ABSTRACTS

Società Italiana Parkinson e Disordini del Movimento
LIMPE-DISMOV ETS

10° Congresso

MILANO
Allianz MiCo - Milano
Convention Centre

10•11•12
APRILE
2024

50 ANNI
LIMPE
1974 - 2024

SOCIETÀ ITALIANA
PARKINSON
E DISORDINI DEL
MOVIMENTO
LIMPE-DISMOV
ETS

Indice generale

Comunicazioni Libere

C1

Combined high - and low - frequency substantia nigra and subthalamic nucleus deep brain stimulation for freezing of gait in Parkinson's disease: a cross-over randomized double-blind trial

Claudia Ledda[1], C.A. Artusi[1,2], S. Gallo[3], D. Rinaldi[4], C. Campisi[1], V. Rousseau[5,6,7], C. Thalamas[8], R. Barbosa[8,9], F. Ory-Magne[8,9], C. Brefel-Courbon[9], O. Rascol[9,10], A. De Barros[11], E. Harroch[9], M. Zibetti[1,2], M.G. Rizzone[1,2], A. Romagnolo[1,2], G. Imbalzano[1,2], L. Lopiano[1,2], J.L. Houeto[12], M. Fabbri[8,9,10]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza di Torino, Turin, Italy
[3]Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[4]Department of Neuroscience, Mental Health and Sense Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[5]Service de Pharmacologie Médicale et Clinique, Centre Hospitalier Universitaire et Faculté de Médecine de Toulouse, Toulouse, France
[6]Centre Midi-Pyrénées de PharmacoVigilance, de Pharmacoépidémiologie et d'Informations sur le Médicament et Pharmacopôle Midi-Pyrénées, Centre Hospitalier Universitaire de Toulouse, Toulouse, France
[7]CIC INSERM 1436, Université et Centre Hospitalier Universitaire de Toulouse, Toulouse, France
[8]Service de Neurologie, Centre Hospitalier Universitaire, Toulouse, France
[9]Centre Expert Parkinson de Toulouse, CHU, Toulouse, France
[10]France CHU de Toulouse, Université de Toulouse-Toulouse 3, INSERM, UMR1214 Toulouse NeuroImaging Centre "TONIC" Center of Excellence in Neurodegeneration (CoEN), NeuroToul, Centre Expert Parkinson de Toulouse, Centre d'Investigation Clinique CIC1436, NS-Park/FCRIN Network, Services de Neurologie et de Pharmacologie Clinique, UMR 1048 Institute for Cardiovascular Diseases, Toulouse, France
[11]Department of Neurosurgery, Toulouse University Hospital, Toulouse, France
[12]Department of Neurology, CIC-INSERM 1402, CHU de Poitiers, Université de Poitiers, Poitiers, France

Introduction: Freezing of gait (FoG) is a disabling Parkinson's disease (PD) symptom, difficult to manage even in patients treated with Deep Brain Stimulation (DBS) and requesting innovative treatments [1–4].

Objective: To assess the efficacy and safety of combined high-frequency (HF) subthalamic (STN) and HF or low-frequency (LF) substantia nigra pars reticulata (SNr) stimulation compared to standard STN stimulation (S) on FoG. Electrode placement in the SNr was confirmed by activated tissue volume models (VTA).

Methods: We performed a double-blind, randomized, cross-over, multicentric trial at the Movement Disorders Center of Turin (Italy) and Toulouse (France). Patients underwent a 1-month period of HF-STN stimulation, combined HF-STN + HF-SNr stimulation (C1), or combined HF-STN + LF-SNr stimulation (C2). Primary endpoint: mean change in New Freezing of Gait Questionnaire (NFOG-Q) score. Secondary endpoints included adverse events (AEs), changes in Timed Up and Go (TUG), MDS-UPDRS I-IV, Hospital Anxiety and Depression Scale (HADS), Parkinson's Disease Sleep Scale-2 (PDSS-2), and patients' preference.

Results: 15 patients participated. NFOG-Q score changes showed no statistically significant differences between S and C1 (p=0.64) or C2 (p=0.19), yet 33.3% of patients obtained an improvement ≥8 points at the NFOG-Q (clinically significant FoG improvement) [5]. Both C1 and C2 improved MDS-UPDRS-IV (p=0.046 and 0.005, respectively) and C1 improved PDSS2 (p=0.04) when compared with S. 80% of patients opted to maintain the combined stimulation after study completion. AEs were all manageable and reversible. Patients maintaining the combined STN-SNr stimulation showed significantly higher SNr coverage by VTA (p=0.004)

Conclusions: This trial enhances understanding of the safety and potential benefits of combined STN+SNr stimulation in PD, not only for FoG but also for motor complications and certain nonmotor features. Further studies, incorporating larger sample sizes and quantitative kinematics, are warranted to refine the role of STN+SNr stimulation in clinical practice.

Reference:

[1] Fasano A, Aquino CC, Krauss JK, Honey CR, Bloem BR. Axial disability and deep brain stimulation in patients with Parkinson disease. Nat Rev Neurol. 2015 Feb;11(2):98-110.
[2] Karl JA, Ouyang B, Goetz S, Metman LV. A Novel DBS Paradigm for Axial Features in Parkinson's Disease: A Randomized Crossover Study. Mov Disord. 2020 Aug;35(8):1369-1378.
[3] Weiss D, Walach M, Meisner C, et al. Nigral stimulation for resistant axial motor impairment in Parkinson's disease? A randomized controlled trial. Brain 2013; 136: 2098-2108.
[4] Valldeoriola F, Muñoz E, Rumià J, et al. Simultaneous lowfrequency deep brain stimulation of the substantia nigra pars reticulata and high-frequency stimulation of the subthalamic nucleus to treat levodopa unresponsive freezing of gait in Parkinson's disease: A pilot study. Parkinsonism Relat Disord 2019; 60: 153-157.
[5] Hulzinga F, Nieuwboer A, Dijkstra BW, Mancini M, Strouwen C, Bloem BR, Ginis P. The New Freezing of Gait Questionnaire: Unsuitable as an Outcome in Clinical Trials? Mov Disord Clin
Pract 2020; 7: 199-205.

C2

Reliability of neurophysiological and cerebral tremor features in Parkinson's disease

Luca Angelini[1, 2], KRE van den Berg[2,3], M.F. Dirkx[2,3], M. Bologna[1, 4], R.C.G. Helmich[2,3]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Donders Institute for Brain, Cognition and Behaviour, Centre for Cognitive Neuroimaging, Radboud University Nijmegen, Nijmegen, the Netherlands
[3]Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology and Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, The Netherlands
[4]IRCCS Neuromed, Pozzilli (IS), Italy

Introduction: Tremor is a cardinal feature of Parkinson's Disease (PD), and the basal ganglia and the cerebello-thalamo-cortical (CTC) circuit both play a key role in its pathophysiology. Better understanding the underlying mechanisms is crucial for advancing tremor treatment strategies.

Objectives: We aim to assess the test-retest reliability of clinical, neurophysiological and neuroimaging tremor parameters on an individualized level in PD.

Methods: We evaluated 26 tremor-dominant PD patients OFF medication in two sessions on average two months apart. Evaluations consisted of standardized clinical scales and quantitative analysis of rest and postural tremor using accelerometry, including tremor amplitude and frequency. For rest tremor, we co-registered a resting state-fMRI with accelerometry. We conducted both group and individual level analyses, using t-tests, Intraclass Correlation Coefficient, and Pearson's correlations.

*Results:*At the group level, clinical and accelerometric data did not change across the two sessions, and showed good to excellent reliability for both rest and postural tremor. Significant tremor-related activity was observed in the three nodes of the CTC circuit, i.e., contralateral motor cortex (MC), contralateral posterior ventral part of ventral lateral thalamic nucleus (VLpv), and ipsilateral cerebellar lobules V and VI (CBLM) (all $p<0.05$). A positive correlation across sessions was also observed for the mean tremor-related activity in MC and CBLM (MC: $r=0.47$, $p=0.02$; CBLM: $r=0.62$, $p<0.01$). At the individual level, voxel-by-voxel tremor-related activity correlated significantly across sessions in 69.23%, 50%, and 76.92% of patients for MC, VLpv and CBLM respectively (all $p<0.01$). As expected, subjects with a higher voxel-by-voxel correlation showed lower distance between activity peaks across sessions (all $p<0.01$).

Conclusions: Our study shows the robust individual-level reliability of neurophysiological and functional neuroimaging measures used to investigate the pathophysiological mechanisms underlying tremor in PD. These findings lay the foundation for personalized treatments and targeted neuromodulation, advancing tremor management in PD patients.

C3

Disentangling bradykinesia and rigidity in Parkinson's Disease: evidence from long-term STN-DBS

Alessandro Zampogna[1,2], A. Suppa[1,3], F. Bove[4], F. Cavallieri[5], A. Castrioto[2], S. Meoni[2], P. Pelissier[2], E. Schmitt[2], S. Chabardes[6], V. Fraix[2], E. Moro[2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Grenoble Alpes University, Division of Neurology, CHU of Grenoble, Grenoble Institute of Neurosciences, INSERM U1216, Grenoble, France
[3]IRCCS Neuromed Institute, Pozzilli, Italy
[4]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Catholic University of the Sacred Heart, Rome, Italy
[5]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[6]Grenoble Alpes University, Division of Neurosurgery, CHU of Grenoble, Grenoble, France

Introduction: Bradykinesia and rigidity are considered closely related cardinal motor signs in Parkinson's disease (PD), but recent neurophysiological findings suggest distinct athophysiological mechanisms [1-2].

Objective : This study aims to examine and compare longitudinal changes in bradykinesia and rigidity in PD patients treated with bilateral subthalamic nucleus deep brain stimulation (STN-DBS).

Methods: In this retrospective cohort study, the clinical progression of appendicular and axial bradykinesia and rigidity was assessed up to 15 years after STN-DBS surgery. The severity of bradykinesia and rigidity was examined using ad hoc composite scores from specific subitems of the Unified Parkinson's Disease Rating Scale motor part (UPDRS-III). Short- and long-term clinical predictors of bradykinesia and rigidity were analysed through linear regression analysis, considering various preoperative demographic and clinical data, including disease duration and severity, phenotype, motor and cognitive scores (e.g., frontal score), and medication.

Results: A total of 301 patients were examined before and one year after STN-DBS surgery. Among them, 101 and 56 individuals were also evaluated at 10-year and 15-year follow-ups, respectively. Bradykinesia significantly worsened after surgery, especially in appendicular segments ($p<0.001$). Conversely, rigidity showed sustained benefit, showing unchanged clinical scores compared to preoperative assessment ($p>0.05$). Preoperative motor disability (e.g., composite scores from the UPDRS-III) predicted short- and longterm outcomes for both bradykinesia and rigidity ($p<0.01$). Executive dysfunction was specifically linked to bradykinesia but not to rigidity ($p<0.05$).

Conclusions: Bradykinesia and rigidity show long-term divergent progression in PD following STN-DBS surgery and are associated with partly independent clinical factors. These findings support partially distinct pathophysiological underpinnings.

References:

[1] Wilkins et al., 2023. Ann Neurol. 93(5):1029-1039.
[2] Asci F et al., 2023. Brain 146(9):3705-3718.

C4

Phenotypic profiles of tremor combined with dystonia by family history: the TITAN study

Maria Russo[1], P. Barone[1], M. Bologna[2,3], A. Castagna[4], R. Ceravolo[5], C. Dallocchio[6], R. De Micco[7], F. Di Biasio[8], A.B. Di Fonzo[9], R. Di Giacopo[10], M. Esposito[11], A.F. Gigante[12], C. Giordano[1], M.C. Malaguti[13], F. Morgante[14,15], V. Moschella[16], C. Sorrentino[1], C. Terranova[17], R. Erro[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Salerno, Italy
[2]Neuromed Institute IRCCS, Pozzilli, IS, Italy
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[4]Centro Disturbi del Movimento-SAFLo IRCCS Fondazione Don Carlo Gnocchi Onlus Milano, Italy
[5]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[6]Neurology Unit, Department of Medical Area, ASST Pavia, Voghera, (PV), Italy
[7]Department of Advanced Medical and Surgical Sciences, Università della Campania "Luigi Vanvitelli", Naples, Italy
[8]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[9]Neurology Unit, Department of Neuroscience, Dino Ferrari Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[10]Neurology Unit, Rovereto Hospital, APSS Trento, Italy
[11]Clinical Neurophysiology Unit, AORN Cardarelli, Naples, Italy
[12]Neurosensory Department, Neurology Unit, San Paolo Hospital, ASL Bari, Bari, Italy
[13]Neurology Department, S. Chiara Hospital, Trento, Italy
[14]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[15]Neurosciences Research Centre, Molecular and Clinical Sciences Institute, St. George's, University of London, London, UK
[16]Neurology Unit, San Filippo Neri Hospital ASL Roma 1, Rome, Italy
[17]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Introduction: Tremor is the only accompanying movement disorder that allows the diagnosis of an isolated dystonia syndrome [1]. Dystonia patients with tremor more likely report a positive family history (FH) for either dystonia or isolated tremor.

Objectives: In this work, we explored The ITAlian Tremor Network (TITAN) database to seek identifying phenotypic features associated with familial clustering of tremor (or other neurological disorders) in subjects with tremor combined with dystonia (TwD).

Methods: All patients were assessed with a standardized protocol [2]. Presence of FH for tremor (FHT) was operationalized as the existence of tremor in either first- or second-degree family members. Only the tremor in the context of a diagnosis of parkinsonism qualified for FH for other neurological disorders (FHOTHER).

Results: A total of 127 patients with TwD were included, of whom 73 (57.4%) were sporadic (FHNO), 33 (25.9%) were identified as FHT and 21 (16.5%) as FHOTHER. The majority (80.9%) of FHOTHER patients were males, while the other two groups were mostly constituted by female patients. Dystonia distribution was significantly different between the groups, with sporadic patients having more commonly upper limb (UL) involvement.
UL tremor at onset was similar between sporadic and FHT patients. Head tremor at onset was often reported and was more severe in FHOTHER patients. Midline tremor was more frequent and more

severe in FHT patients. No differences were found in terms of UL tremor except for the rest component that was more common in FHT patients.

Conclusions: The finding of a higher FH for tremor than for dystonia in patients with TwD could suggest the existence of a hereditable dystonia-tremor syndrome. Familial cases had higher rates and severity of head/midline tremor which matches the knowledge that head tremor is the most common type of tremor in cervical dystonia and that tremulous cervical dystonia is likely to be familial.

References:

[1] A. Albanese, M. Di Giovanni, S. Lalli. Dystonia: diagnosis and management. Eur J Neurol. 2019 Jan;26(1):5-17. doi: 10.1111/ene.13762. Epub 2018 Aug 18.

[2] R. Erro, A. Pilotto, M. Esposito, E. Olivola, A. Nicoletti, G. Lazzeri, L. Magistrelli, C. Dallocchio, R. Marchese, M. Bologna, A. Tessitore, S. Misceo, A.F. Gigante, C. Terranova, V. Moschella, L. di Biase, R. Di Giacopo, F. Morgante, F. Valentino, A. De Rosa, A. Trinchillo, M.C. Malaguti, L. Brusa, A. Matinella, F. Di Biasio, G. Paparella, R. De Micco, E. Contaldi, N. Modugno, A. Di Fonzo, A. Padovani, P. Barone, TITAN Study Group, The Italian tremor Network (TITAN): rationale, design and preliminary findings. Neurol Sci. 2022 Sep;43(9):5369-5376. doi: 10.1007/s10072-022-06104-w. Epub 2022 May 24.

C5

Neural correlates of bradykinesia in Parkinson's disease: a kinematic and fMRI study

Lucia Zenere[1], E. Sarasso[1,5,6], A. Gardoni[1], D. Emedoli[7], A. Grassi[1,5], S. Basaia[1], R. Balestrino[3,5,8], D. Corbetta[7], M. Filippi[1,2,3,4,5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy;
[2]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy;
[3]NeurorehabilitationUnit, IRCCS San Raffaele Scientific Institute, Milan, Italy;
[4]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy;
[5]Vita-SaluteSan Raffaele University, Milan, Italy;
[6]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy;
[7]Department of Rehabilitation and Functional Recovery; IRCCS San Raffaele Scientific Institute, Milan, Italy;
[8]Neurosurgery and Gamma Knife Radiosurgery Unit, IRCCS Ospedale San Raffaele, Milan, Italy.

Introduction: Bradykinesia is defined as a "complex" of motor alterations including reduced movement amplitude and/or speed and tendency to reduce them with task repetition (sequence effect).

Objectives: The aim of the study was to investigate the neural correlates of bradykinesia assessed during a hand tapping performance in people with Parkinson's disease (pwPD) relative to healthy controls.

Methods: Twenty-five pwPD and 25 age- and sex-matched healthy controls were included. All subjects underwent brain functional magnetic resonance imaging (fMRI) including a hand tapping task: subjects alternatively opened and closed their right hand as fast and as ample as possible. Hand tapping speed and amplitude was measured during the fMRI task using an optical fiber data glove.

Results: During the fMRI hand tapping task, pwPD showed reduced hand tapping amplitude (hypokinesia) and a greater sequence effect. PwPD relative to healthy controls showed a reduced activity of frontoparietal areas, supplementary motor area, middle cingulum, parahippocampus, pallidum, thalamus, and motor cerebellar areas. Moreover, pwPD showed an increased activity of cognitive areas: superior temporal gyrus, posterior cingulum, and cerebellum crus I. The decreased activity of cerebellum IV-V-VI, vermis IV-V, inferior frontal gyrus, and cingulum correlated with hypokinesia and with the sequence effect.

Conclusions: PwPD showed a worse hand tapping performance in terms of reduced movement amplitude and tendency to reduce amplitude with movement repetition relative to healthy controls. Interestingly, these manifestations correlated with altered brain activity: a reduced activity of areas involved in motor planning and timing correlated both with hypokinesia and with the presence of the sequence effect in pwPD. This study has the major strength of collecting objective motor parameters and brain activity simultaneously, providing a unique opportunity to investigate the neural correlates of the "bradykinesia complex".

Funding: Italian Ministry of Health grant GR-2018-12366005.

C6

A mechanistic mathematical model to investigate genotypicphenotypic relationship in GBA-PD patients

Federico Reali[1], E. Righetti[1,2], D. Boaretti[1], E. Domenici[1,2], L. Marchetti[1,2]

[1]Fondazione The Microsoft Research - University of Trento Centre for Computational and Systems Biology (COSBI), Trento, Italy
[2]University of Trento, Department of Cellular, Computational and Integrative Biology (CIBIO), Trento, Italy

Introduction: Quantitative Systems Pharmacology (QSP) deploys mechanistic mathematical models to understand complex biological systems and drug responses, synthesizing data from diverse sources [1]. This approach holds promise for addressing challenges in Parkinson's disease (PD), a neurodegenerative disorder lacking a disease-modifying therapy. About 10% of PD cases involve GBA gene mutations [2], contributing to a substantial gap in therapeutic knowledge. QSP modeling aims to bridge the disconnection between in vitro and in vivo studies, facilitating experimental research and therapeutic strategy design [3], and offering mechanistic insights into PD's biology [4].

Objectives: We extend an existing QSP model for sphingolipidoses [3] to investigate molecular and cellular interactions over time between GBA mutations and PD clinical manifestations.

Methods: Implemented through ordinary differential equations, our QSP model is calibrated using preclinical and clinical data, including plasma and cerebrospinal fluid (CSF) biomarkers, and clinical manifestations. Variability is introduced through genetic factors, physiological parameters, demographics, and disease severity to create virtual patient populations and simulate their behavior over time.

Results: The preliminary findings demonstrate the model dynamics to be consistent with the literature data under healthy and pathological conditions. This allows detailed analysis of simulated sphingolipids dynamics in the brain, liver, plasma, and CSF. Moreover, the model accurately recapitulates the correlations between GBA mutation severity and sphingolipid accumulation [5].

Conclusions: QSP modeling can provide insights into the intricate interplay between neurodegeneration and sphingolipid metabolism. Our model is a potential tool for improving our understanding of GBAPD by addressing patient heterogeneity, optimizing treatment strategies, and informing clinical trial design. Including additional clinical data, such as alpha-synuclein measurements, would enhance the reliability of model simulations and further elucidate protein aggregation mechanisms occurring in GBA-PD.

References:

[1] Azer, K., et al. History and future perspectives on the discipline of quantitative systems pharmacology modeling and its applications, Frontiers in Physiology, 12, 127, (2021).
[2] Smith, L., & Schapira, A. H. V. GBA Variants and Parkinson Disease: Mechanisms and Treatments. Cells, 11(8), 1261, (2022).
[3] Abrams, R., et al. A Quantitative Systems Pharmacology Model of Gaucher Disease Type 1 Provides Mechanistic Insight Into the Response to Substrate Reduction Therapy With Eliglustat t, CPT: Pharmacometrics & Systems Pharmacology, 9, 374–383, (2020).
[4] Righetti, E., et al. Mechanistic models of α-synuclein homeostasis for Parkinson’s disease: A blueprint for therapeutic intervention, Frontiers in Applied Mathematics and Statistics, 8, (2022).
[5] den Heijer, J.M., et al., A Biomarker Study in Patients with GBA1-Parkinson's Disease and Healthy Controls Movement Disorders, 38, (2023).

C7

Stepwise functional brain architecture from disease epicenter correlates with atrophy in progressive supranuclear palsy

Edoardo Gioele Spinelli[1,2,3], A. Ghirelli[1,2,3], I. Bottale[1,2,3], S. Basaia[1], E. Canu[1], V. Castelnovo[1], M.A. Volontè[3], S. Galantucci[3], G. Magnani[3], F. Caso[3], G. Cecchetti[1,3,7], P. Caroppo[4], S. Prioni[4], C. Villa[4], K.A. Josephs[5], J.L. Whitwell[6], M. Filippi[1,2,3,5,7], F. Agosta[1,2,3]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Vita-Salute San Raffaele University, Milan, Italy
[3]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Unit of Neurology 5 - Neuropathology, Milan, Italy
[5]Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA
[6]Department of Radiology, Mayo Clinic, Rochester, Minnesota, USA
[7]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy

Introduction: Stepwise functional connectivity (SFC) is a graphtheory-based neuroimaging method, which detects whole-brain functional couplings of a selected region of interest, at increasing linkstep topological distances.

Objectives: This study applied SFC to test the hypothesis that topological stepwise architecture propagating from the disease epicenter would shape patterns of grey matter (GM) atrophy in patients with progressive supranuclear palsy (PSP).

Methods: Thirty-six patients with PSP-Richardson's syndrome and 44 age-matched healthy controls underwent brain MRI on a 3T scanner. The disease epicenter was defined as the peak of atrophy observed in an independent cohort of 13 cases with post-mortem confirmation of PSP pathology, and used as seed region for SFC analysis. First, we explored SFC rearrangements in PSP patients, as compared with agematched controls. Subsequently, we tested SFC architecture propagating from the disease epicenter as a determinant of brain atrophy distribution.

Results: The disease epicenter was identified in the left midbrain tegmental region. In PSP patients, a pattern of mostly increased functional connectivity of the midbrain within direct connections was mirrored by a progressively widespread decreased connectivity through indirect connections with sensorimotor cortical regions. For each GM region, a correlation was found between average link-step distance from the left midbrain in controls and mean normalized GM volume in PSP patients ($r=0.38$, $p<0.001$).

Conclusions: This study provides comprehensive insights into the topology of functional network rearrangements in PSP and demonstrates that the brain architectural topology, as described by SFC propagating from the disease epicenter, shapes the pattern of atrophic changes in PSP. Our findings support the view of a networkbased pathology propagation in this primary tauopathy.

Funding. European Research Council (StG-2016_714388_NeuroTRACK); US National Institutes of Health (R01-DC010367, R01-DC12519, R01-DC14942, R01-NS89757, R21-NS94684); Foundation Research on Alzheimer Disease; Next Generation EU, National Recovery and Resilience Plan, Investment PE8 - Project Age-It.

C8

Brain metabolic correlates of STN-DBS on gait in Parkinson's disease: FDG-PET study of gait with dynamic obstacle avoidance

Ioannis Ugo Isaias[1,2], I. Hanafi[1], R. Habib[2], C. Palmisano[1], G. Marotta[2], J. Del Vecchio[1], A. Buck[3], G. Pezzoli[2], J. Volkmann[1], N.G. Pozzi[1]

[1]Department of Neurology, University Hospital Würzburg and Julius Maximilian University, Würzburg, Germany
[2]Parkinson's Institute Milan, ASST G. Pini-CTO, Milan, Italy
[3]Department of Nuclear Medicine, University Hospital Würzburg and Julius Maximilian University, Würzburg, Germany

Introduction: Subthalamic deep brain stimulation (STN-DBS) is a mainstay treatment for Parkinson's disease (PD), but poorly effective on gait and posture (PIGD). This may stem from our limited understanding of the impact of STN-DBS on the supraspinal locomotor control, which deserves specific studies.

Objectives: To correlate DBS-induced changes of brain metabolic activity during dynamic obstacle avoidance and PIGD improvement in PD.

Methods: Twelve PD patients (age: 61±7; disease duration: 10±4; UPDRS-III meds-off: 44±15) with STN-DBS performed two (18) Ffluorodeoxyglucose (FDG)-positron emission tomography (PET) scans. Between FDG injection and PET, patients performed a dynamic obstacle avoidance task in a validated virtual reality environment, which consisted of walking back-and-forth adjusting gait to avoid collision with a virtual agent crossing their trajectory [1]. The PET scans were conducted in (overnight) meds-off/stim-on and meds-off/stim-off (45min after pausing DBS). PET images were co-registered with individual MRIs and analyzed using SPM12.

Results: Patients were classified with severe (SGI, n=6, PIGD subscore: 6.8±2.6) or mild gait impairment (MGI, n=6, PIGD subscore: 2.7±1.9). In SGI patients, STN-DBS increased FDG uptake in the left superior frontal gyrus, which correlated negatively (τb=-0.89, $p<0.05$) with gait improvement (33.9±17.4% gait subscore). In contrast, MGI patients showed higher DBS-related FDG uptake in the orbitomedial frontal region than SGI patients ($p<0.05$).

Conclusions: We showed that the beneficial effect of STN-DBS on walking in the SGI group associates with poorer stimulation-induced metabolic activity in the left superior frontal gyrus. Conversely, STNDBS increases orbitomedial frontal metabolism in patients with a relatively preserved supraspinal locomotor network (LGI group). Our results highlight the fundamental role of the frontal lobe in locomotor control in PD and provide insights on the impact of STN-DBS on parkinsonian gait.

References:

[1] Palmisano C, et al. Front Hum Neurosci. 2022;16:783452.

C9

Phosphoproteomic profiling of peripheral immune cells from patients with Parkinson's disease

Tommaso Schirinzi[1], G. Massacci[2], J. Bissacco[1], R. Cerroni[1], R. Bovenzi[1], M. Zwiebel[3], M. Wahle[3], V. Venafra[2], M. Mann[3], F. Sacco[2,4]

[1]Unit of Neurology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Department of Biology, University of Rome Tor Vergata, Rome, Italy
[3]Department Proteomics and Signal Transduction, Max Planck Institute of Biochemistry, Martinsried, Germany
[4]Telethon Institute of Genetics and Medicine (TIGEM), Pozzuoli (NA), Italy

Introduction: Evidence on the involvement of the peripheral immune response in mechanisms underlying Parkinson's disease (PD) is dramatically increasing. Peripheral blood immune cells may directly participate in pathogenic processes or rather reflect neuropathological events. Regardless, substantial functional changes occur in PD patients' peripheral blood mononucleate cells (PBMCs), which may be theoretically targeted for therapeutic or biomarker purposes. State-of-the-art mass spectrometry (MS)-based (phospho)proteomics allows for profiling the global changes in the phosphorylation and concentration level of thousands of proteins in cells, uncovering activated signaling networks and novel molecular targets.

Objectives: To perform a (MS)-based (phospho)proteomics analysis of PBMCs from PD patients at various disease stages.

Methods: The study included ten healthy controls and 20 PD patients assessed through conventional scores for disease severity (e.g., MDSUPDRS part 3, H&Y). PBMCs were isolated from each participant and processed for high sensitive (MS)-based total proteome and phosphoproteome quantification. Principal component analysis (PCA) was run to cluster patients.

Results: The case-control analysis of the (phospho)proteomic PBMCs profile revealed a global rewiring of pathways involved in oxidative phosphorylation and inflammation. In addition, expression of asynuclein, septin-5, and DJ-1 was upregulated in the PD group. The PCA of about 8000 proteins and 12000 phosphosites identified three distinct subgroups at different clinical stages. In particular, crucial kinases involved in the antigen presentation/processing, MAPK, and calcium signaling pathways were differently modulated according to PD severity.

Conclusions: This unbiased analysis enabled shaping the global (phospho)proteomic profile of PD patients PBMCs, recognizing differential (phospho)proteomic signatures associated with different disease stages, and identifying some biological pathways majorly involved in PD immune cells. A large-scale MS-based characterization of PBMCs might allow for a better understanding of the role of peripheral immunity in PD and discover molecular targets consistent with the disease status.

C10

Predictors of clinical outcome of focused ultrasound VIM thalamotomy in Parkinson's disease

Arianna Braccia[1], N. Golfrè Andreasi[1], R. Cilia[1], L.M. Romito[1], A.E. Elia[1], V. Levi[2], G. Devigili[1], S. Rinaldo[1], E.F.M. Ciceri[3], M.G. Bruzzone[4], F. Ghielmetti[5], M. Fusar Poli[6], S. Prioni[6], P. Amami[6], S.H.M.J. Piacentini[6], M. Grisoli[4], M. Stanziano[4], R. Eleopra[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[2]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neurosurgery Department, Functional Neurosurgery Unit, Milan, Italy
[3]Fondazione IRCCS Istituto Neurologico Carlo Besta, Diagnostic Radiology and Interventional Neuroradiology, Milan, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neuroradiology Unit, Milan, Italy
[5]Fondazione IRCCS Istituto Neurologico Carlo Besta, Health Department, Milan, Italy
[6]Fondazione IRCCS Istituto Neurologico Carlo Besta, Clinical Neuropsychology Unit, Milan, Italy

Introduction: Tremor response to medical treatment can often be unsatisfactory in Parkinson's disease (PD). Data about long-term efficacy and predictors of clinical response and recurrence after the procedure of MRgFUS Vim thalamotomy in tremor dominant Parkinson's disease (TDPD) are still limited [1].

Objectives: To investigate the role of clinico-demographical (including MDSUPDRS part III tremor scores in med-off and med-on conditions, skull density ratio), procedural (number and duration of sonications, temperature reached, energy and power delivered) and neuroradiological variables (lesion volume after 1 day) in determining MRgFUS clinical outcome. To estimate the rate of adverse events (AE) and percentage of relapsers.

Methods: 52 TDPD patients who underwent MRgFUS VIM thalamotomy were prospectively followed for 6 months after treatment.

Results: Tremor severity significantly decreased in all patients after 1 day from MRgFUS VIM thalamotomy (tremor scores improved > 30% in all cases). The degree of improvement correlated with older age and with a larger lesion volume 1 day after treatment. Mean lesion volume was 172 mm3. Total recurrence rate (tremor's improvement <30% after 6 months) was 21%. Critically, all relapsers manifested worsening of tremor during the 1st month after treatment (80% during the first 15 days). Sonication's parameters did not differ between responders and relapsers. In the follow-up AEs were: at 1-month 42% (22 patients, mild in majority); at 6-months 19% (10 patients, all mild); at 1 year 17%.

Conclusions: MRgFUS thalamotomy is effective to treat tremor in PD patients [2]. The greater rate of relapse among younger subjects could be explained by the lower lesion's volume, which -in turn- was associated with a favorable AEs profile. Mean lesion volume in two recent studies on TDPD was larger [494.9 mm3 (1), 335,5 mm3 (2)] than in our cohort, but the number of total AE was greater.

References:

[1] Chua MMJ, Blitz SE, Ng PR, Segar DJ, McDannold NJ, White PJ, Christie S, Hayes MT, Rolston JD, Cosgrove GR. Focused Ultrasound Thalamotomy for Tremor in Parkinson's Disease: Outcomes in a Large, Prospective Cohort. Mov Disord. 2023 Oct;38(10):1962-1967. doi: 10.1002/mds.29569. Epub 2023 Aug 4. PMID: 37539721

[2] Lak AM, Segar DJ, McDannold N, White PJ, Cosgrove GR. Magnetic Resonance Image Guided Focused Ultrasound Thalamotomy. A Single Center Experience With 160 Procedures. Front Neurol. 2022 Feb 18;13:743649. doi: 10.3389/fneur.2022.743649. PMID: 35250802; PMCID: PMC8894664.

C11

Analysis of family history in Parkinson's disease: an Italian population based cross sectional study

Federica Arienti[1,2], G. Casazza[3,4], G. Lazzeri[1,2], E. Monfrini[1,2], A. Di Maio[1,2], R. Erro[5], P. Barone[5], F. Tamma[6], E. Caputo[6], M.A. Volontè[7], L. Cacciaguerra[7], A. Pilotto[8], A. Padovani[8], C. Comi[9], L. Magistrelli[9], F. Valzania[10], F. Cavallieri[10], L. Avanzino[11,12], R. Marchese[12], M. Sensi[13], G. Carroli[13], R. Eleopra[14], R. Cilia[14], F. Spagnolo[15], A. Tessitore[16], R. De Micco[16], R. Ceravolo[17], G. Palermo[17], M.C. Malaguti[18], L. Lopiano[19,20], P. Tocco[21], C. Sorbera[22], M. Tinazzi[23], A. Ciammola[24], D. Ottaviani[25], A. Albanese[26], M. Canesi[27], A. Antonini[28], M. Carecchio[28], V. Fetoni[29], C. Colosimo[30], M. Zappia[31], N. Tambasco[32], G. Cossu[33], D. Volpe[34], E.M. Valente[35], G. Franco[1,2], A.B. Di Fonzo[1,2]

[1]Neurology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[2]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[3]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy
[4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[5]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Salerno, Italy
[6]Department of Neurology, "F. Miulli" General Hospital, Acquaviva delle Fonti, Italy
[7]Department of Neurology, IRCCS San Raffaele Scientific Institute, Milan, Italy
[8]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, and Department of Continuity of Care and Frailty, ASST Spedali Civili Brescia Hospital, Italy Brescia, Italy
[9]Department of Translational Medicine, Section of Neurology, University of Piemonte Orientale, Novara, Italy
[10]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[11]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genova, Italy
[12]IRCCS Ospedale Policlinico San Martino, UOC Genetica Medica, Genoa, Italy
[13]Department of Neuroscience and Rehabilitation, Azienda Ospedaliera Universitaria S. Anna, Ferrara, Italy
[14]Fondazione IRCCS Istituto Neurologico Carlo Besta, Parkinson and Movement Disorders Unit, Milan, Italy
[15]Neurological Department, A. Perrino's Hospital, Brindisi, Italy
[16]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[17]Center for Neurodegenerative Diseases, Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[18]Neurology Unit, Trento Hospital, Azienda Provinciale per i Servizi Sanitari di Trento, Trento, Italy
[19]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[20]Neurology 2 Unit, A.O.U. Città della Salute e della Scienza di Torino, Turin, Italy
[21]Neurology and Stroke Unit, Pescara Hospital, Pescara, Italy
[22]Neurorehabilitation Unit IRCCS Centro Neurolesi "Bonino Pulejo," Messina, Italy
[23]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

[24]Department of Neurology and Laboratory of Neuroscience, Istituto Auxologico Italiano IRCCS, Milan, Italy
[25]Neurology Unit, Rovereto Hospital, Azienda Provinciale per i Servizi Sanitari di Trento, Trento, Italy
[26]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, (MI), Italy
[27]Department of Parkinson's Disease, Movement Disorders and Brain Injury Rehabilitation, Moriggia Pelascini Hospital, Gravedona, Italy
[28]Parkinson and Movement Disorders Unit, Center for Neurodegenerative Diseases (CENSE), Department of Neuroscience, University of Padua, Padua, Italy
[29]Neurology Department, ASST Fatebenefratelli Sacco, Milan, Italy
[30]Department of Neurology, Santa Maria University Hospital, Terni, Italy
[31]Department G.F. Ingrassia, University of Catania, Catania, Italy
[32]Movement Disorders Center, Neurology Department, General Hospital and University of Perugia, Perugia, Italy
[33]Department of Neuroscience, Brotzu Hospital, Cagliari, Italy
[34]Department of Neurorehabilitation, Parkinson's Disease Excellence Center, Casa di Cura Villa Margherita, Arcugnano, (VI), Italy
[35]Department of Molecular Medicine, University of Pavia, Pavia, Italy

Parkinson's disease (PD) is a neurodegenerative disease with an increasing epidemiological and social relevance. Positive family history is a well-known risk factor for PD development and, according to literature, familial forms recur in up to 5-15% of cases [1]. Cognitive and mood disorders also appear to be more frequent in PD families, possibly suggesting a greater fragility and propensity towards neurodegenerative and neuropsychiatric manifestations [2].

In this study, we examined in depth the family history of PD patients and compared demographic, genetic and clinical features between familial (fPD) and sporadic (sPD) forms. Family history of other neurological and psychiatric disorders (essential tremor, cognitive impairment, depression, bipolar disorder) was also investigated.

A cross-sectional study enrolling 2,035 PD patients in a 30-month period was conducted in twenty-eight Italian Centres. Clinical data and family history up to the third degree of kinship were collected, entered an electronic database, and analysed through descriptive and inferential statistics (SAS software).

A remarkable 34.5% of patients reported a positive family history for PD. In fPD the mean age at onset was significantly lower and the genetic test resulted more often positive than in sporadic forms (36.4% of fPD patients tested). The higher rate of positive family history encountered may suggest either a major role played by genetic factors in the Italian PD population, or a possible underestimation in previous studies with data collection limited to first-degree relatives.

No significant difference emerged in the distribution of motor and non-motor symptoms, except for hyposmia which was more frequently reported in the fPD group. This finding is difficult to interpret, and requires further analysis in order to exclude possible confounding factors (e.g. cigarette smoking).

Considering the other neuropsychiatric disorders investigated, 2% of patients reported a certain positive family history for essential tremor, 12% for cognitive impairment, 32% for depression, 31% for anxiety disorder and 0.7% for bipolar disorder. Although the prevalence of cognitive impairment has not been investigated in relatives of healthy controls, and a rigorous comparison is therefore impossible, it appears higher than previously reported in the general Italian population [3], suggesting

a possible familial predisposition to neurodegenerative diseases. This hypothesis is supported by the presence of genetic risk factors shared between PD and other dementias (i.e., GBA1, C9ORF72, MAPT, PSEN1, etc.) [4]. The prevalence of depressive and anxiety disorders was also higher than expected [5].

In conclusion, this study shows that a positive PD family history recurs more frequently than previously reported in PD patients, involving approximately one-third of the total study population.

This work suggests an in-depth collection of family history, including second and third degrees of kinship, with the aim of identifying family clusters that represent an ideal population to investigate genetic and environmental risk factors for neurological and psychiatric disorders.

References:

[1] de Lau, L. M. L.; Breteler, M. M. B. Epidemiology of Parkinson's Disease. Lancet Neurol. 2006, 5 (6), 525–535. https://doi.org/10.1016/S1474-4422(06)70471-9.
[2] Wareham, L. K.; Liddelow, S. A.; et al. Solving Neurodegeneration: Common Mechanisms and Strategies for New Treatments. Mol. Neurodegener. 2022, 17 (1), 23. https://doi.org/10.1186/s13024-022-00524-0
[3] Ravaglia G, Forti P, Montesi F, Lucicesare A, Pisacane N, Rietti E, Dalmonte E, Bianchin M, Mecocci P. Mild cognitive impairment: epidemiology and dementia risk in an elderly Italian population. J Am Geriatr Soc. 2008 Jan;56(1):51-8. doi: 10.1111/j.1532-5415.2007.01503.x. Epub 2007 Nov 20. PMID: 18028343.
[4] Tsuang, D.; Leverenz, J. B.; Lopez, O. L.; Hamilton, R. L.; Bennett, D. A.; Schneider, J. A.; Buchman, A. S.; Larson, E. B.; Crane, P. K.; Kaye, J. A.; Kramer, P.; Woltjer, R.; Kukull, W.; Nelson, P. T.; Jicha, G. A.; Neltner, J. H.; Galasko, D.; Masliah, E.; Trojanowski, J. Q.; Schellenberg, G. D.; Yearout, D.; Huston, H.; Fritts-Penniman, A.; Mata, I. F.; Wan, J. Y.; Edwards, K. L.; Montine, T. J.; Zabetian, C. P. GBA Mutations Increase Risk for Lewy Body Disease with and without Alzheimer Disease Pathology. Neurology 2012, 79 (19), 1944–1950. https://doi.org/10.1212/WNL.0b013e3182735e9a.
[5] de Girolamo, G.; Polidori, G.; Morosini, P.; Scarpino, V.; Reda, V.; Serra, G.; Mazzi, F.; Alonso, J.; Vilagut, G.; Visonà, G.; Falsirollo, F.; Rossi, A.; Warner, R. Prevalence of Common Mental Disorders in Italy: Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD). Soc. Psychiatry Psychiatr. Epidemiol. 2006, 41 (11), 853–861. https://doi.org/10.1007/s00127-006-0097-4.

C12

Effect of sex on the association between GBA mutations and cognitive decline in Parkinson's disease

Silvia Paola Caminiti[1], M. Avenali[1,2], A. Galli[3], R. Malito[4], G. Cuconato[3], A. Pilotto[4], D. Perani[5,6], C. Tassorelli[1], F. Blandini[1,7], E.M. Valente[3,8]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]Parkinson and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[4]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]IRCCS San Raffaele Scientific Institute, Milan, Italy
[7]Ca' Granda IRCCS Foundation, Ospedale Maggiore Policlinico, Milan, Italy
[8]Neurogenetics Research Center, IRCCS Mondino Foundation, Pavia, Italy

Introduction: In Parkinson's disease (PD) cognitive decline may occur, substantially affecting patients' quality of life.

Objectives: We aimed to assess the impact of sex and glucocerebrosidase (GBA) mutations on clinical phenotype, dopaminergic integrity, and PD clinical trajectories.

Methods: Included 568 PD patients from Parkinson's Progression Markers Initiative database, of whom 118 (20.8%) bearing GBA mutations. PD patients were also genotyped for at APOE-ε4 and LRRK mutations. Dopaminergic activity was assessed in a subset of patients with available 123I-FP-CIT SPECT scans (248, 65%). We stratified the PD group by males and females, then further subdivided each sex by GBA carrier status and compared clinical features in each stratification. Patients were clinically followed for up to 6.5 years (median 6 years). Cox regression (adjusted for age, disease duration and education) was used to model the effect of [1] GBA and non-GBA genetic mutations, [2] sex, [3] gene-sex interactions on cognitive decline.

Results: The p.N409S variant was the prevailing GBA-mutation (50%), with no differences between sex distribution. As expected, individuals with GBA-PD showed a more severe phenotype and reduced dopamine uptake in the bilateral putamen. Although similar clinical phenotype among GBA-PD patients, females showed a greater dopaminergic deficit as compared to the HC population. Cox Regression revealed that sex (HR=0.675, $p<0.01$), GBA mutations (HR=0.514 $p<0.001$), the interaction between sex and GBA mutations (HR=0.756 $p<0.05$) and between APOE- ε4 and GBA mutations (HR=0.630 $p<0.001$) were associated with a steeper cognitive decline.

Conclusions: The results suggest that both GBA mutations and sex drive phenotype, with GBA-PD males being characterized by a more malignant trajectory. Notably, the greater dopaminergic impairment in GBA-PD females, together with a more benign phenotype than GBA-PD males may be explained by the action of estrogen on neuronal reserve in females. The modulation of sex on genotype should be considered for future trial selection.

C13

Adaptive versus conventional chronic deep brain stimulation in Parkinson's disease

Ioannis Ugo Isaias[1,2], S. Marceglia[3], L. Romito[4], R. Eleopra[4], L. Borellini[5], V. Levi[4], M. Locatelli[5], T. Mandat[6], E. Pirola[5], A. Ampollini[5], M. Lanotte[7], L. Lopiano[7], M. Zibetti[7], A.R. Bentivoglio[8], C. Piano[8], A. Izzo[8], F. Tamma[9], C. Palmisano[2], L. Caffi[1,2], G. Foffani[10], A. Lozano[11], E. Moro[12], J. Volkmann[2], C. Conti[13], M. Arlotti[13], L. Krinke[13,14], L. Rossi[13], A. Priori[15]

[1]Centro Parkinson e Parkinsonismi, ASST G.Pini-CTO, Milan, Italy
[2]University Hospital Würzburg and Julius Maximilian University of Würzburg, Würzburg, Germany
[3]University of Trieste, Dipartimento di Ingegneria e Architettura, Trieste, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[6]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie, Warsaw, Poland
[7]Università degli Studi di Torino, Turin, Italy
[8]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[9]Dipartimento di Neurologia, Ospedale Regionale F. Miulli, Acquaviva delle Fonti, Bari, Italy
[10]Fundacion del Hospital Nacional de Parapléjicos para la Investigacion y la Integracion, Toledo, Spain
[11]Division of Neurosurgery, Department of Surgery, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada
[12]Grenoble Institute of Neurosciences, INSERM U1216, University Grenoble Alpes, Grenoble, France
[13]Newronika SpA, Milan, Italy
[14]West Virginia University, Morgantown, West Virginia, USA
[15]Università degli Studi di Milano, Aldo Ravelli Research Center for Neurotechnology and Experimental Neurotherapeutics, Milan, Italy

Introduction: Adaptive deep brain stimulation (aDBS) is one of the most promising innovations in the field of DBS. The possibility to automatically adapt stimulation parameters, moment-by-moment to the clinical condition of a patient potentially offers several advantages over conventional DBS (cDBS) but still needs long-term clinical validation.

Objectives: To report the intraindividual comparative evaluation between aDBS and cDBS of the subthalamic nucleus in 14 patients with Parkinson's disease (PD).

Methods: Patients were implanted with the AlphaDBS device (Newronika SpA, Milano, Italy) in the context of the clinical trial NCT04681534 and were followed-up for one day (short term follow-up, ST-FP) and for two weeks (long term follow-up, LT-FUP) in each mode (aDBS or cDBS in random order). Clinical assessment was performed with the UPDRS-III and UDysRS scales and a 3-days diary. Data are reported as mean±SD.

Results: aDBS improved patients as much as cDBS (UPDRS-III %improvement MedOFF/StimOFF to MedON/StimON cDBS vs aDBS: 0.66±0.15 vs 0.61±0.17; Good-On-Time cDBS vs aDBS: 11.7±4.3 vs 13.1±4.9). When patients were stratified for the severity of dyskinesias, cDBS-induced UPDRS-III improvement did not correlate with dyskinesias (Spearman's rho: -0.385, p=0.282), aDBS-induced UPDRS-III had a negative correlation with dyskinesias, implying that patients with milder dyskinesias have a greater UPDRS-III improvement (Spearman's rho: -0.771, p=0.006). The ON time without dyskinesia in aDBS was higher than 1SD of the average ON time without dyskinesia with cDBS in 50% of patients. In the end, 90% of patients chose (blinded) to continue with aDBS.

Conclusions: Our preliminary results suggest that (i) PD patients have similar UPDRSIII improvement with aDBS and cDBS, (ii) patients with mild dyskinesias undergoing aDBS have a greater UPDRS-III improvement than cDBS, (iii) with aDBS the ON time is higher than cDBS in half of the patients, and (iv) the majority of PD patients preferred aDBS.

C14

Pain in multiple system atrophy: a community-based survey

Nicole Campese[1], B. Caliò[1,2], F. Leys[1], L. Kaltenbach[3], G. Göbel[3], J. Wanschitz[1], A. Schlager[4], P. Bower[5], L. Kellerman[5], L. Zamarian[1], K. Bannister[6], K. Ray Chaudhuri[6,7], A. Schrag[8], R. Freeman[9], H. Kaufmann[10], R. Granata[1], S. Kiechl[1], W. Poewe[1], K. Seppi[1], G. Wenning[1], A. Fanciulli[1]

[1]Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[3]Institute for Medical Statistics and Informatics, Medical University of Innsbruck, Innsbruck, Austria
[4]Department of Anesthesiology and Intensive Care Medicine, Medical University of Innsbruck, Innsbruck, Austria
[5]The Multiple System Atrophy Coalition, Inc., McLean, VA, USA
[6]Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[7]Parkinson Foundation International Centre of Excellence, Kings College Hospital, London, UK
[8]Department of Clinical and Movement Neurosciences, University College London, London, UK
[9]Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA
[10]Department of Neurology, Dysautonomia Center, New York University Grossman School of Medicine, New York, New York, USA

Introduction: A recent meta-analysis indicates that pain affects up to 60% of individuals with multiple system atrophy (MSA), but its prevalence, features, risk factors and best treatment options in this rare disorder remain unclear.

Objectives: To assess prevalence, characteristics, associated features, and treatments for pain in MSA.

Methods: We performed a community-based cross-sectional observational study. Following a whole population sampling approach, individuals with MSA and their informal caregivers were invited, via patient advocacy newsletters and social media, to participate in an online survey, available between February and May 2023. Two hundred sixty-four individuals with MSA and 178 caregivers accessed the survey. After checking for data completeness and plausibility, questionnaires from 194 individuals with MSA and 114 caregivers were included in the final analysis.

Results: Eighty-seven percent of individuals with MSA reported pain. Pain occurred more frequently in women [OR: 6.38 (95% C.I. 1.27-32.08), p=0.025] and in individuals with a self-reported annual income below the average of the country [OR: 5.02 (95% C.I. 1.32-19.08), p=0.018]. Pain was mostly located in the neck and shoulders (58%, n=111), back (45%, n=86) and legs (45%, n=86). Among individuals suffering from pain, 69% received any kind of targeted pain treatment, most frequently non-steroidal anti-inflammatory drugs (30%, n=49), acetaminophen (25%, n=41) and opioids (17%, n=29) but only 52% of them reported to be at least partially satisfied with current pain management. Pain mostly affected patients' work, household activities, and hobbies and caregivers' social activities.

Conclusions: Our findings indicate that pain is even more common than previously reported in MSA, is mostly located in the neck and shoulders, back and legs, and especially affects women and individuals with lower income. Despite the frequent occurrence, pain remains undertreated or not satisfactorily managed in MSA, pinpointing an important unmet need to be addressed in MSA.

C15

Clinical features of α-synucleinopathies in a large cohort of Gaucher's disease patients

Marco Percetti[1-3], E. Monfrini[3,4], G. Franco[4], I. Trezzi[4], M.C. Malaguti[5], F. Cavallieri[6], F. Valzania[6], G. Cossu[7], S. Ramat[8], A. Govoni[8], C. Comi[9], A. Tessitore[10], R. De Micco[10], A. Barbato[11], P. Tirelli[12], F. Spagnolo[13], M.D. Cappellini[14], E. Cassinerio[14], I. Motta[14], F. Carubbi[15], F. Nascimbeni[16], L. Borin[17], A.B. Di Fonzo[4]

[1]School of Medicine and Surgery and Milan Center for Neuroscience, University of Milan-Bicocca, Milan, Italy
[2]Foundation IRCCS San Gerardo dei Tintori, Monza, Italy
[3]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[4]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[5]Dipartimento di Scienze Neurologiche, Ospedale Santa Chiara, Trento, Italy
[6]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[7]Neurology Service and Stroke Unit, Department of Neuroscience, AO Brotzu Cagliari Italy
[8]Parkinson Unit, Neuromuscular-Skeletal and Sensory Organs Department, AOU Careggi, Florence, Italy
[9]Neurology Unit, S. Andrea Hospital, Department of Translational Medicine, University of Piemonte Orientale, Vercelli, Italy
[10]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[11]Department of Clinical Medicine and Surgery, "Federico II" University Hospital, Naples, Italy
[12]UOC Medicina Generale Ospedale del Mare, ASL Na 1, Naples, Italy
[13]Neurological Department, Antonio Perrino's Hospital, Brindisi, Italy
[14]Unit of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[15]U.O.C. Medicina Metabolica AOU Modena, Metabolic Medicine Unit, Modena University Hospital, Modena, Italy
[16]Regional Referral Centre for Lysosomal Storage Diseases, Division of Internal Medicine and Metabolism, University Hospital of Baggiovara, AOU of Modena, Modena, Italy
[17]Department of Hematology, Asst Monza, San Gerardo Hospital, Monza, Italy

Background: Gaucher's disease (GD) is a lysosomal storage disorder caused by biallelic GBA1 mutations. In addition, mono- and biallelic GBA1 mutations are the major genetic risk factor for α-synucleinopathies, such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Although only a minority of GD patients develop PD or DLB, in-depth characterization of these patients may help to elucidate pathogenetic mechanisms, identify new biomarkers, and to test neuroprotective therapies for PD.

Objective: To investigate the prevalence of motor and non-motor clinical features of PD in a cohort of GD patients.

Methods: Neurological examination, non-motor clinical scales (i.e. RBDSQ, UMSARS, BDI), and family history for PD or dementia were evaluated in a consecutive cohort of GD patients.

Results: 147 GD patients form several Italian referral centers for GD were evaluated by movement disorders specialists. The mean age-at examination (AaE) was 47.3±15.9y. Twenty patients (14%)

were diagnosed with PD, whereas five patients (3%) with DLB. The mean AaO of PD and DLB was 58.7±11.6 and 49.8±13.6y, respectively. The occurrence of PD or DLB was higher according to AaE (30% over 61y vs 5% 21-40y, p=0.026) and AaO of GD (50% over 61y vs 8% 0-20y, p=0.006). 16% of GD patients showed a mild extrapyramidal syndrome, with higher occurrence according to AaO of GD (78% 41-60 vs 18% 0-20, p=0.007). 30% of GD patients presented at least one non-motor symptom, especially REM sleep behavior disorder (35%) and depression (31%).

Conclusions: A high portion of GD patients display motor and, more frequently, non-motor symptoms of PD. This study highlights the potentialities of studying the GD population to identify specific biomarkers defining the prodromal phase and risk of conversion to PD.

C16

Plasma neurofilament light chain level in isolated REM sleep behavior disorders

Alessandra Calculli[1,2], D. Di Martino[1,2], G. Ongari[2], S. Gagliardi[2], P. Grillo[1], E. Capriglia[1,2], C. Fazio[1,2], D. Comolli[1,2], M. Terzaghi[1,2], S. Cerri[2], A. Pisani[1,2]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy

Introduction: Rapid-Eye-Movement (REM) sleep behavior disorder (RBD) has emerged as a specific prodromal sign of α-synucleinopathies, including Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). Individuals with isolated RBD represent an ideal population for the identification of biomarkers capable of monitoring the neurodegenerative process. The neurofilament light chain protein (NfL), a neuron-specific component of the axons, is a promising biomarker in various neurodegenerative diseases.

Objectives: Investigate the role of NfLs in iRBD population.

Methods: Plasma-NfL levels in iRBD, PD, MSA patients, and healthy controls (HC) were assessed using Ella. Statistical analysis employed PRISM9, with data comparisons via the Mann-Whitney and Spearman test.

Results: Plasma-NfL levels were measured in 69 subjects (PD:19, M:14 F:5; iRBD:19, M:18 F:1; MSA:12, M:5 F:7; HC:19, M:14 F:5). As expected, PD and MSA groups exhibited elevated plasma-NfL levels compared to HC (PDvs.HC $p=0.0005$; MSAvs.HC $p<0.0001$). Notably, plasma-NfL levels were significantly elevated in iRBD compared to HC (iRBDvs.HC $p=0.0392$) and in MSA compared to iRBD (MSAvs.iRBD $p=0.0472$). No significant difference existed between PD and iRBD patients ($p=0.8007$). Correlation analyses showed no significance between plasma-NfL levels and nonparametric variables (UPDRS-III and MMSE). Within iRBD, a comparative analysis evaluated differences based on hyposmia, constipation, or orthostatic hypotension, with no evidence of significance.

Conclusions: Results suggest individuals with iRBD exhibit axonal damage, hinting at an ongoing neurodegenerative process. This hypothesis aligns with the statistical nonsignificance found in plasma-NfL levels between PD and iRBD, suggesting a constancy in NfL levels during phenoconversion process to PD. Moreover, the observed trend in elevated NfL levels in iRBD patients with orthostatic hypotension ($p= 0,0620$) suggest a potential link to MSA, requiring confirmation through a larger sample size for robust analysis. Plasma-NfLs emerge as a promising biomarker for identifying irreversible CNS damage, especially when integrated with clinical and instrumental data.

C17

Cerebral amyloid-β deposition, axial features and cognitive alterations in Parkinson's disease patients treated with bilateral STN-DBS: a long-term cohort study

Francesco Cavallieri[1], A. Fraternali[2], A. Arnone[2], A. Marti[1], I. Campanini[3], A. Gessani[4], V. Fioravanti[1], G. Di Rauso[1,5], F. Antonelli[4], V. Rispoli[4], A. Feletti[6,7], R. Stanzani[7], B. Damiano[3], S. Scaltriti[3], E. Bardi[4], M.G. Corni[4], F. Cavalleri[8], M.A. Molinari[4], S. Contardi[9], E. Menozzi[10], G. Biagini[11], G. Pavesi[7], C. Budriesi[4], A. Merlo[3], E. Moro[12], A. Versari[2], F. Valzania[1]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Nuclear Medicine Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3]LAM-Motion Analysis Laboratory, Department of Neuromotor and Rehabilitation, Azienda USL-IRCCS di Reggio Emilia, S. Sebastiano Hospital, Correggio, Italy
[4]Neurology Unit, Department of Neuroscience, S. Agostino Estense Hospital, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[5]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Italy
[6]Department of Neurosciences, Biomedicine, and Movement Sciences, Institute of Neurosurgery, University of Verona, Verona, Italy
[7]Neurosurgery Unit, Azienda Ospedaliero-Universitaria of Modena, Ospedale Civile Baggiovara, Modena, Italy
[8]Division of Neuroradiology, Department of Neuroscience, Nuovo Ospedale Civile S. Agostino Estense, Modena, Italy
[9]IRCCS Istituto delle Scienze Neurologiche di Bologna, Department of Neurology and Stroke Center, Maggiore Hospital, Bologna, Italy
[10]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK
[11]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[12]Grenoble Institut Neurosciences, CHU Grenoble Alpes, University Grenoble Alpes, Grenoble, France

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) represents a long-term effective treatment in complicated Parkinson's disease (PD). However, its effects on axial symptoms and cognitive decline are limited. Pathological data have confirmed that the neurodegeneration of central dopaminergic pathways, the hallmark of PD, can be accompanied by a contemporary involvement of other neurotransmitter pathways. Prevalent involvement of the cholinergic system could be associated with a clinical "cholinergic" phenotype dominated by axial symptoms, cognitive deterioration and cerebral amyloid-β deposition.

Objectives: To evaluate the possible long-term cerebral deposition of amyloid-β in PD patients treated with STN-DBS and its possible influence on axial and cognitive variables.

Methods: Consecutive PD patients treated with bilateral STN-DBS with a long-term follow-up were included. Amyloid-β deposition was evaluated postoperatively through a 18Fflutemetamol positron emission tomography (PET) study. Axial symptoms have been assessed using a standardized clinical-instrumental approach. Speech was assessed by perceptual and acoustic analysis while gait by means of the instrumented timed up and go test (iTUG). Motor severity was evaluated applying the UPDRS part III score and subscores while cognitive functions through a complete neuropsychological

assessment. Different stimulation and drug conditions were assessed: on stimulation/off-medication, off-stimulation/off-medication, on-stimulation/on medication conditions (single and dual task).

Results: 19 PD patients (male:11; age:63.52 years; on-stimulation/on-medication UPDRSIII: 17.05) with a five-year postoperative follow-up were included. Amyloid-β deposition was found in 21% of patients (4/19) with a prevalent involvement of prefrontal, limbic and parietal areas. Compared with patients without amyloid-β deposition, PD patients with positive 18F-flutemetamol PET study showed higher preoperative UPDRS-I (p=.037) score and lower postoperative Raven's matrices scores (p=.05).

Conclusions: Our results suggest that in the long-term after STN-DBS a significant percentage of PD patients may develop brain amyloid-β deposition. However, larger samples are needed to evaluate the possible role of amyloid-β deposition in the development of axial and cognitive alterations after surgery.

C18

Discriminating between Brain-first and Body-first Parkinson's disease using conventional and radiomics-enhanced dopamine transporter SPECT image analysis

Giovanni Palermo[1], G. Aghakhanyan[2], G. Bellini[1], M.G. Tedeschi[1], G. Nonne[2], R. Morganti[3], D. Frosini[1], D. Volterrani[2], R. Ceravolo[1]

[1]Center for Neurodegenerative Diseases – Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Regional Center of Nuclear Medicine, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[3]Section of Statistics, University of Pisa, Pisa, Italy

Introduction: Recently, two new Parkinson's disease (PD) subtypes, Brain-First and a Body-First type, have been proposed based on a variable disease initiation site. Body-First PD patients are characterized by prodromal REM behaviour disorder (RBD), a substantial burden of autonomic symptoms (e.g. constipation and orthostatic hypotension) and more symmetric striatal dopaminergic loss.

Objectives: We aimed to assess in a large PD cohort whether clinical markers of Body-First subtype (considered individually or as a whole) correlate with a more symmetrical [123I]-FP-CIT binding and to differentiate the two subtypes through the integration of clinical data and dopamine transporter (DAT)-SPECT image analysis, based on the application of both DaTQUANT and Radiomics.

Methods: We retrospectively included 158 early PD patients who underwent DAT-SPECT at diagnosis. They were recruited if they had been assessed at least once annually and had a minimum follow-up period of six years. Motor and non-motor symptoms were regularly evaluated with common scales. Body-First patients were subdivided on the basis of RBD, dysautonomia status, and constipation at baseline. We utilized DaTQUANT software semi-quantitative outputs, such as specific binding ratios, asymmetry indexes, and Z-scores, alongside a machine learning algorithm employing radiomics features from DAT-SPECT images for distinguishing between the two subtypes.

Results: Body-First patients did not exhibit greater symmetrical [123I]-FP-CIT reduction compared to Body-First ones, even though PD patients with a more symmetric DAT deficit tended to be older, have worse motor and cognitive performance at baseline as well as increased cognitive decline at follow-up. Both DaTQUANT analyses ($p > 0.05$) and Radiomics (AUC = 0.47±0.1) were unsuccessful in differentiating the two subtypes.

Conclusions: Baseline increased symmetry on DAT-SPECT was associated with a more "malignant" PD phenotype but it was not prevalent in the clinically Body-First type. Similarly, radiomics and DaTQUANT analyses showed limited discriminative capacity for categorizing Brain-First and Body-First PD patients.

C19

Dopaminergic deficits along the spectrum of Alzheimer's disease

Alice Galli[1,2], A. Pilotto[1-3], A. Sala[4], S.P. Caminiti[5], L. Presotto[6], C. Liguori[7], N.B. Mercuri[7], E. Premi[8], V. Garibotto[9], G. Frisoni[10], A. Chiaravallotti[11], O. Schillaci[11], M. D'Amelio[12], B. Paghera[13], S. Lucchini[13], F. Bertagna[13], D. Perani[14], A. Padovani[1-3]

[1]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Brescia, Italy
[2]Laboratory of Digital Neurology and Biosensors, University of Brescia, Brescia, Italy
[3]Neurology Unit, Department of Continuity of Care and Frailty, ASST Spedali Civili Brescia Hospital, Brescia, Italy
[4]Coma Science Group, University of Liege, Liege, Belgium
[5]Department of Brain and Behavioral Sciences, Univeristy of Pavia, Pavia, Italy
[6]Department of Applied Physics, University of Milan - Bicocca, Milan, Italy
[7]Neurophysiology Unit, Sleep and Epilepsy Center, University of Rome Tor Vergata, Rome, Italy
[8]Stroke Unit, ASST Spedali Civili Brescia Hospital, Brescia, Italy
[9]Department of Radiology and Medical Informatics, Geneva University Hospital, Geneva, Switzerland
[10]Department of Psychiatry, Geneva University Hospital, Geneva, Switzerland
[11]Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy
[12]Department of Experimental Neurosciences, IRCCS Santa Lucia Foundation, Rome, Italy
[13]Nuclear Medicine Unit, University of Brescia, Brescia, Italy
[14]University Vita-Salute San Raffaele, IRCCS San Raffaele Hospital, Milan, Italy

Introduction: Both post-mortem and in vivo data argue for dopamine dysfunction in patients with Alzheimer's Disease (AD). However, the timing and regional progresssion of dopaminergic systems alterations in AD are still debated.

Objectives: To investigate in vivo the pattern of dopaminergic changes and connectivity using 123I-FP-CIT imaging in patients across the AD spectrum.

Methods: Fifty-nine A+T+N+ AD patients (n=21 MCI-AD; n=38 ADDEM) and n=45 age and sex-matched controls (CG) entered the study and underwent 123I-FP-CIT dopaminergic imaging. The occipital binding was used as reference region to obtain single-subject binding in different brain regions. Between-groups differences in 123I-FP-CIT binding in both mesolimbic and nigrostriatal dopaminergic pathways were assessed using an ANCOVA test-adjusting for the effect of center of imaging acquisition, age, and sex. Regions resulting from the voxel-wise direct comparison between MCI-AD and AD-DEM were considered as a seed of interest for a voxel-wise interregional correlation analysis.

Results: Both MCI-AD and AD-DEM patients showed dopaminergic depletion within the basal ganglia, whereas cortico-limbic regions (namely hippocampus, amygdala, anterior and middle cingulate, frontal cortex and thalamus) resulted impaired only in the dementia phase. The brain voxel-wise interregional correlation analysis showed a progressive pattern of disruption of caudate/thalamus dopaminergic connectivity to hippocampus and amygdala from MCI-AD to AD-DEM stages.

Conclusions: This study indicates basal ganglia dopaminergic alterations and connectivity disruption in the nigrostriatal and mesolimbic systems already in prodromal AD, extending to several cortico-limbic regions in dementia phases.

C20

Modelling pathology progression in Parkinson's disease phenotypes

Massimiliano Passaretti[1,2], H. Zhao[1,3], M. Mijalkov[1], B.Z. Gerboles[1], A. Canal Garcia[1], J. Sun[1], D. Vereb[1], N. Rivera[4,5], G. Volpe[3], M. Bologna[2,6], J.B. Pereira[1]

[1]Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
[2]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[3]University of Gothenburg, Department of Physics, Soft Matter Lab, Gothenburg, Sweden
[4]Department of Medicine Solna, Respiratory Medicine Division, Karolinska Institutet, Stockholm, Sweden
[5]Rheumatology Division, Department of Medicine Solna, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
[6]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: Understanding the relationship between phenotypic heterogeneity and the spread of pathology in Parkinson's disease (PD) is challenging. The α-Synuclein Origin site and Connectome (SOC) model postulate that α-synuclein aggregation first localization and spreading determine disease evolution. Accordingly, two PD subtypes have been proposed: brain-first-PD and body-first-PD. The former originates from the central nervous system, while the latter originates from peripheral nervous structures.

Objectives: We aim to establish whether using the SOC model we can differentiate PD phenotypes predicting disease progression.

Methods: 1120 de novo- PD patients, 910 prodromal-cases, and 263 healthy controls were included in the Parkinson's progression markers initiative. Patients and prodromal cases with REM behavior disorder and/or autonomic symptoms at baseline were classified as body-first, otherwise as brain-first. All subjects underwent a detailed longitudinal (12-year) clinical protocol and magnetic resonance imaging. Clinical data were analyzed through linear-mixed effects models, and group comparisons were employed for longitudinal gray matter atrophy.

Results: Body-first-PD cases (667) demonstrated higher motor burden and complications, worse cognitive evolution, and more severe depression compared to brain-first-PD. Body-first-PD cases showed bilateral medial and lateral temporal atrophy involving the amygdala, para-hippocampus, and temporoparietal junction. Brainfirst PD patients demonstrated more circumscribed atrophy of the left hemisphere, involving the angular gyrus, sensory-motor cortex, and inferior frontal gyrus. Body-first-prodromal-cases (519) demonstrated similar results to body-first-PD cases, i.e. greater motor and cognitive impairment, involving the same domains, and grey matter atrophy in lateral temporal areas.

Conclusions: Consistent with the SOC model, the study results indicate that body-first-PD and prodromal cases had worse disease progression and more severe brain atrophy compared to brain-first-PD and prodromal cases. The results underscore the importance of PD patient phenotyping since the prodromal phases. Hence, the application of the model would enable tailored therapeutic approaches and disease prevention interventions in high-risk individuals in the future.

References:

[1] Borghammer P. The α-Synuclein Origin and Connectome Model (SOC Model) of Parkinson's Disease: Explaining Motor Asymmetry, Non-Motor Phenotypes, and Cognitive Decline. J Parkinsons Dis. 2021;11(2):455-474. doi: 10.3233/JPD-202481. PMID: 33682732; PMCID: PMC8150555.

C21

Continuous gait monitoring of Parkinson's disease patients during STN DBS under chronic sensing: a pilot study

Gaia Anzini[1], R. Battaglia[2], G. Leogrande[3], F. Bressi[2], R. Ricciuti[4], M. Paniccia[5], A. Belli[6], V. Di Lazzaro[1], P. Pierleoni[6], S. Raggiunto[7], M. Marano[1]

[1]Neurology, Fondazione Policlinico Universitario Campus Bio-Medico di Roma, Roma, Italy
[2]Physical Medicine and Rehabilitation, Fondazione Policlinico Universitario Campus Bio-Medico di Roma, Roma, Italy
[3]Medtronic EMEA Corporate Technology and Innovation, Maastricht, Netherlands
[4]Neurosurgery, Belcolle Hospital, ASL Viterbo, Viterbo, Italy
[5]Rehabilitation Center S. Stefano, Potenza Picena, Italy
[6]Department of Information Engineering (DII), Università Politecnica delle Marche, Ancona, Italy
[7]National Inter-University Consortium for Telecommunications (CNIT), Research Unit of Università Politecnica delle Marche, Ancona, Italy

Introduction: Subthalamic nucleus (STN) Deep Brain Stimulation (DBS) is effective for the treatment of fluctuations in Parkinson's disease (PD). The adoption of STN Local Field Potential (LFP) in clinical practice is possible through available DBS devices [1]. DBS management of gait issues has a variable outcome, and LFP (beta band) show low correlation with gait parameters [2].

Objective: Exploring the correlation between macroscopic beta changes and gait.

Methods: We recruited 7 subjects treated with STN-DBS. Subjects were equipped with 3 IMUs (feet and back), recording 10 hours of walking bouts (step number, step/stride duration, variability, and regularity). Chronic sensing was enabled with the frequency of interest set on the patient known beta value. LFPs recorder collected a mean beta power value for each consecutive block of 10 minutes along the recording, which was then normalized. Mean values of walking episodes were collected during the same time span.

Results: All patients successfully completed the experiment. Mean age was 58±7.8 and disease duration 10±2.5 years, UPDRS-III 10±7 (ON), H&Y 2±0.5 (ON), LEDD 297±179 mgs. Mean LFP STN frequency was 18.6 (left) and 17.5 Hz (right). We found a low-grade correlation between step/stride variability and left beta power (R 0.15, $p<0.05$), and stride duration and right beta power (R 0.15, $p<0.05$). On the other hand, a more robust correlation was present between step/stride regularity and right beta power (R -0.30, $p<0.01$).

Discussion: These results inform on the role of chronic beta sensing for the potential optimization of DBS parameters in PD with a focus on gait. The finding of asymmetric correlation between parameters supports the hypothesis of brain lateralization (right) of axial functions [3]. Studies are warranted on the effect of the stimulation on the correlation between the beta power and the gait. Data on other oscillatory activities are under collection.

References:

[1] Binder T, Lange F, Pozzi N, Musacchio T, Daniels C, Odorfer T, Fricke P, Matthies C, Volkmann J, Capetian P. Feasibility of local field potential-guided programming for deep brain stimulation in Parkinson's disease: A comparison with clinical and neuro-imaging guided approaches in a randomized, controlled pilot trial. Brain Stimul. 2023 Sep-Oct;16(5):1243-1251. doi: 10.1016/j.brs.2023.08.017.

[2] Morelli N. Effect and Relationship of Gait on Subcortical Local Field Potentials in Parkinson's Disease: A Systematic Review. Neuromodulation. 2023 Feb;26(2):271-279. doi: 10.1016/j.neurom.2022.09.001. Epub 2022 Oct 14. PMID: 36244929.
[3] Lizarraga KJ, Jagid JR, Luca CC. Comparative effects of unilateral and bilateral subthalamic nucleus deep brain stimulation on gait kinematics in Parkinson's disease: a randomized, blinded study. J Neurol. 2016 Aug;263(8):1652-6. doi: 10.1007/s00415-016-8191-3.

C22

Skin calcium deposits in primary familial brain calcification (PFBC): a novel potential biomarker?

Giulia Bonato[1,2], A. Emmi[1,2,3], A. Tushevski[3], C. Bertolin[4], A. Porzionato[3], L. Salviati[4], A. Antonini[1,2], M. Carecchio[1,2]

[1]Parkinson and Movement Disorders Unit, Centre for Rare Neurological Diseases (ERN-RND), Department of Neuroscience, University of Padova, Padova, Italy
[2]Center for Neurodegenerative Disease Research (CESNE), University of Padova, Padova, Italy
[3]Institute of Human Anatomy, Department of Neurosciences, University of Padova, Padova, Italy
[4]Clinical Genetics Unit, Department of Women's and Children's Health, University of Padova, Padova, Italy

Introduction: PFBC is a rare genetic neurodegenerative disorder of adulthood characterized by calcium deposition in basal ganglia, causing movement disorders, cognitive deficits or psychiatric features [1,2].
Perivascular skin calcifications have been reported in single cases of PDGFB and XPR1 gene mutations [3,4], but it is currently unknown whether they are a hallmark of all PFBC genetic subtypes.

Objective: Evaluating skin biopsies of PFBC patients, determining differences based on symptoms and genetic features; comparing with other neurodegenerative conditions.

Methods:
- Cohort: 10 PFBC (5 males, 5 females), 10 PD, 7 healthy controls
- Testing: neurologic examination, CT scans, PTH, Ca, P, creatinine, CPK, NGS panel (>100 genes for movement disorders, Illumina Nextseq550)
- Skin biopsy: 3mm ø - 5mm deep punch skin samples; Haematoxylin-Eosin, von-Kossa, immunoperoxidase CD31/PECAM-1 staining; optical microscopy.

Results: 9/10 PFBC patients had pathogenic mutations (3 MYORG, 3 SLC20A2, 1 PDGFB, 1 PDGFRB, 1 XPR1), 6 variants were novel. 50% of the subjects were symptomatic: 4 had parkinsonism (in 3 combined with other movement disorders), 1 paroxysmal dystonia; 4 had psychiatric or cognitive features. All subjects had extensive calcifications in multiple brain areas (mean TCS score 27).
Skin biopsies showed small granular von Kossa+ argyrophilic calcium-phosphate deposits in the intimal layer, near the basal lamina and within the cytoplasm of CD31+ endothelial cells and pericytes of dermal capillaries and arterioles, and in the basement membrane of dermal sweat glands.
4/7 controls and 6/10 PD had calcium in the basal layer of epidermis (melanin cross-reactivity), but not in vascular walls or glands.

Conclusions: PFBC patients show a consistent pattern of perivascular calcium deposits in skin capillaries, that is independent from genetic and clinical features, suggesting convergent pathways and a multisystem disease. Skin biopsy may represent a novel diagnostic and research tool and a potential biomarker for future chelating therapies.

References:

[1] Tadic V et al (2015) Primary familial brain calcification with known gene mutations: a systematic review and challenges of phenotypic characterization. JAMA Neurol 72:460–467 .

[2] Balck A et al (2021) Genotype-phenotype relations in primary familial brain calcification: systematic MDSGene review. Mov Disord 36(11):2468–2480.
[3] Nicolas G, Marguet F, Laquerrière A, et al. Microangiopathy in primary familial brain calcification: Evidence from skin biopsies. Neurol Genet. 2017;3(2):e134.
[4] Biancheri R, Severino M, Robbiano A, et al. White matter involvement in a family with a novel PDGFB mutation. Neurol Genet. 2016;2(3):e77.

C23

Tell me how you walk and I tell you how your brain (will) work: new path to intercept future cognitive impairment - cognitive dual task as possible marker of precocious and subclinical cognitive alterations

Federico Di Filippo[1], G. De Biasi[1], C. Ricciardi[2], M. Russo[2], A. Volzone[1], G. Ricciardelli[1], S. Cuoco[1], M. Romano[2], F. Amato[2], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Fisciano, Italy
[2]Department of Electrical Engineering and Information Technology, University of Naples "Federico II", Naples, Italy

Introduction: Gait impairments are extremely common in Parkinson's disease (PD), even before most evident clinical manifestations [1]. These alterations follow the history of disease, so they can be studied as hypothetical phenotypical and prognostic/progression markers.

Objectives: To evaluate spatiotemporal gait parameters in PD patients with and without mild or subjective cognitive impairment (MCI and SCI) in three different gait settings.

Methods: One hundred PD patients were divided in three groups: 15 PD patients with self-referred cognitive impairment at the first item of MDS-UPDRS part I without objective cognitive decline (PD-SCI), 41 PD patients without subjective or objective cognitive impairment (PD-noCI), 44 PD patients with MCI (PD-MCI). They were evaluated with gait analysis acquired in three different conditions (normal gait, motor and cognitive dual-task). Spatiotemporal variables were extracted from the analysis. A univariate statistical analysis (parametric ANOVA test or non-parametric Kruskal-Wallis test, as appropriate) with post-hoc analysis was carried out in order to evaluate the significant differences among the groups.

Results: The three groups were comparable except for age (greater in PD-MCI), levodopa equivalent daily dose (lower in PD-SCI), MDS-UPDRS total score and Part I and III scores (higher in PD-MCI). In normal gait task, the three groups showed several differences, all due to the comparison between PD-MCI and PD-noCI, as disclosed by post-hoc analysis. In dual task conditions, mostly in the cognitive dual-task, the three groups showed increased gait alterations that, at post-hoc analysis, mirrored the magnitude of cognitive dysfunction (PD-noCI<PD-SCI<PD-MCI).

Conclusions: PD patients display progressive alterations of spatiotemporal parameters of gait in relationship with the cognitive status [2]. Even more importantly, our findings suggest that some prodromic gait alterations – especially the ones highlighted by cognitive dualtask – could eventually be considered possible markers to objectify symptoms-based construct, such as SCI, and to precociously intercept subjects at risk of future cognitive impairment.

References:

[1] Amboni M, Barone P, Hausdorff JM. Cognitive contributions to gait and implications. Mov Dis ofradll.s: 2vi0d1e3n ce Saenpd 15;28(11):1520-33.
[2] Joseph B. Webster, Benjamin J. Darter Principles of Normal and Pathologic Gait, Chapter IV. 2019.

C24

One-year global improvement after deep brain stimulation for Parkinson's Disease: patient versus clinician impression. What matters?

Pietro Antenucci[1], A. Gozzi[1], F. Colucci[1,2], I. Casetta[1], M. Sensi[3]

[1]Department of Neurosciences and Rehabilitation, University of Ferrara, Ferrara, Italy.
[2]Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[3]Department of Neurosciences and Rehabilitation, Ferrara University Hospital, Ferrara, Italy

Introduction: Several different factors can affect the global impression of improvement after deep brain stimulation (DBS) for Parkinson's disease (PD) and evaluation of clinicians could differ from the patient awareness. [1, 2]

Objective: To evaluate similarities and differences between clinician and PD patients point of view on global improvement at one year of DBS.

Methods: Patients' Global Impression of Change Scale (PGIC) [3] and Clinical Global Impressions Scale of Improvement (CGI) [4,5] were administered at 1 year following DBS surgery. We retrospectively collected and evaluated which parameters differ between groups with different degrees of impression of improvement (A: Very Much Improved, B: Much Improved, C: Minimally Improved-Unchanged-Worse)

Results: Results from 57 patients were collected. No significant differences between groups were found in age, sex, years of disease, UPDRS III, UPDRS IV, LEDD, UPDRS III reduction, LEDD reduction, number of tablets and number of administrations per day. Significant differences at one year in reduction UPDRS IV and number of outpatient accesses for stimulation reglage were found between both PGIC groups and CGI groups. Furthermore, significant difference was detected for the presence of stimulus-induced complications between CGI groups, unlike PGIC groups.

Conclusion: At one year reduction in UPDRS IV and the number of accesses in outpatient clinic for stimulation reglage appear to be key factors for the evaluation of the degree of improvement for both clinician and patients. On the other hand, the presence of stimulus-induced complications accounts only for the clinician point of view on improvement, whereas it does not affect self-assessment of the patient.

References:

[1] Abboud, H., Genc, G., Thompson, N. R., Oravivattanakul, S., Alsallom, F., Reyes, D., Wilson, K., Cerejo, R., Yu, X. X., Floden, D., Ahmed, A., Gostkowski, M., Ezzeldin, A., Marouf, H., Mansour, O. Y., Machado, A., & Fernandez, H. H. (2017). Predictors of Functional and Quality of Life Outcomes following Deep Brain Stimulation Surgery in Parkinson's Disease Patients: Disease, Patient, and Surgical Factors. Parkinson's Disease, 2017, 5609163. https://doi.org/10.1155/2017/5609163.

[2] Martinez-Martin, P., Deuschl, G., Tonder, L., Schnitzler, A., Houeto, J.-L., Timmermann, L., Rau, J., Schade-Brittinger, C., Stoker, V., Vidailhet, M., Krack, P., & EARLYSTIM Study Group. (2020). Interpretation of health-related quality of life outcomes in Parkinson's disease from the EARLYSTIM Study. PloS One, 15(8), e0237498. https://doi.org/10.1371/journal.pone.0237498.

[3] Maier, F., Lewis, C. J., Horstkoetter, N., Eggers, C., Dembek, T. A., Visser-Vandewalle, V., Kuhn, J., Zurowski, M., Moro, E., Woopen, C., & Timmermann, L. (2016). Subjective perceived outcome of subthalamic deep brain stimulation in Parkinson's disease one year after surgery. Parkinsonism & Related Disorders, 24, 41–47. https://doi.org/10.1016/j.parkreldis.2016.01.019.

[4] Kamper, S. J., Maher, C. G., & Mackay, G. (2009). Global rating of change scales: a review of strengths and weaknesses and considerations for design. The Journal of Manual & Manipulative Therapy, 17(3), 163–170. https://doi.org/10.1179/jmt.2009.17.3.163.
[5] Busner, J., & Targum, S. D. (2007). The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry (Edgmont (Pa. : Township)), 4(7), 28–37.

C25

Dopamine neuron dysfunction and loss in the PrknR275W mouse model of juvenile parkinsonism

Jenny Sassone[1,2], M. Regoni[1,2], L. Zanetti[1,2], M. Sevegnani[3], C. Domenicale[4], S. Magnabosco[4], J.C. Patel[5], M.K. Fernandes[5], E. Monzani[1], S. Comai[1,6], C. Laura[1], A. Ciammola[7], F. Valtorta[1,2], M. Morari[4], G. Piccoli[3], M.E. Rice[5]

[1]San Raffaele Scientific Institute, Milan, Italy
[2]Vita-Salute San Raffaele University, Milan, Italy
[3]Dulbecco Telethon Institute, Laboratory of Biology of Synapse, Center for Integrative Biology (CIBIO), University of Trento, Trento, Italy
[4]Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy
[5]Department of Neurosurgery, New York University Grossman School of Medicine, New York, NY, USA
[6]Department of Biomedical Sciences, University of Padova, Padova, Italy
[7]IRCCS Istituto Auxologico Italiano, Department of Neurology and Laboratory of Neuroscience, Milan

Introduction: Mutations in the PRKN gene cause Autosomal Recessive Juvenile Parkinsonism (ARJP) [1]. To date, there is no animal model able to recapitulate the disease features, its creation is fundamental to clarify the neurodegeneration mechanisms and to test neuroprotective strategies.

Objectives: We created a knock-in mouse model carrying the p.Arg275Trp (R275W) mutation, i.e. the missense mutation with the highest allelic frequency in PRKN patients [2]. We analysed the anatomical and functional integrity of the nigrostriatal pathway of homozygous Prkn R275W mice as well as their motor phenotype over the entire lifespan.

Methods: The number of dopamine (DA) neurons in the SNc of WT and PrknR275W mice was counted by unbiased stereology. DA content in striatum was determined by high-performance liquid chromatography. Dynamic DA release in ex vivo corticostriatal slices was examined by fast-scan cyclic voltammetry.

Results: Young WT and Prkn R275W mice (1 month of age) had similar DA neuron counts, however, examination of SNc DA neurons from Prkn R275W mice revealed early pathophysiological changes including cytoplasmic vacuolization and alteration of burst firing. Adult Prkn R275W mice (6 and 12 months of age) showed a ~25% decrease in DA neurons. Total tissue DA content and evoked DA in dorsal striatum were significantly lower in adult Prkn R275W mice as compared to WT mice. Adult Prkn R275W mice were significantly impaired in the balance beam and pole test. Old Prkn R275W mice (18 months of age) showed a 40% decrease in the number of DA neurons and performed significantly worse than WT mice in the rotarod and balance beam test.

Conclusions: The Prkn R275W mouse recapitulates key features of ARJP. This study fills a critical need in the field by introducing a new murine PD model in which to study causative mechanisms of the disease, as well as test therapeutic strategies.

References:

[1] Bonifati V. Autosomal recessive parkinsonism. Parkinsonism Relat Disord. 2012;18:S4-S6. doi:10.1016/S1353-8020(11)70004-9.
[2] Mitsuyama S, Ohtsubo M, Minoshima S, Shimizu N. The KMparkin- DB: A Sub-set MutationView Database Specialized for PARK2 (PARKIN) Variants. Hum Mutat. 2015;36(8):E2430-E2440. doi:10.1002/humu.22803.

C26

Structural and functional connectivity predicts MRgFUS thalamotomy outcome in Parkinson's disease

Alberto Cacciola[1], G.A. Basile[1], G. Acri[1], L. Bonanno[2], A. Ielo[2], S. Marino[2], A. Brigandì[2], C. Sorbera[2], R. Morabito[2], S. Cammaroto[2], G. Di Lorenzo[2], A. Cerasa[3,4,5], A. Quartarone[2]

[1]Brain Mapping Lab, Department of Biomedical, Dental Sciences and Morphological and Functional Imaging, University of Messina, Messina, Italy
[2]IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy
[3]S. Anna Institute, Crotone, Italy
[4]Institute for Biomedical Research and Innovation (IRIB), National Research Council of Italy, Messina, Italy
[5]Pharmacotechnology Documentation and Transfer Unit, Preclinical and Translational Pharmacology, Department of Pharmacy, Health Science and Nutrition, University of Calabria, Rende, Italy

Introduction: Magnetic Resonance-guided Focused UltraSound (MRgFUS) thalamotomy is effective in alleviating tremor symptoms in Parkinson's disease (PD), with emerging evidence suggesting that treatment outcomes may be influenced by brain connectivity rather than the choice of target site alone. However, it remains unclear whether brain connectivity can predict clinical outcomes in tremordominant PD patients.

Objectives: To characterize structural and functional connectivity associated with successful MRgFUS ablation of the Ventral intermediate thalamic nucleus (Vim) and assess its potential to predict treatment outcomes.

Methods: Twelve tremor-dominant PD patients underwent unilateral MRgFUS thalamotomy. Treatment outcome was measured as the percentage change in motor score of the UPDRS-III one week post treatment. Different standard ablation features were tested for correlation with clinical outcome. We then combined our PD data set with normative human connectome data (diffusion tractography and resting state functional connectivity) to identify connectivity patterns associated with clinical improvement. Structural and functional connectivity profiles were then independently employed to predict clinical outcome in a leave-one-patient-out cross-validation (LOOCV) design.

Results: No significant correlations were found between standard ablation features and clinical outcome. However, connectivity between the ablation site and a network of brain regions, including structural connectivity to pre-supplementary motor area, supplementary motor area, superior frontal gyrus, and cerebellum, correlated with clinical improvement. Similar patterns were observed in functional connectivity, with anticorrelation between the ablation area and primary somatosensory cortex and the most lateral part of primary motor cortex. LOOCV demonstrated that both structural ($R2 = 0.53$; $R = 0.73$; $p = 0.002$) and functional connectivity ($R2 = 0.23$; $R = 0.48$; $p = 0.007$) fingerprints predicted clinical improvement within the cohort.

Conclusions: Both target structural and functional connectivity are independent predictors of clinical improvement in tremor-dominant PD patients undergoing MRgFUS thalamotomy. This pilot study suggests the future potential for patient-specific connectomics surgical targeting, while warranting further validation in independent cohorts.

C27

Serum neurofilament light chain, GFAP and pTau181 as biomarkers in Parkinson's disease patients with and without cognitive deficits

Eleonora Fiorenzato[1], G. Musso[2], R. Biundo[3], M. Campagnolo[1], M. Carecchio[1], S. Cauzzo[1], A. Emmi[4,5], M. Garon[1], A. Guerra[1], V. Misenti[1], S. Moz[2], S. Mozzetta[1], A. Pilotto[6], A. Cagnin[1], D. Basso[2], A. Antonini[1,4]

[1]Department of Neuroscience (DNS), University of Padova, Padova, Italy
[2]Department of Medicine (DIMED), University of Padova, Padova, Italy
[3]Department of General Psychology, University of Padova, Padova, Italy
[4]Center for Neurodegenerative Disease Research (CESNE), Department of Neuroscience, University of Padova, Padova, Italy
[5]Institute of Human Anatomy, Department of Neuroscience, University of Padova, Padova, Italy
[6]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Brescia, Italy

Introduction: Neurofilament light chain protein (NfL) is a biomarker of neurodegeneration and high values may predict later development of mild cognitive impairment (MCI) or dementia even in subjects with baseline normal cognitive (NC) status. The combined role of glial fibrillary acidic protein (GFAP) and phosphorylated tau at residue 181 (pTau181) measures in Parkinson's disease (PD) is not fully explored.

Objectives: We measured serum NfL, GFAP and pTau181 in PD patients with and without cognitive deficits with the objective to detect those who may be at risk of worse cognitive ad motor progression.

Methods: Serum NfL, GFAP and pTau181 were measured in 92 PD patients as well as in 20 age, education and sex-matched healthy controls (HC). A subgroup of PD patients (n=65) underwent a comprehensive neuropsychological assessment, 44 were classified as PD-NC and 21 as PD-MCI. NfL, GFAP and pTau181 concentrations were measured using the commercially available Simoa kits. Normality distribution assumption was tested with Shapiro-Wilk tests, the Spearman's correlations and non-parametric ANOVA model (Kruskal-Wallis) were run for between group comparisons.

Results: Each serum NfL, GFAP and pTau181 were more elevated in PD overall compared to HC. NfL levels positively correlated with PD disease duration (r2=0.29, p=0.011), while NfL and GFAP negatively correlated with MoCA (r2=–0.30, p=0.010 and r2=–0.27, p=0.026, respectively). Further analyses focused on PD-subgroups highlighted that NfL and GFAP levels were higher in PD-MCI compared to PD-NC (p=0.006 and p=0.034, respectively), while there was no difference in the pTau181. In addition, NfL concentration negatively correlated with the attentive domain (compound z score) (r 2=–0.38, pFDR=0.040), but not with other cognitive domains.

Conclusions: Our findings support that neurodegeneration biomarkers are higher in PD vs. HC. Serum NfL and GFAP have a potential value for distinguishing PD patients with MCI, and higher NfL levels were associated with worse performance in the attentive domain. These results indicate these biomarkers may help detecting PD at greater risk of cognitive and motor deterioration. The role of pTau181 in PD and its relationship with cognition needs further elucidation.

C28

Gut microbiota alterations as potential biomarker of severity and progression in Parkinson's disease

Rocco Cerroni[1], J.A. Campone[1], D. Pietrucci[2], M. Conti[1], C. Liguori[1], M. Pierantozzi[1], N.B. Mercuri[4,5], G. Chillemi[2], T. Schirinzi[1], A. Stefani[1]

[1]Parkinson Centre, Department of System Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]Department for Innovation in Biological, Agro-Food and Forest Systems (DIBAF), University of Tuscia, Viterbo, Italy
[3]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[4]Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) "Fondazione Santa Lucia", Rome, Italy

Introduction: Several studies underlined dysbiosis of gut microbiota in Parkinson's disease (PD) [1], remaining still unclear whether microbiota alterations represent a pathogenetic starting point or a consequence of disease [2].

Objectives: To investigate microbiota alterations as a potential biomarker of severity and progression in PD.

Methods: Microbiota compositions was studied through 16rRNA amplicon sequencing and classified to taxonomic rank. To identify dysbiosis as a severity biomarker, we compared faecal samples collected from three groups, representing three different times in natural history of disease: healthy controls (HC), PD patients at time of diagnosis (de-novo PD), PD patients in advanced stages, defined by H&Y stage≥3 and/or LEED>900mg (advPD). A multivaristatistical analysis was performed to identify differential abundant taxa between three groups. To identify dysbiosis as a prognostic biomarker, we followed longitudinally 2 groups of de-novo PD: a group with dysbiosis and a group without dysbiosis at time of diagnosis. The two groups underwent motor, non-motor and cognitive assessment at baseline and follow-up of 2 years.

Results: In the first study we enrolled 79 HC, 30 de-novo PD and 38 advPD. We found a progressive reduction in alfa and in beta-diversity and a progressive reduction in Lachnospiraceae, Bacteroidaceae, Prevotellaceae and Clostridiaceae families moving from HC to denovo PD and finally to advPD, with a reverse trend in Enterobacteriaceae and Lactobacillaceae families. In the second research line we enrolled 13 dysbiotic and 11 eubiotic de-novo PD. At two years follow-up, dysbiotics showed a more severe worsening of motor impairment, non-motor symptoms and in some cognitive domains compared to eubiotics. Moreover, dysbiotic patients needed more LEED respect to patients without dysbiosis.

Conclusions: We showed how, moving from the early to advanced stages of PD, gut microbiota become gradually destructured, assuming a pathologic and pro-inflammatory arrangement, probably underlying a more severe phenotype of the disease.

References:

[1] J.M. Boertien, P.A.B. Pereira, V.T.E. Aho, F. Scheperjans. Increasing Comparability and Utility of Gut Microbiome Studies in Parkinson's Disease: A Systematic Review. Journal of Parkinson's Disease 9 (2019) S297-S312. doi: 10.3233/JPD-191711.
[2] A. Keshavarzian, P Engen, S Bonvegna, R Cilia. The gut microbiome in Parkinson's disease: A culprit or a bystander? Prog Brain Res. 252 (2020) 357-450. doi: 10.1016/bs.pbr.2020.01.004.

C29

Exploring the nigrostriatal pathway in patients with iNPH and parkinsonism

Alessio Francesconi[1], G. Palermo[1], J. Pasquini[1], G. Bellini[1], G. Migaleddu[2], P. Perrini[3], D. Volterrani[4], M. Cosottini[5], R. Ceravolo[1]

[1]Center for Neurodegenerative Diseases - Parkinson's disease and Movement Disorders, Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Neuroradiology Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[3]Neurosurgery Unit, Department of Translational Research on New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
[4]Nuclear Medicine Unit, Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa, Italy
[5]Neuroradiology Unit, Department of Translational Research on New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Introduction: Idiopathic normal pressure hydrocephalus (iNPH) is typically characterized by gait disorder, cognitive impairment and urinary incontinence in the presence of a dilation of the ventricular system with normal intracranial pressure. iNPH can also present with parkinsonism but it is not clear if parkinsonian features are part of the clinical syndrome of iNPH or the result of a concomitant a-synucleinopathy nor what be the exact role of the dopaminergic pathway in iNPH [1].

Objective: To explore the integrity of the nigrostriatal pathway using both DaTSPECT and nigrosome imaging in patients with iNPH.

Methods: In this retrospective study, we included 20 iNPH and 20 early PD patients. iNPH participants had a diagnosis of probable iNPH with parkinsonism, all with available clinical (iNPHGS, MDS-UPDRS III and MMSE) and DaTSPECT data. Twelve iNPH patients had also performed 3T MRI with specific sequences to evaluate nigrosome [2]. In iNPH patients, the correlation between striatal DAT binding and clinical variables was assessed. The putamen/caudate ratio (P/C) and the asymmetry index (AI) were both compared between iNPH and PD patients to investigate potential differences in the striatal uptake pattern.

Results: None of the 12 iNPH patients who performed 3T MRI showed alterations of substantia nigra. A reduced DAT uptake was observed in 45% ofiNPH patients but with a prevalent involvement of the caudate in contrast to the pattern seen typically in PD. Additionally, a correlation between DAT availability and severity of motor symptoms was found in iNPH subjects.

Conclusions: These findings support the hypothesis that striatal dopaminergic dysfunction may contribute to parkinsonism in iNPH [3]. However, the nigrosome integrity in patients with abnormal dopaminergic imaging seems to support the non-neurodegenerative basis of parkinsonism in iNPH suggesting the contribute of a mechanical compression by the enlarged ventricles [4]. Hence, DAT deficit in iNPH should not reduce confidence of the iNPH diagnosis nor restrict access to shunt surgery.

References:

[1] A. J. Espay, “Deconstructing normal pressure hydrocephalus: Ventriculomegaly as early sign of neurodegeneration,” Ann. Neurol., 2017.

[2] M. Cosottini et al., “Comparison of 3T and 7T susceptibility-weighted angiography of the substantia nigra in diagnosing Parkinson disease,” Am. J. Neuroradiol., 2015.
[3] N. G. Pozzi et al., “Striatal Dopamine Deficit and Motor Impairment in Idiopathic Normal Pressure Hydrocephalus,” Mov. Disord., vol. 36, no. 1, pp. 124–132, 2021.
[4] C. Del Gamba et al., “Is DAT imaging abnormality in normal pressure hydrocephalus always suggestive of degeneration?,” Neurol. Sci., vol. 42, no. 2, pp. 723–726, 2021.

C30

Hypokinetic dysarthria, intransitive/verb ratio, and silent pauses predict the clinical diagnosis of Parkinson's disease: a machine learning study

Simona Aresta[1,2], C. Salvatore[3,4], S. Tagliente[1], C. Palmirotta[1], G. Lagravinese[1,2], D. Mongelli[1,2], C. Gelao[2], R. Falcone[1,2], I. Castiglioni[5], P. Fiore[2,6], F. Tamma[7], B. Minafra[2], P. Battista[1,8]

[1]Istituti Clinici Scientifici Maugeri IRCCS, Laboratory of Neuropsychology, Bari Institute, Bari, Italy
[2]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Bari Institute, Bari, Italy
[3]Department of Science, Technology and Society, University School for Advanced Studies IUSS Pavia, Pavia, Italy
[4]DeepTrace Technologies S.R.L., Milan, Italy
[5]Department of Physics G. Occhialini, University of Milan-Bicocca, Milan, Italy
[6]Department of Physical and Rehabilitation Medicine, University of Foggia, Foggia, Italy
[7]Neurology Unit, Miulli Hospital, Acquaviva delle Fonti, Bari, Italy
[8]Global Brain Health Institute (GBHI), University of California San Francisco, San Francisco, CA, USA

Introduction: Previous works highlighted the relevance of automated language analysis for predicting clinical diagnosis in neurodegenerative diseases, such as Alzheimer's dementia and frontotemporal dementia, but a deeper language-based data-driven investigation of the language profile of patients with Parkinson's disease (PD) [1] has been generally neglected compared to the investigation of motor speech symptoms (i.e., dysphonia and dysarthria).

Objective: To evaluate whether quantitative linguistic measures effectively identify patients with PD, we used a semi-automated multidimensional linguistic analysis innovatively combined with a machinelearning (ML) approach to characterize the narrative discourse of individuals with PD.

Methods: We recruited N=39 patients with PD (age: 69.5 ± 7.2 years; H&Y: 3.2 ± 1.3; MDS-UPDRSIII: 37.3 ± 21.4) and N=40 age-matched controls (age: 64.4 ± 10.5) at the Maugeri Institute IRCCS Bari, from whom we obtained speech samples based on the Summer Time picture description task. We processed all individual transcriptions with the computational language analysis software (CLAN) and a total of 42 linguistic features, belonging to different linguistic levels, were extracted. Univariate statistical analysis was performed, followed by an ML approach i.e., Support Vector Machine (SVM), dividing the dataset into 80% for training and 20% for testing. Furthermore, feature selection, hyperparameter tuning, and SHAP explainability analysis were performed.

Results: The most significant differences were silent pauses, intransitive verbs ratio, utterances without verbs ratio, and hypokinetic dysarthria condition. The SVM model achieved good performances, accuracy (%) 87.5, sensibility (%) 75.0, specificity (%) 100, AUC (%) 87.5, Precision (%) 100, and F1-score (%) 87.5. The optimal ML predictors were hypokinetic dysarthria, intransitive/verb ratio, and silent pauses.

Conclusions: These findings highlight the importance of considering language disturbances in PD and approaching them in automated and data-driven ways.

References:

[1] Miller, Nick, 2017. Practical neurology.

C31

Vibro-tactile stimulation of the neck reduces pain in people with cervical dystonia

Matteo Costanzo[1,2], J. Xu[3], L. Avanzino[4,5], D. Martino[6], P. Salehi[7], S. Standal[7], N. Manzo[8], P. Alizadeh[6], S. Terranova[4], G. Bonassi[9], J. Oh[3], A. Conte[2,10], J. Konczak[3,11]

[1]Department of Neurosciences, Istituto Superiore di Sanità, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]School of Kinesiology, Human Sensorimotor Control Laboratory, University of Minnesota, Minneapolis, USA
[4]Department of Experimental Medicine at the University of Genoa, Genoa, Italy
[5]IRCCS Policlinico San Martino, Genoa, Italy
[6]Department of Clinical Neurosciences, University of Calgary, Calgary, Canada
[7]Department of Physical Medicine & Rehabilitation, University of Minnesota, Minneapolis, USA
[8]IRCCS San Camillo Hospital, Venice, Italy
[9]Department of Neuroscience, University of Genoa, Genoa, Italy
[10]IRCCS Neuromed, Pozzilli (IS), Italy
[11]Center for Clinical Movement Science, University of Minnesota, Minneapolis, USA

Background: Pain is a common non-motor symptom in patients affected by cervical dystonia (CD) which impacts severely their quality of life [1,2]. Its pathophysiology is incompletely understood yet involves motor and somatosensory components, such as altered processing of proprioceptive and pain signals [3,4]. Finding effective pain therapies, as alternatives or complementary treatments to botulinum toxin injections, is crucial for managing this complex disorder.

Objectives: To determine if vibro-tactile stimulation (VTS) as a non-invasive form of neuromodulation targeting the somatosensory system can modulate pain processing in people with CD.

Methods: In a multi-center study, 44 CD patients received VTS to sternocleidomastoid and/or trapezius muscles for up to 45 minutes under 9 stimulation conditions. The primary outcome measure was a perceived pain score (PPS) rated by participants on a 100-point analogue scale.

Results: During VTS, 29/44 (66%) of these patients experienced a reduction in PPS of at least 10% with 17/44 (39%) reporting a reduction in pain of 50% or higher. After cessation of VTS, 57% of participants reported a 10% or higher reduction in PPS. Effects were significant at the group level and persisted for up to 20 minutes post-treatment. For each CD phenotype, no distinct optimal stimulation profiles were identified. Clinical markers of disease severity or duration did not predict the degree of VTS-induced pain reduction.

Conclusions: This study demonstrates the potential of VTS as a new treatment option for neck pain associated with CD. Further research should delineate optimal dosage and long-term effects.

References:

[1] Kutvonen O, Dastidar P, Nurmikko T. Pain in spasmodic torticollis. Pain 1997;69(3):279-286. doi:10.1016/S0304-3959(96)03296-4.
[2] van den Dool J, Tijssen MAJ, Koelman JHTM, Engelbert RHH, Visser B. Determinants of disability in cervical dystonia. Parkinsonism & Related Disorders 2016;32:48-53. doi:10.1016/j.parkreldis.2016.08.014.
[3] Tinazzi M, Squintani GM, Bhatia KP, et al. Pain in cervical dystonia: Evidence of abnormal inhibitory control. Parkinsonism & Related Disorders 2019;65:252-255. doi:10.1016/j.parkreldis.2019.06.009.

[4] Tinazzi M, Erro R, Mascia MM, et al. Demographic and clinical determinants of neck pain in idiopathic cervical dystonia. J Neural Transm 2020;127(10):1435-1439. doi:10.1007/s00702-020-02245-4.

C32

Motor and nonmotor correlates of iron deposition within subcortical nuclei in early drug-naïve Parkinson's disease patients

Emilia Norma Mosca[1], R. De Micco[1], N. Piramide[1], F. Di Nardo[1], M.A. Pirozzi[1], M. Siciliano[1,2], G. Tedeschi[1], F. Esposito[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]Neuropsychology Laboratory, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Introduction: Iron deposition using Quantitative Susceptibility Mapping (QSM) has been reported within cortical and subcortical areas in patients with Parkinson's disease (PD) [1].

Objectives: To explore the association between 3TMRI-derived iron deposition content within 12 bilateral subcortical nuclei and several motor, nonmotor and neuropsychological features in a cohort of 58 early drug-naïve PD patients.

Methods: Disease severity was assessed by UPDRS-III and modified Hoehn&Yahr, nonmotor symptoms by the Nonmotor symptoms scale (NMSS), autonomic dysfunction by the Scale for Outcomes in Parkinson's disease for Autonomic symptoms (SCOPA-AUT), behavioral symptoms by Beck Depression Inventory (BDI-II), Parkinson Anxiety Scale (PAS) and Apathy Evaluation scale (AES). An extensive neuropsychological assessment was also acquired and a z-score for each cognitive domain was calculated. QSM values were extracted from 12 bilateral subcortical nuclei by applying the HybraPD atlas2. A partial correlation analysis was run between MRI and clinical data.

Results: UPDRS-III scores positively correlated with higher iron deposition within bilateral dentate nuclei. AES scores positively correlated with higher iron deposition within the left externus globus pallidus and right red nucleus. Z-score executive positively correlated with higher iron deposition within left subthalamic nucleus and externus globus pallidus. Z-score attention positively correlated with higher iron deposition within bilateral putamina and right externus globus pallidus. PAS scores positively correlated with higher iron deposition within the left substantia nigra pars reticulata. BDI-II scores positively correlated with higher iron deposition within the right substantia nigra pars compacta. SCOPA-AUT scores positively correlated with higher iron deposition within the right red nucleus and different thalamic subregions.

Conclusions: The presence of specific clinical features is associated with increased iron deposition within different subcortical nuclei in PD patients, even in the early stages. These findings may be associated with a more severe clinical picture at baseline and may potentially lead to more rapid worsening over time.

References:

[1] Langkammer C, Pirpamer L, Seiler S, Deistung A, Schweser F, Franthal S, Homayoon N, Katschnig-Winter P, Koegl-Wallner M, Pendl T, Stoegerer EM, Wenzel K, Fazekas F, Ropele S, Reichenbach JR, Schmidt R, Schwingenschuh P. Quantitative Susceptibility Mapping in Parkinson's Disease. PLoS One. 2016 Sep 6;11(9):e0162460. doi: 10.1371/journal.pone.0162460. PMID: 27598250; PMCID: PMC5012676.
[2] Yu B, Li L, Guan X, Xu X, Liu X, Yang Q, Wei H, Zuo C, Zhang Y. HybraPD atlas: Towards precise subcortical nuclei segmentation using multimodality medical images in patients with Parkinson disease. Hum Brain Mapp. 2021 Sep;42(13):4399-4421. doi: 10.1002/hbm.25556. Epub 2021 Jun 8. PMID: 34101297; PMCID: PMC8357000.

C33

The role of metabotropic glutamate receptors type 3 and 5 in Parkinson's disease: analysis of GRM3 and GRM5 genbe variants

Marika Alborghetti[1], E. Bianchini[1], D. Rinaldi[1], L. Di Menna[2], N. Palomba[2], L. de Carolis[1], S. Galli[1], F.E. Pontieri[1], G. Battaglia[2], V. Bruno[2], T. Esposito[3], M. Borro[1], M. Simmaco[1], F. Nicoletti[2]

[1]Sapienza, University of Rome, Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Rome, Italy
[2]IRCSS Neuromed, Pozzilli, IS, Isernia, Italy
[3]Institute of Genetics and Biophysics CNR, Biomedicine, Napoli, Italy

Type-3 metabotropic glutamate (mGlu3) receptors exert pleiotropic functions in the CNS depending on their anatomical localization [1]. Presynaptic mGlu3 receptors inhibit glutamate release, whereas postsynaptic mGlu3 receptors boost mGlu5 receptors signaling [1,2]. In addition, activation of mGlu3 receptors in astrocytes stimulates the production of GDNF and TGF-β and drives microglia towards an anti-inflammatory phenotype [3,4].
The aim of the study was to examine the association between polymorphic variants of GRM3 and GRM5 and Parkinson's disease (PD) and motor and non-motor symptoms. The study sample included 960 PD patients and 706 age/gendermatched healthy controls. The DNA was extracted from the blood samples and the WES analysis allowed a massive and simultaneous genotyping of all the samples under examination.
The GRM3 gene haplotype was significantly associated with PD [OR 95% CI 3.34 (1.57-7.10); p-value 0.0018]. The mutated variants are rs1527768 (G,A), rs187993 (G,T), rs274622 (T,C), rs724226 (G,A), while rs13242038, rs1468412, rs2228595, rs2237562 and rs906415 are wild-type. The rs60954128 polymorphism of the GRM5 gene is associated with the development of PD [OR 95% CI 1.95 (1.16-3.29); p-value 0.0084]. Ad interim analysis suggests an association between the GRM3 and GRM5 variants and PD phenotype.
These findings suggest that mGlu3 and mGlu5 receptors might shape the balance between neurodegeneration and neuroprotection in PD and might be targeted by therapeutic intervention.

References:

[1] Bruno V, Caraci F, Copani A, Matrisciano F, Nicoletti F, Battaglia G. The impact of metabotropic glutamate receptors into active neurodegenerative processes: A "dark side" in the development of new symptomatic treatments for neurologic and psychiatric disorders. Neuropharmacology. 2017 Mar 15;115:180-192.
[2] Di Menna L, Joffe ME, Iacovelli L, Orlando R, Lindsley CW, Mairesse J, Gressèns P, Cannella M, Caraci F, Copani A, Bruno V, Battaglia G, Conn PJ, Nicoletti F. Functional partnership between mGlu3 and mGlu5 metabotropic glutamate receptors in the central nervous system. Neuropharmacology. 2018 Jan;128:301-313.
[3] Battaglia G, Riozzi B, Bucci D, Di Menna L, Molinaro G, Pallottino S, Nicoletti F, Bruno V. Activation of mGlu3 metabotropic glutamate receptors enhances GDNF and GLT-1 formation in the spinal cord and rescues motor neurons in the SOD-1 mouse model of amyotrophic lateral sclerosis. Neurobiol Dis. 2015 Feb;74:126-36.
[4] Zinni M, Mairesse J, Pansiot J, Fazio F, Iacovelli L, Antenucci N, Orlando R, Nicoletti F, Vaiman D, Baud O. mGlu3 receptor regulates microglial cell reactivity in neonatal rats. J Neuroinflammation. 2021 Jan 6;18(1):13.

C34

Functional motor disorders in pediatrics: motor patterns and clinical correlates

Valentina Baglioni[1], C. Geroin[2], D. Esposito[1], F. Teatini[3], A. Tessitore[4], G. Calandra Buonaura[5,6], M. Zibetti[7], R. Erro[8], F. Morgante[9,10], A. Albanese[11], F. Bono[11], M. Zappia[13], G. Defazio[14], E. Marcuzzo[2], M. Tinazzi[2]

[1]Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy
[2]Department of Neuroscience, Biomedicine, and Movement, University of Verona, Verona, Italy
[3]Functional Movement Disorders Outpt. Clinic, Clinical Neurology and Stroke Unit Department, Central Country Hospital, Bolzano, Italy
[4]Department of Advanced Medical and Surgery Sciences, University of Campania Luigi Vanvitelli, Naples, Italy
[5]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[6]IRCCS, Institute of Neurological Sciences of Bologna, Bologna, Italy
[7]Department of Neuroscience Rita Levi Montalcini, University of Turin, Turin, Italy
[8]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry Scuola Medica Salernitana, University of Salerno, Baronissi, SA, Italy
[9]Neurosciences Research Centre, Molecular and Clinical Sciences Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[10]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy
[11]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano Milan, Italy
[12]Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[13]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy

Introduction: Functional Motor Disorders (FMDs) represent an increasing challenge also in pediatric age [1,2].

Objectives: Our aim was to describe FMDs clinical manifestations in pediatrics, including non-motor symptoms and other functional neurological disorders (FND) and to report the frequency of isolated and combined FMDs and their relationship with demographic and clinical variables.

Methods: For this cross-sectional study, data were extracted from the Italian Registry of Functional Motor Disorders and from the pediatric database of the Unit of Neuropsychiatry of Sapienza University of Rome, collecting 74 FMD pediatric (7-18 years) inpatients and outpatients, assessed by a complete neurological and psychiatric evaluation.

Results: Out of 74 FMDs (68.9% females; mean age 13.8±2.31years) the most common phenotypes were weakness (55.4%, n=41) and gait disorders (55.4%, n=41) Among the hyperkinetic FMDs, functional tremor (33.8%; n=25) represented the highest expressed manifestations, then dystonia (14.9%, n=11); myoclonus/jerks (16.2%, n=12) and Tic (10.8%, n=8). An isolated pattern was reported in the 67.6% (n=50), related with a lower onset age (p 0.03) and spontaneous symptoms remissions (p.0.012). Combined pattern was significatively associated with weakness (p.< 0.001), functional tremor (p. 0.002), perceptual disorders (p.0.004), pain (p.0.011) and functional seizures (p. 005). The 73% of FMDs had associated other FND. Moreover, pain was in the 74.4% (n=55) of which headache represented the 17.6% (n=13). Almost half of FMDs presented comorbid medical conditions, mostly represented by psychiatric diagnosis (32.4%, n=24). A history of childhood trauma (23%, n=17)) and family neurological disease (13.5%, n=10)) was highlighted.

Conclusions: These data expanded the knowledge of FMDs clinical correlates in the pediatric age [3], mainly represented by an isolated pattern of functional gait disorders and weakness. Moreover, a need for a neuropsychiatric assessment was highlighted in pediatric FMDs patients, given the high frequency of non-motor symptoms and other FND, especially in patients with combined FMDs.

References:

[1] Schwingenschuh P, Pont-Sunyer C, Surtees R, Edwards MJ, Bhatia KP. Psychogenic movement disorders in children: a report of 15 cases and a review of the literature. Mov Disord. 2008;23(13):1882-1888. doi:10.1002/mds.222802).
[2] Raucci U, Parisi P, Vanacore N, et al. Acute hyperkinetic movement disorders in Italian paediatric emergency departments. Arch Dis Child. 2018;103(8):790-794. doi:10.1136/archdischild-2017-314464.
[3] Canavese C, Ciano C, Zibordi F, Zorzi G, Cavallera V, Nardocci N. Phenomenology of psychogenic movement disorders in children. Mov Disord . 2012;27(9):1153-1157. doi:10.1002/mds.24947.

C35

Evaluation of non-motor fluctuations in Parkinson's disease during pharmacological ON phase. Is always the "ON" condition beneficial?

Giulia Donzuso, G. Mostile, A. Luca, C.E. Cicero, A. Nicoletti, M. Zappia

Department of Medical, Surgical Sciences and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy

Objectives: Non-motor symptoms (NMS) and fluctuations (NMF) are very common in Parkinson's disease (PD) occurring in ON and OFF state and affecting patients' quality of life [1]. Aim of the study was to evaluate NMS occurring during ON pharmacological state.

Methods: Patients with diagnosis of PD according to MDS criteria were consecutively enrolled at the Movement Disorders Center of the University of Catania. For this purpose, a new questionnaire was developed considering 17 items including the main symptoms experienced by PD patients in the ON state. PD patients were evaluated in ON state, 90' after the first morning dose of dopaminergic therapy and were asked if the symptoms were present during the ON state. PD patients who experienced at least one symptom in ON were defined ON Non-Motor Fluctuators (ONMF). Additionally, clinical features, MDS-UPDRS, Hoehn and Yahr stage and levodopa-equivalent dose were collected.

Results: One-hundred and thirty-seven PD patients with a mild to moderate disease stage were enrolled (79 man and 58 woman, age 69.4 ± 9.5 years (mean ± SD), disease duration 8.0 ± 4.6 years). Seventy-seven patients were ONMF (56.6%). ONMF were associated with female gender (OR 2.81, 95%CI 1.37-5.77, p-value 0.005) and with motor fluctuations (OR 2.41, 95%CI 1.20-4.83, p-value 0.013). PD patients with short disease duration (<7 years) showed the presence of "negative" NMS such as "sonnolenza/sleepiness", "sensazione di testa vuota/light-headedness", nausea/vomito/nausea/vomiting". PD patients with longer disease duration experienced more "positive" NSM including "sentirsi pieno di energie/feel lot of energy" and "sensazione di benessere fisico/feel physical well-being".

Conclusions: In this study we demonstrated the presence of a different pattern of NMS occurring during ON response in PD patients. PD patients with short disease duration (<7 years) showed the presence of "negative" NMS whereas PD patients with longer disease duration experienced more "positive" NSM. This could help the physician in the therapy management of PD patients.

References:

[1] Martínez-Fernández R, Schmitt E, Martinez-Martin P, Krack P. The hidden sister of motor fluctuations in Parkinson's disease: a review on nonmotor fluctuations. Mov Disord 2016;31(8):1080–1094.

C36

Virtual Reality (VR) and Parkinson's disease: an innovative approach

Daniele Sartini, E. Pramaggiore, G. Nada, F. Garini, M. Sacchetti, L. Binaschi

S.S.V.D.O Psicologia Clinica, A.O.U. Maggiore della Carità di Novara, Italy

Introduction: Parkinson's disease is a neurodegenerative disorder characterized by motor and cognitive dysfunctions. The search for new therapeutic strategies aimed at improving the quality of life for patients is crucial. In this context, virtual reality (VR) emerges as a powerful tool for cognitive stimulation, providing an interactive and engaging environment [1].

Objectives: The study aims to assess the effectiveness of cognitive stimulation through virtual reality in improving cognitive functions [2] in patients with Parkinson's disease experiencing mild cognitive impairment (MCI). The primary objective is to investigate the impact of VR on memory, attention, visuospatial abilities, and executive functions.

Methods: A sample of Parkinson's patients underwent a cognitive stimulation program use VR applications [3]. The sessions were customized according to each patient's cognitive needs, utilizing the
Oculus Quest 2 hardware from Meta and Idego's Cerebrum applications. Standardized neuropsychological tests were employed to assess cognitive performance before and after the intervention period (T0 and T1 at 6 months).

Results: The collected data suggest a significant improvement in the cognitive abilities of patients who participated in the cognitive stimulation program with VR. Considerable improvements were observed in memory, attention, and visuospatial abilities. Interestingly, the VR group exhibited better performance compared to the group undergoing traditional stimulation using pen and paper.

Conclusions: Cognitive stimulation through virtual reality presents itself as an innovative and promising therapeutic procedure for individuals with Parkinson's disease [4]. The encouraging results of our study propose that regular use of virtual reality could contribute to slowing down the cognitive deterioration associated with the disease, with superior outcomes compared to traditional stimulation methods. Further research is needed to confirm and expand upon these findings.

References:

[1] Hwang J, Lee S. The effect of virtual reality program on the cognitive function and balance of the people with mild cognitive impairment. J Phys Ther Sci. 2017 Aug;29(8):1283-1286. doi: 10.1589/jpts.29.1283. Epub 2017 Aug 10. PMID: 28878448; PMCID: PMC5574359.
[2] Oliveira J, Gamito P, Souto T, Conde R, Ferreira M, Corotnean T, Fernandes A, Silva H, Neto T. Virtual Reality-Based Cognitive Stimulation on People with Mild to Moderate Dementia due to Alzheimer's Disease: A Pilot Randomized Controlled Trial. Int J Environ Res Public Health. 2021 May 16;18(10):5290. doi: 10.3390/ijerph18105290. PMID: 34065698; PMCID: PMC8156930.
[3] Maggio MG, De Cola MC, Latella D, et al. What About the Role of Virtual Reality in Parkinson Disease's Cognitive Rehabilitation? Preliminary Findings From a Randomized Clinical Trial. Journal of Geriatric Psychiatry and Neurology. 2018;31(6):312-318. doi:10.1177/0891988718807973
[4] Kwon, SH., Park, J.K. & Koh, Y.H. A systematic review and metaanalysis on the effect of virtual reality-based rehabilitation for people with Parkinson's disease. J NeuroEngineering Rehabil 20, 94 (2023). https://doi.org/10.1186/s12984-023-01219-3.

C37

Post-thrombectomy movement disorders in basal ganglia stroke

Leonardo Rigon[1] and Danilo Genovese[2,3], C. Piano[2], V. Brunetti[2], V. Guglielmi[2], A.T. Cimmino[1], I. Scala[1], S. Citro[1], A.R. Bentivoglio[1,2], G. Masone[2], P. Calabresi[1,2], G. Della Marca[1,2]

[1]Dipartimento di Neuroscienze, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Dipartimento di neuroscienze, Organi di Senso e Torace, Fondazione Policlinico Universitario A. Gemelli IRCCS - UOC Neurologia, Rome, Italy
[3]The Marlene and Paolo Fresco Institute for Parkinson's Disease and Movement Disorders, New York University Langone Health, New York, NY, USA

Background and purpose: Post-stroke movement disorders (PMDs) following ischemic lesions of the basal ganglia (BG) are a known entity, but data regarding incidence are missing [1-4]. Ischemic strokes secondary to proximal middle cerebral artery (MCA) occlusion treated with thrombectomy represent a model of selective damage of the BG [5-8]. Aim of this study was to assess prevalence and features of movement disorders after selective BG ischemia in patients with successfully reperfused acute ischemic stroke.

*Methods***:** We enrolled 64 consecutive subjects with acute ischemic stroke of the basal ganglia due to proximal MCA occlusion treated with thrombectomy. Patients were clinically evaluated by a movement disorders specialist for PMDs onset at baseline, after 6 and 12 months.

Results: None of the subjects showed an identifiable movement disorder in the subacute phase of the stroke. At 6- and 12-months respectively 28% and 53.8% of patients developed PMDs. The clinical spectrum of PMDs encompassed parkinsonism, dystonia and chorea, either isolated or combined. In most patients, symptoms were contralateral to the lesion, although a subset of patients presented with bilateral involvement and prominent axial signs.

Conclusion: PMDs are not uncommon in a long-term follow-up of successfully reperfused acute ischemic strokes. A prosecution of follow-up in a multidisciplinary team is strongly advisable in patients with selective lesions of the BG after AIS, even if asymptomatic at discharge.

References:

[1] Suri, R. et al. Post-stroke Movement Disorders: The Clinical, Neuroanatomic, and Demographic Portrait of 284 Published Cases. Journal of Stroke and Cerebrovascular Diseases **27**, (2018).
[2] Mehanna, R. & Jankovic, J. Movement disorders in cerebrovascular disease. Lancet Neurol **12**, 597–608 (2013).
[3] Tater, P. & Pandey, S. Post-stroke Movement Disorders: Clinical Spectrum, Pathogenesis, and Management. Neurology India vol. 69 Preprint at https://doi.org/10.4103/0028-3886.314574 (2021).
[4] Alarcón, F., Zijlmans, J. C. M., Dueñas, G. & Cevallos, N. Post-stroke movement disorders: Report of 56 patients. Journal of Neurology, Neurosurgery and Psychiatry vol. 75 Preprint at https://doi.org/10.1136/jnnp.2003.011874 (2004).
[5] Tambasco, N., Romoli, M. & Calabresi, P. Selective basal ganglia vulnerability to energy deprivation: Experimental and clinical evidences. Prog Neurobiol **169**, 55–75 (2018).
[6] Kaesmacher, J. et al. Isolated striatocapsular infarcts after endovascular treatment of acute proximal middle cerebral artery occlusions: Prevalence, enabling factors, and clinical outcome. Front Neurol **8**, (2017).
[7] Kleine, J. F., Beller, E., Zimmer, C. & Kaesmacher, J. Lenticulostriate infarctions after successful mechanical thrombectomy in middle cerebral artery occlusion. J Neurointerv Surg **9**, (2017).
[8] Kaesmacher, J. et al. Early Thrombectomy Protects the Internal Capsule in Patients with Proximal Middle Cerebral Artery Occlusion. Stroke (2021) doi:10.1161/STROKEAHA.120.031977.

C38

Are dietary components potential risk/protective factors of Parkinson's disease?

Barbara Vitucci[1], R. Pellicciari[1], S. Altomare[2], M. Costanzo[3], C. Cutrona[3], A. Fabbrini[4], S. Pietracupa[3], T. Giloni[3], N. Modugno[3], F. Magrinelli[5], C. Dallocchio[6], T. Ercoli[7], A. Nicoletti[8], M. Zappia[8], P. Solla[7], G. Iliceto[1], G. Fabbrini[3,4], M. Tinazzi[5], A. Conte[3,4], A. Berardelli[3,4], G. Defazio[1], D. Belvisi[3,4]

[1]Department of Basic Medical Sciences, Neuroscience and Sense Organs "Aldo Moro", University of Bari, Bari, Italy
[2]Neurology Unit, Ospedale Dimiccoli, ASL BT, Barletta, Italy
[3]Department of Neurology, IRCCS Neuromed, Pozzilli, Italy
[4] Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[5]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[6]Neurology Unit, ASST Pavia, Ospedale Civile, Voghera, Italy
[7]Department of Medical Sciences and Public Health, University of Cagliari, Monserrato, Cagliari, Italy
[8]Department G.F. Ingrassia, Neuroscience Section University of Catania, Catania, Italy

***Introduction*:** Parkinson's disease (PD) is a multifactorial disease [1]. Previous studies identified several modifiable risk and protective factors for developing PD [2]. Among possible modifiable factors, dietary components may play a relevant role but the relationship between PD risk and diet factors/patterns is still poorly understood.

***Objective*:** To investigate the potential influence of dietary components and patterns on PD development in a large sample of patients.

***Methods*:** 694 PD patients who attended six Italian Movement Disorders Centers and 612 healthy controls were enrolled. PD diagnosis was established by experienced neurologists using standard criteria. Healthy controls were frequency-matched to cases by 5-year age stratum, sex, and referral center. Dietary factors were explored using a validated 77-item food-frequency questionnaire [3]. The questionnaire was personally administered by a medical interviewer in each center.

***Results*:** The multivariate logistic regression models showed that eight dietary factors had an independent positive association with PD. These included pizza, prosciutto, artichoke, cruciferae, biscuits, chocolate snacks, sugar and soft drinks. Five factors were inversely associated with PD development and included whole wheat bread, raw carrots, citrus fruits, coffee and beer. The factor analysis identified two diet patterns. The first one ("Western pattern") included meat, sweets, pasta, pizza and potatoes and was positively associated with PD risk. The second one ("Prudent pattern") included vegetables and fruits and there was a trend for an inverse association with PD risk.

***Conclusions*:** Our data demonstrated a relationship between PD risk and dietary components and patterns. This relationship may depend on the ability of different foods to influence the "gut-brain axis" that is thought to play a pivotal role in PD pathogenesis. Future strategies aimed at preventing PD development should take into account diet components among the modifiable risk/protective factors of PD.

References:

[1] de Lau L, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurology (2006);5(6):525-35.

[2] Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurology (2016);15(12):1257-72.
[3] Franceschi S, Negri E, Salvini S, Decarli A, Ferraroni M, Filiberti R, Giacosa A, Talamini R, Nanni O, Panarello G, La Vecchia C. Reproducibility of an Italian Food Frequency Questionnaire for Cancer Studies: Results for Specific Food Items. European Journal of Cancer (1993);29A(16):2298-2305.

C39

Prognostic role of ambulatory blood pressure monitoring in predicting disability and mortality in Parkinson's Disease: a long-term retrospective study

Marta Maria Tangari[1], A. Covolo[1], G. Imbalzano[1], C. Ledda[1], E. Montanaro[1,2], C. Campisi[1], M. Laudadio[1], C.A. Artusi[1,2], M. Bozzali[1,2], M.G. Rizzone[1,2], M. Zibetti[1,2], M. Valente[3], S. Maule[3], F. Vallelonga[3], L. Lopiano[1,2], A. Romagnolo[1,2]

[1] Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy
[3]Autonomic Unit and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy

Introduction: Neurogenic orthostatic hypotension (nOH) is a non-motor feature of Parkinson's disease (PD), associated with severe complications and shorter survival [1,2]. Recently, the presence of at least 2 hypotensive episodes (SBP drop ≥ 15 mmHg compared to the average 24-h SBP) at 24-h ambulatory BP monitoring (ABPM) has showed high accuracy in detecting nOH [3].

Objectives: To evaluate the prognostic role of ABPM-hypotensive episodes in predicting disability milestones and mortality, and to compare it to the prognostic role of bedside nOH.

Methods: PD patients who underwent ABPM from Jan 2012 to Dec 2014 were retrospectively enrolled and evaluated for main clinical features at baseline, and for the development of disability milestones (falls, fractures, dementia, bed/wheelchair confinement, hospitalization) and mortality during an up-to-10-year follow-up. Kaplan-Meyer analysis and Cox regression analysis (corrected for age, PD duration, Charlson Comorbidity Index, and H&Y stage at baseline) evaluated the association between ABPM-hypotensive episodes or bedside nOH and disability milestones/mortality.

Results: We included 99 PD patients; the mean follow-up was 5.9±2.7 years (range 1-10). At baseline, 38.4% of patients had ≥2 ABPM-hypotensive episodes. In patients with ABPM-hypotensive episodes, Kaplan-Meier analysis showed earlier onset of all complications and shorter survival (8.0 vs. 9.5 years; p=0.009); while bedside nOH was only associated with earlier development of dementia. Adjusted Cox-Regression analysis showed significant association between ABPM-hypotensive episodes and falls (OR:3.626; p<0.001), hospitalizations (OR:2.016; p=0.038), and dementia (OR:2.926; p=0.008), while bedside nOH was associated only with dementia (OR:2.100; p=0.025)

Conclusion: Although prospective confirmatory studies are needed, our observations support the usefulness of ABPM in clinical practice, as hypotensive episodes have a stronger prognostic value than simple bedside evaluation in predicting the development of falls, dementia and hospitalization.

References:

[1] Ricci F, Fedorowski A, Radico F, et al (2015) Cardiovascular morbidity and mortality related to orthostatic hypotension: A metaanalysis of prospective observational studies. Eur Heart J 36:1609– 1617. https://doi.org/10.1093/eurheartj/ehv093.
[2] Romagnolo A, Zibetti M, Merola A, et al (2019) Cardiovascular autonomic neuropathy and falls in Parkinson disease: a prospective cohort study. J Neurol 266:85–91. https://doi.org/10.1007/s00415-018- 9104-4.

[3] Vallelonga F, Romagnolo A, Merola A, et al (2019) Detection of orthostatic hypotension with ambulatory blood pressure monitoring in parkinson’s disease. Hypertens Res 42:1552–1560. https://doi.org/10.1038/s41440-019-0267-x.

C40

Analysing the role of patient's fatigue on caregiver burden in Parkinson's disease

Salvatore Landolfo[1], D. Urso[2], V. Gnoni[2], C. Santoro[1], F. Amati[1], A. Giugno[2], G. Logroscino[1,2]

[1]Department of Basic Medical Sciences, Neuroscience and Organ Sense, University "Aldo Moro", Bari, Italy
[2]Center for Neurodegenerative Diseases and the Aging Brain, Department of Clinical Research in Neurology, University of Bari Aldo Moro', "Pia Fondazione Cardinale G. Panico", Tricase, Lecce, Italy

Introduction: Fatigue is a prevalent and disabling non-motor symptom (NMS) in Parkinson's disease (PD) [1], impacting both patients' and caregivers' well-being [2].

Objective: The aim of this study was to explore the role of PD-related fatigue as a determinant of caregiver burden.

Methods: Participants included PD patients and their primary caregivers recruited from the outpatient clinic at the Centre for Neurodegenerative Diseases and the Aging Brain in Tricase. Level of fatigue experienced by PD patients was measured using the Fatigue Severity Scale (FSS-9) [3], while caregivers completed the Caregiver Burden Inventory (CBI) [4]. Univariate and multivariate linear regression models were employed to examine the potential predictive role of patient-related fatigue on caregiver burden. Factors such as age, sex, disease duration, motor and non-motor symptom burden, anxiety, depression, and cognitive performance were taken into consideration in the analysis.

Results: The study enrolled a total of 61 patients, the majority of whom were male (70.5 %) with a mean age of 67.84±10.33 years. In univariate linear regression model, disease duration ($p<0.001$), NMS burden ($p<0.001$), anxiety and depression scores ($p<0.001$), cognitive performance ($p=0.008$), and FSS score ($p<0.001$) emerged as notable predictors of CBI scores. These variables were subsequently included in a multivariate linear regression model, revealing that only FSS score ($p< 0.001$) and disease duration ($p=0.003$) retained their significance as predictors of caregiver burden.

Conclusion: Our investigation revealed that disease duration, NMS burden, anxiety and depression scores, cognitive performance and fatigue emerged as clinical contributors of caregiver burden [5]. However, only disease duration and fatigue were found to be independent predictors of caregiver burden. Noteworthy is fatigue's distinct impact, asserting itself as a pivotal determinant.

References:

[1] Kluger BM. Fatigue in Parkinson's Disease. In: International Review of Neurobiology. Vol 133. Elsevier; 2017:743-768. doi:10.1016/bs.irn.2017.05.007.
[2] Martinez-Martin P, Arroyo S, Rojo-Abuin JM, et al. Burden, perceived health status, and mood among caregivers of Parkinson's disease patients. Mov Disord. 2008;23(12):1673-1680. doi:10.1002/mds.22106.
[3] Krupp LB. The Fatigue Severity Scale: Application to Patients With Multiple Sclerosis and Systemic Lupus Erythematosus. Arch Neurol. 1989;46(10):1121. doi:10.1001/archneur.1989.00520460115022.
[4]Novak M, Guest C. Application of a Multidimensional Caregiver Burden Inventory. The Gerontologist. 1989;29(6):798-803. doi:10.1093/geront/29.6.798.
[5] Mosley PE, Moodie R, Dissanayaka N. Caregiver Burden in Parkinson Disease: A Critical Review of Recent Literature. J Geriatr Psychiatry Neurol. 2017;30(5):235-252. doi:10.1177/0891988717720302.


Società Italiana Parkinson e Disordini del Movimento
LIMPE-DISMOV ETS
10°
Congresso
MILANO
Allianz MiCo - Milano
Convention Centre
10•11•12
APRILE
2024
50
LIMPE
1974 - 2024

Poster

P1

The cut-off values of the Montreal Cognitive Assessment (MoCA) for discriminating patients with Progressive Supranuclear Palsy

Arianna Cappiello[1], S. Cuoco[1], M.L. Restaino[2], P. Barone[1], M. Picillo[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Salerno, Italy
[2]Department of Economics and Statistics, University of Salerno, Baronissi, Italy

Introduction: Progressive Supranuclear Palsy (PSP) is a rapidly progressive atypical parkinsonism clinically characterized by ocular and motor symptoms as well as cognitive impairment [1]. The Montreal Cognitive Assessment (MoCA) is a valid tool in detecting cognitive impairment in a variety of neurodegenerative diseases.

Objectives: We sought to determine the discriminatory power of the MoCA items and sub-domains for screening cognitive functions in PSP compared to an age-and education-matched cohort of healthy controls (HC).

Methods: Three hundred and two PSP patients diagnosed according to the Movement Disorder Society (MDS) Criteria and 152 healthy controls underwent MoCA. Data were collected from several centres throughout Italy within the PSP-NET supported by Fondazione LIMPE. To identify cut-off values for the MOCA (total and sub-domains), Classification and Regression Trees (CART) analysis was performed. The diagnostic accuracy of each score was assessed using the area under the Receiver Operating Characteristic curve (AUC), accuracy, precision, and recall estimates.

Results: As for MOCA items, the item measuring the ability to draw a clock is the first and most discriminating item (precision: 0.78; precision: 0.87; AUC: 0.78), followed by the fluency item (accuracy: 0.78; precision: 0.83; AUC: 0.75). As such, having a score less than 3 on the clock item together with a score less than 1 on the fluency task determine a 42% of chances to be allocated to the PSP group. As for MOCA sub-domains, we found that the visuospatial one is the first and the most discriminating compared to the others (accuracy: 0.76; precision: 0.80; AUC: 0.81). As such a score lower than 3 has 48% of chances of discriminating between PSP and HC.

Conclusions: Specific MoCA items and subdomains are sensitive in detecting PSP cognitive impairment. In particular, clock draw, fluency and orientation items and visuospatial abilities sub-domain have the highest discriminatory power compared to an age- and educationmatched cohort of HC.

References:

[1] Höglinger G.U., Respondek G., Stamelou M. et al (2017) Clinical diagnosis of progressive supranuclear palsy: the Movement Disorder Society criteria. Mov Disord. 32(6):853–86.: Doi: 10.1002/mds.26987. PMID: 28467028.

P2

Clinical applicability of telephone-based cognitive screening tests in Parkinson's disease: preliminary data in an Italian patient cohort

Angelica De Sandi[1], E.N. Aiello[2], F. Verardo[3], F. Mameli[1], F. Ruggiero[1], E. Zirone[1], D. Mellace[3], A. Marfoli[3], A. Tomaselli[1], S. Diotti[4], A. Giust[4], D. Alimonti[5], B. Poletti[2,3], F. Pisano[4], S. Barbieri[1], R. Ferrucci[1,3]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2]IRCCS Istituto Auxologico Italiano, Milan, Italy
[3]Università degli Studi di Milano, Milan, Italy
[4]Policlinico San Marco, Gruppo San Donato, Zingonia, Bergamo, Italy
[5]Ospedale Papa Giovanni XXIII, Bergamo, Italy

Introduction: Telephone-based cognitive screening (TBCS) procedures have the potential to improve clinical practice and research on brain disorders by bridging geographical, logistical, socio-demographic and economic barriers [1]. Their use appears to be particularly relevant for patients with motor disabilities – such as Parkinson's disease (PD) [1].

Objectives: To provide preliminary evidence for the clinical applicability of Italian TBCS tests in PD patients.

Methods: N = 21 PD patients (12 men; age: 66.2±8.7 years; education: 13.1±4.3; disease duration: 126.3±71.4 months) who had the Montreal Cognitive Assessment (MoCA) in the last 6 months were included. Patients were tested with a TBCS battery that included the Telephone Cognitive Status Interview (TICS) [2], the telephone-based frontal assessment battery (t-FAB) [3], and the telephone verbal fluency battery (t-VFB) – including phonemic, semantic and alternate fluency tests (t-PVF/-SVF/-AVF) [4]. Eleven patients had previously undergone deep brain stimulation (DBS) (average time since surgery: 15.9±7.4 months). The convergent validity and diagnostic accuracy of the TBCS measurements were tested using the MoCA.

Results: DBS and non-DBS patients were comparable on demographic and cognitive measures ($p \geq 0.067$). The results showed that the MoCA converged with TICS ($rs=.72$; $p < 0.001$), t-FAB ($rs=0.59$; $p = 0.009$), t-PVF ($rs=0.56$; $p = 0.015$), t-AVF ($rs=0.64$; $p = 0.004$) and t-CSI ($rs=0.51$; $p = 0.032$) scores, but not with the t-SVF ($p = 0.280$). When detecting patients with deficient [5] or borderline [5] MoCA scores (19%), all TBCS measurements showed optimal performance (AUC=0.77-0.97), except for t-PVF (AUC=0.65) and the -SVF (AUC=0.63).

Conclusions: This study provides promising, although preliminary, evidence for the clinimetric reliability of Italian TBCS tests for screening cognitive dysfunction in PD patients and therefore warrants further research on this topic.

References:

[1] Zanin et al., 2022. Neurol Sci; 43: 125-138.
[2] Aiello et al. Neurol Sci; 43: 3071-3077.
[3] Aiello et al., 2022. Aging Clin Exp Res; 34: 1635-1644.
[4] Aiello et al., 2022. Front Psychol; 13: 963164.
[5] D'Iorio et al., 2023. Aging Clin Exp Res; 35; 2157-2163.

P3

Cognitive correlates of dysphagia in Parkinson's disease

Serena Tagliente[1], P. Battista[1], S. Aresta[1,3], F. Merlo[2], D. Mongelli[1], G. Lagravinese[1], R. Falcone[1], C. Palmirotta[1], G. Turi[1], M. Castellari[4], A. Zonno[3], C. Gelao[3], P. Fiore[4,5], I. Battel[6], B. Minafra[3]

[1]Istituti Clinici Scientifici Maugeri IRCCS, Laboratory of Neuropsychology, Bari Institute, Bari, Italy
[2]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[3]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Bari Institute, Bari, Italy
[4]Department of Physical and Rehabilitation Medicine, University of Foggia, Foggia, Italy
[5]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Milan Institute, Italy
[6]Department of Biomedical, Surgical and Dental Sciences, University "La Statale," Milan, Milan, Italy

Introduction: Dysphagia refers to swallowing disorders that are frequent and fatal symptoms in people with Parkinson's Disease (PD) [1]. Cognitive changes can manifest at all stages of PD and can play a crucial role in swallowing. Specifically, attention and executive dysfunction can be involved in involuntary and voluntary swallowing actions. However, there is a gap in knowledge on the contribution of cognitive impairment to swallowing dysfunction.

Objective: We investigated the relationship between attentive/executive functions and dysphagia in people with PD.

Methods: We recruited n=21 patients with PD (age 69.38± 6.58 years, H&Y 3.79±1.07; MDS-UPDRS-III 43.95±24.18) at the Maugeri Institute IRCCS of Bari. We administered a neuropsychological assessment to all patients together with a fiberoptic endoscopic evaluation of swallowing. Moreover, the Penetration Aspiration Scale (PAS); the Yale Pharyngeal Residue Severity Rating Scale (YPRSR), and the Functional Oral Intake Scale (FOIS) were used to evaluate swallowing function. Spearman's correlation and linear regression analysis were performed.

Results: The most significant correlations were found between Stroop Time, Raven's Progressive Matrices, Digit Backward, Semantic Fluency, and FOIS, PAS, and YPRSR. Linear regression showed an association between FOIS and Semantic Fluency (beta= 0.10 CI 95% 0.05 to 0.14) and Stroop Time (beta= -0.02, CI 95% -0.03 to -0.002). The Digit Backward (beta= -2.14, CI 95% -3.43 to -0.86) was significantly associated with the PAS. Raven was significantly associated with the YPRSRS (beta= -0.12, CI 95% -0.22 to -0.01). These associations were not influenced by disease duration.

Conclusions: Attention and executive functions are associated with the ability to coordinate, plan, and organize movements required for chewing, lingual motion, laryngeal elevation, and pharyngeal contraction.

References:

[1] Kalf et al., 2012. Parkinsonism Relat Disord 18:311–315.

P4

Effects of a tailored tablet-based rehabilitation on cognition in Parkinson's disease: a pilot study

Serena Tagliente[1], B. Minafra[2], C. Palmirotta[1], G. Lagravinese[1], S. Aresta[2], G. Turi[1], D. Mongelli[1], R. Falcone[1], C. Gelao[2], A. Buccoliero[4], S. Pazzi[5], D. Scrutinio[2], P. Baiardi[3], P. Battista[1]

[1]Istituti Clinici Scientifici Maugeri IRCCS, Laboratory of Neuropsychology, Bari Institute, Bari, Italy
[2]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Bari Institute, Bari, Italy
[3]Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy
[4]Vision & Innovation Manager - R&D dept GPI spa (Università degli Studi di Verona), Bari, Italy
[5]Consorzio di Bioingegneria e Informatica Medica CBIM, Pavia, Italy

Introduction: Cognitive functions can be affected in Parkinson's Disease (PD) early in the disease, specifically attention and executive functions. Traditionally, paper and pencil paper exercises have been used to address cognitive impairment. Recently, digital technologies have opened new opportunities to ameliorate cognitive dysfunctions [1], allowing new computerized training tools to be developed and paper and pencil tools to be translated into new computerized devices.

Objective: To evaluate the effectiveness of a new computerized home-based cognitive training delivered on Neurotablet in patients with PD.

Methods: We enrolled n=13 patients with PD (age 66±8 years; education 13±4.98 years) in a pre-post design pilot study, recruited at the Maugeri Institute IRCCS of Bari. Beyond PD diagnosis, the Montreal Cognitive Assessment (MoCA) score ≥15 was imposed as inclusionary criteria. Based on the neuropsychological profile that each patient presented, we developed a tailored intervention targeting attention, memory, executive functions, perception, and language, providing all patients with a tablet containing an innovative app (Neurotablet). Patients performed a 5-week training using Neurotablet at home, for 5 days of the week, each of 45 minutes. At baseline and post-training, we administered a full neuropsychological assessment as the outcome measure. Normalization with min-max scaling and the Shapiro-Wilk test were performed to verify the normality of distribution. Comparison pre-post measures were calculated by paired samples t-test.

Results: We found significant differences pre-post test in the following cognitive measures: Word Learning ($t=-2.69$; $p<.05$), Semantic Fluency ($t=-3.575$; $p<.05$), Figure Recall ($t=-3.525$; $p<.05$).

Conclusions: This study documents the positive effects of table-based cognitive training at home using Neurotablet for a group of patients with PD, demonstrating the usefulness of restitutive and compensatory interventions in facing neurodegeneration.
Bibliography

References:

[1] Gavelin et al., 2022. Ageing Research Reviews, 80, 10167.

P5

Psychological and psychoeducational support interventions for caregivers

Francesca Garini, E. Pramaggiore, D. Sartini, G. Nada, M. Sacchetti

SSVDO Psicologia Clinica, Ospedale Maggiore della Carità di Novara, Novara, Italy

Introduction: Cognitive decline in patients with Mild Cognitive Impairment (MCI) not only affects the patient's daily life but also significantly impacts the family members who care for them [1]. Caregivers of individuals with MCI often experience symptoms of anxiety, depression, and face caregiver burden. This study aims to assess the effects of psychological and psychoeducational support interventions aimed at alleviating these symptoms and improving the well-being of caregivers.

Objectives: Aim of the present work is to present the results of a psychological and psycho-educational intervention program on a population of Mild Cognitive Impairment (MCI) caregivers. In particular, our aim was to evaluate changes in stress levels, anxiety, depression, and the perception of caregiver burden before and after the support intervention.

Methods: For this purpose, we selected 20 caregivers of MCI patients from the AOU Maggiore della Carità di Novara. Caregivers were assessed using the Caregiver Burden Inventory (CBI), Zarit Burden Interview (ZBI) questionnaire, and Zung's self-rating anxiety and depression scales, both at the beginning and upon completion of the cognitive stimulation program for their relatives with MCI. Psychological and psychoeducational support interventions were conducted taking inspiration from Strategies for Relatives (START) [3] and The Savvy Caregiver programs [2].

Results: Following participation in the support interventions, all caregivers showed clinically significant improvements in the questionnaire scores, indicating a significant reduction in perceived caregiver burden and levels of anxiety and depression. Particularly, notable improvements were observed in the emotional aspects assessed by the self-rating scales.

Conclusions: Psychological and psychoeducational support interventions have demonstrated a positive impact on caregivers of individuals with MCI, reducing perceived caregiver burden and enhancing emotional well-being. These findings underscore the importance of integrating such interventions in caregiver support, aiming to improve their quality of life and the support provided to their loved ones affected by MCI.

References:

[1] Connors MH, Seeher K, Teixeira-Pinto A, Woodward M, Ames D, Brodaty H. Mild Cognitive Impairment and Caregiver Burden: A 3-Year-Longitudinal Study. Am J Geriatr Psychiatry. 2019 Nov;27(11):1206-1215.
[2] Griffiths PC, Kovaleva M, Higgins M, Langston AH, Hepburn K. Tele-Savvy: An Online Program for Dementia Caregivers. Am J Alzheimers Dis Other Demen. 2018 Aug;33(5):269-276.
[3] Livingston G, Barber J, Rapaport P, Knapp M, Griffin M, Romeo R, King D, Livingston D, Lewis-Holmes E, Mummery C, Walker Z, Hoe J, Cooper C. START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of a manual-based coping strategy programme in promoting the mental health of carers of people with dementia. Health Technol Assess. 2014 Oct;18(61):1-242.

P6

The cognitive effect of RehaCom training on a Parkinson's disease: a single-case study

Giulia Nada, F. Garini, E. Pramaggiore, D. Sartini, M. Sacchetti

S.S.D.O Psicologia Clinica, AOU Maggiore della Carità, Novara, Italy

Introduction: Cognitive impairment is one of the most important non-motor features of Parkinson's disease (PD) and negatively affects patient quality of life and caregiver burden. Cognitive symptoms can occur in both the early and advanced stages of the disease and mainly concern attention, memory and executive function. Mild cognitive impairment concerns approximately 25% of PD patients and it increases the risk of developing dementia (PDD) whose prevalence is between 30% and 40% [1,3]. Lately, several non-pharmacological methods have been developed: cognitive therapies, physical exercise, non-invasive brain stimulation and invasive brain stimulation. Recent studies have shown that multidomain computer-based cognitive training can bring benefits in the domains primarily impaired in PD [2].

Objectives: This work aims to investigate the effect of computerized software on neuropsychological performance in a PD patient.

Methods: This study employed an ABA single-case design in which the participant was evaluated at the beginning (T0) and the end of training (T1). He was treated by RehaCom for eight weeks, two 60- minute sessions per week.

Results: The results shown that RehaCom treatment leads to improvements in several cognitive domains such as attention, memory and fluency.

Conclusions: RehaCom appears to be a promising tool to improve cognitive performance for individuals with PD. Furthermore, given the presence of specially designated keyboards, it is particularly suitable for PD patients characterized by motor difficulties. Further studies could delve deeper into the topic but our data provide preliminary evidence for the use of this specific computer-based cognitive training.

References:

[1] [1] Aarsland, D. et al., 2021. Nature Reviews Disease Primers , 7(1), 47.
[2] Nousia, A. et al., 2020. Archives of Clinical Neuropsychology , 35(4), 434-447.
[3] Rektorova, I., 2019. Parkinsonism & Related Disorders, 59, 65-73.

P7

Feasibility of a telematic version of the Parkinson's Disease – Cognitive Rating Scale (PD - CRS): preliminary data

Elisa Pini[1], F. Pepe[1], V. Laini[1,2], M. Ingiardi[1,2], N. Ciccarelli[3] E. Magni[1]

[1]Department of Neuroscience, Poliambulanza Foundation, Brescia, Italy
[2]Department of Psychology, Catholic University, Milan, Italy
[3]Faculty of Psychology eCampus Università, Como, Italy

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms [4]. Among the latter, cognitive disorders can be present from the early stages, often becoming prominent as the disease progresses [4]. Approximately 25% of new diagnosed PD patients may present alterations in one or more cognitive domains. Consequently, the early assessment of cognitive functioning with the use of a screening tool that considers the entire spectrum of cognitive functions appears to be a priority [1,2,3,4]. In this respect, the Parkinson's Disease – Cognitive Rating Scale (PD-CRS) was developed [5,6]. Yet, the Covid-19 pandemic has made it necessary to design and implement new methods to conduct neuropsychological assessments due to difficulties in seeing patients in presence.

Objective: The aim of the study was to evaluate the feasibility of an electronic online version of the PD-CRS.

Methods: Eighty PD patients were recruited during routine neurological outpatient consultation at Poliambulanza Foundation (Brescia, Italy). The electronic version of the PD-CRS was administered to patients staying at their home using a call with Google Meet platform. At the end of the call the examiner and the patient reported on a Visuo-Analogue Scale (scoring 0-10) the perceived subjective difficulty in completing the neuropsychological battery.

Results: In general, both patients and examiner did not encounter significant difficulties during the online screening (mean = 1.75, standard deviation = 3.75) with no statistically significant differences in the perception of the difficulties between patients and examiner ($p = 0.890$).

Conclusion: The telematic version of the PD-CRS seems to be feasible and well tolerated by patients. The use of a telematic screening tool could facilitate the evaluation of many more patients, also reaching those with severe motor disability or living far from the reference centers.

References:

[1] Aarsland, D., Bronnick, K., Williams-Gray, C., Weintraub, D., Marder, K., Kulisevsky, J., ... & Emre, M. (2010). Mild cognitive impairment in Parkinson disease: a multicenter pooled analysis. Neurology, 75(12), 1062-1069.
[2] Barone, P., Aarsland, D., Burn, D., Emre, M., Kulisevsky, J., & Weintraub, D. (2011). Cognitive impairment in nondemented Parkinson's disease. Movement Disorders, 26(14), 2483-2495.
[3] Marras C, Armstrong MJ, Meaney CA, Fox S, Rothberg B, Reginold W, Tang-Wai DF, Gill D, Eslinger PJ, adikoff C, Kennedy N, Marshall FJ, Mapstone M, Chou KL, Persad C, Litvan I, Mast BT, Gerstenecker AT, Weintraub S, Duff-Canning S. Measuring mild cognitive impairment in patients with Parkinson's disease. Mov Disord. 2013 May;28(5):626-33. doi: 10.1002/mds.25426. Epub 2013 Mar 20. PMID: 23520128; PMCID: PMC4524474.
[4] Papagno, C., & Trojano, L. (2018). Cognitive and behavioral disorders in Parkinson's disease: an update. I: cognitive impairments. Neurological Sciences, 39(2), 215-223.
[5] Pagonabarraga, J., Kulisevsky, J., Llebaria, G., García-Sánchez, C., Pascual-Sedano, B., & Gironell, A. (2008). Parkinson's disease-cognitive rating scale: a new cognitive scale specific for Parkinson's disease. Movement disorders: official journal of the Movement Disorder Society, 23(7), 998-1005.
[6] Santangelo, G., Barone, P., Abbruzzese, G., Ferini-Strambi, L., & Antonini, A. (2014). Validation of the Italian version of Parkinson's disease-cognitive rating scale (PD-CRS). Neurological Sciences, 35(4), 537-544.

P8

Automated tablet scoring of Rey Complex figure in PD patients: differences between spatial, cinematic and procedural abilities

Silvia Gobbo[1], M. Petilli[2], M. Rabuffetti[1], R. Daini[1,2], F.L. Saibene[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano, Italy
[2]Università degli Studi di Milano-Bicocca, Milano, Italy

A commonly used test to assess visuo-constructional skills is the copy of Rey-Osterreith Complex figure (RCF). However, its scoring is solely based on the accuracy of the graphical output not allowing for a quantitative assessment of other abilities involved as motor and procedural skills. This represents a limitation in the assessment of patients, especially those affected by Parkinson's Disease (PD). This because they do not show a deficit limited to accuracy, but show visuomotor delay and an altered copy procedure. To overcome this limitation, a tablet method for scoring RCF (TRCF) was developed. It allows to extract quantitative indexes about a spatial (SPA), a procedural (PRO), and a kinematic (KIN) performance in RCF copy and recall. In the present study we administered the TRFC to PD patients, a group of control patients (with right acquired lesion), or to healthy controls (HC). We aimed at investigating the ability of the TRFC to discriminate the three indexes in the three groups. Results reveal that the KIN index is the most impaired in PD patients, while the SPA index is the most impaired in the control patients. No differences between the indexes are observed in the HCs. In addition, both KIN and SPA indexes are able to discriminate between PD patients and HCs and between PD and control patients. These results confirm the usefulness of TRFC in PD patients: it allows not only to describe their performance in greater detail, but also to discriminate PD patients from other categories of patients.

References:

[1] Müller, S., Preische, O., Heymann, P., Elbing, U., & Laske, C. (2017). Increased diagnostic accuracy of digital vs. conventional clock drawing test for discrimination of patients in the early course of Alzheimer's disease from cognitively healthy individuals. Frontiers in aging neuroscience, 9, 101. Petilli, M. A., Daini, R., Saibene, F. L., & Rabuffetti, M. (2021).

[2] Automated scoring for a Tablet-based Rey Figure copy task differentiates constructional, organisational, and motor abilities. Scientific Reports, 11(1), 14895. [6] Santangelo, G., Barone, P., Abbruzzese, G., Ferini-Strambi, L., & Antonini, A. (2014). Validation of the Italian version of Parkinson's disease-cognitive rating scale (PD-CRS). Neurological Sciences, 35(4), 537-544.

P9

Correlations between CSF biomarkers of Alzheimer's disease, neuropsychological tests and UPDRS-III in a cohort of Parkinson disease patients

Francesco Musso[1], A.T. Cimmino[1], A. Scalese[1], G.M. Giuffrè[2], M. Petracca[2], A.R. Bentivoglio[2], P. Calabresi[2], G. Di Lazzaro[2]

[1]Sezione di Neurologia, Dipartimento di Neuroscienze, Facoltà di Medicina e Chirurgia, Università Cattolica del Sacro Cuore, Roma, Italia
[2]Neurologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italia

Introduction: Cerebrospinal fluid (CSF) biomarkers for a biological diagnosis of Parkinson's Disease (PD) are still lacking a wide clinical application. CSF biomarkers of amyloidopathy (Aβ42 and Aβ42/40), tauopathy (p-tau) and neurodegeneration (t-tau) have been widely used in the last decades as a measure of Alzheimer's disease (AD) pathology in vivo and as a predictor of cognitive impairment in AD. These biomarkers have been proven to predict cognitive decline in PD as well.

Objective: To assess the correlations between CSF biomarkers of AD pathology and cognitive/motor impairment in a cohort of PD patients.

Methods: We consecutively recruited 89 subjects who had a clinical diagnosis of PD. A lumbar puncture was performed and AD CSF biomarkers were quantified. At the time of lumbar puncture, a complete neuropsychological battery and UPDRS-III motor scale were used to assess cognitive and motor domains respectively. Follow-up of at least 9 months was available for every patient. Correlations between CSF biomarkers, neuropsychological tests and UPDRS-III at the time of lumbar puncture and at last follow-up were carried out.

Results: Our results revealed a statistically significant correlation between biomarkers of amyloidopathy (Aβ42 and Aβ42/40) and poorer performances in MMSE, RAVLT delayed recall, Spatial Span, Raven matrices, MFTC, semantic verbal fluency, ROCF delayed recall. Interestingly, t-tau and p-tau levels were found to predict the % change between the UPDRS-III score at the baseline and follow-up, also when corrected with follow-up duration, LEDD and baseline UPDRS score.

Discussion & Conclusion: Amyloidopathy is a frequent PD copathology. This study highlighted the role of CSF biomarkers of amyloidopathy as a tool to predict worse performances in some common neuropsychological tests. Furthermore, tau species showed potential in identifying PD patients at risk of accelerated motor decline over time, suggesting a possible synergistic role of tau with alpha-synuclein in the clinical progression of Parkinson's disease.

P10

Subjective cognitive complaints in Parkinson's disease: a systematic review and meta-analysis

Mattia Siciliano[1,2,3], A. Tessitore[1], F. Morgante[3], J.G. Goldman[4], L. Ricciardi[3]

[1]Department of Advanced Medical and Surgical Sciences – MRI Research Center Vanvitelli-FISM, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[3]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[4]JPG Enterprises LLC, Medical Division, Chicago, USA

Introduction: Subjective cognitive complaints (SCCs) in Parkinson's disease (PD) are reported frequently [1], but their prevalence and association with changes on objective testing are not fully known [2].

Objectives: We conducted a systematic review and meta-analysis to determine the prevalence, clinical correlates, and predictive value of SCCs in PD.

Methods: A systematic review of research-based literature catalogued in PubMed, Scopus, Web of Science, and PsycINFO (ProQuest) was restricted to peer-reviewed articles in English, supplemented by hand searches of reference lists of all included papers.

Results: From 204 abstracts, we selected 31 studies (n=3441 patients). The meta-analysis showed a SCCs prevalence of 36%. This prevalence, however, was significantly moderated by study heterogeneity regarding female sex, disease severity, levodopa equivalent daily dosage, exclusion from the overall sample of patients with objective cognitive impairment, and measurement instrument. SCCs prevalence did not differ between de novo and treated PD patients. SCCs were weakly and negligibly associated with cognitive changes on objective testing in cross-sectional studies. However, in cognitively normal patients, SCCs had a risk ratio of 2.71 for later cognitive decline over a mean follow-up of 3.16 years. Moreover, SCCs were moderately related to co-occurring symptoms of depression, anxiety, or apathy and were more strongly related to these neuropsychiatric symptoms than objective cognitive functioning.

Conclusions: Our analyses suggest that SCCs in patients with and without objective cognitive impairment are frequent, occurring in more than one-third of PD patients. Establishing uniform measurement instruments for identifying PD-related SCCs is critical to understand their implications. Even in cases lacking evidence of objective cognitive impairment and where SCCs might reflect underlying neuropsychiatric symptoms, the possibility of later cognitive deterioration should not be excluded. As such, SCCs in PD patients warrant close monitoring for opportunities for targeted and effective interventions.

References:

[1] Kjeldsen PL, Damholdt MF. Subjective cognitive complaints in patients with Parkinson's disease. Acta Neurol Scand 2019; 140: 375-389.
[2] Litvan I, Goldman JG, Tröster AI, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord 2012; 27: 349-356.

P11

Speech analysis in parkinsonism: detecting linguistic patterns through Natural Language Processing

Francesca Petrini[1], F. Dell'Orletta[2], E. Del Prete[1], D. Brunato[2], E. Benevento[3], D. Frosini[1], R. Ceravolo[3]

[1]Department of Medical Specialties, Neurology Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy
[2]Istituto di Linguistica Computazionale "Antonio Zampolli" (CNR-ILC) / ItaliaNLP Lab, Pisa, Italy
[3]Department of Clinical and Experimental Medicine, Neurology Unit – University of Pisa, Pisa, Italy

Introduction: Progressive Supranuclear Palsy (PSP) is an atypical parkinsonism characterized by motor and cognitive impairment, which often presents speech and language disorders. The prevalence and linguistic profile of these disorders are currently under investigation. The application of Natural Language Processing (NLP) techniques to neurodegenerative disorders shows promise in exploring language disorders and enhancing diagnostic accuracy [1].

Objectives: The aim of our investigation is to assess the effectiveness of NLP techniques in delineating a specific linguistic profile in individuals with PSP.

Methods: 30 PSP, 17 Parkinson's Disease patients, and 17 healthy controls were recruited. They were asked to describe the Screening for Aphasia in NeuroDegeneration [2] picture and their descriptions were recorded and transcribed verbatim. State-of-the-art NLP methods were employed to extract a comprehensive linguistic profile, encompassing a diverse range of features, including shallow text features (e.g. average length of words and sentences), vocabulary type and richness, lexical density (calculated as the ratio between content and functional morpho-syntactic categories), as well as the occurrence of different syntactic constructions along with their internal complexity [3]. Many of these features have been informed by literature on linguistic complexity, language acquisition and neurolinguistics, and have been successfully applied in a wide range of scenarios [4,5], including the prediction of behavioral and cognitive impairments based on the detection of relevant linguistic markers from clinical tests [6,7,8]. Additionally, we employed various methodologies, such as word embeddings, topic modeling, and information extraction to automatically compute discourse-related properties, encompassing both global and local aspects of text coherence [9].

Results/Conclusions: Although the study is still in progress, the preliminary qualitative results are encouraging, suggesting the potential of NLP techniques in the identification of peculiar linguistic features in PSP patients and the possibility of using them to aid the diagnostic process.

References:

[1] Beltrami et al., 2018. Front. Aging Neurosci. 10:369.
[2] Catricalà et al., 2017. Neurol. Sci.; 38(8):1469-1483.
[3] Brunato et al., 2020. In: Proceedings of the Twelfth Language Resources and Evaluation Conference, 7145–7151, Marseille, France. European Language Resources Association.
[4] X Lu, 2009. International Journal of Corpus Linguistics;14:3–28.
[5] Lubetich et al., 2014. In: Proceedings of COLING, the 25th International Conference on Computational Linguistics: Technical Papers. 2014: 2151–60.
[6] Roark et al., 2007. BioNLP 2007:1–8.
[7] Prud'hommeaux et al., 2011. In: Proceedings of the 2nd Workshop on Cognitive Modeling and Computational Linguistics 2011:88–96.
[8] Shellikeri et al., 2022. Parkinsonism Relat. Disord.; 102:94-100.
[9] Corcoran et al., 2020. Schizophr. Res.; 226:158–66.

P12

Evaluation of autonomic, imaging and genetic biomarkers for dementia in Parkinson's disease: a cohort description

Paola Polverino[1], T. De Santis[1], A. Cocco[1], S. Lalli[1], E. Perdixi[1], A. Albanese[1,2]

[1]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[2]Department of Neuroscience, Catholic University, Rome, Italy

Introduction: Among the wide spectrum of non-motor symptoms, Cognitive Impairment (CI) is a major feature of PD, and its diagnosis is often complex, as no reliable diagnostic biomarkers have been described yet [1]. Mild cognitive dysfunction may present since the early stages [2], while dementia will occur in over 80% of patients after 20 years of disease, severely affecting the quality of life [3]. Detection of early predictors of CI could help to stratify patients and set appropriate early interventions.

Objectives: We aimed to extensively characterize an early nondemented PD (NDPD) cohort to be studied prospectively, in order to identify potential predictors of CI in PD. Here we report baseline clinical, biological and instrumental assessments.

Methods: Patients referring to Neurology Department of Humanitas Research Hospital (Rozzano, Milano) were consecutively screened for inclusion. Study protocol was based on a multidimensional approach, including clinical, biological, and imaging variables. Patients underwent a baseline evaluation including motor and non-motor scales (MDS-UPDPRS I-IV, NMSS, SCOPA-AUT), neuropsychological assessment, autonomic testing, cardiac scintigraphy with 123I-MIBG, brain PET with 18F-FDG and genetic testing.

Results: 58 NDPD patients were enrolled. Average disease duration was 4,2±2,7 years. H&Y average score was 1,87±0,6. Neuropsychological assessment revealed an average MoCA score of 26,8±2,3. 18FDG-PET scans showed a DLB-like pattern in 55% of cases. SCOPA-AUT median value was 4 (range 0-22). 123I-MIBG imaging demonstrated 64% of patients showing pathological findings both in the early and delayed ratio. Genetic testing revealed the presence of genetic variants in 15% of patients, including 6 GBA, 1 SNCA, 1 PRKN, 1 LRRK2 and 1 PINK1 variants.

Conclusions: A multidimensional characterization of an early NDPD cohort represents the baseline assessment for a longitudinal observation, in order to detect early biomarkers of phenoconversion and define predictive models to be applied in clinical practice.

References:

[1] Chaudhuri KR, Healy DG, Schapira AH; National Institute for Clinical Excellence. Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol. 2006 Mar;5(3):235-45. doi: 10.1016/S1474-4422(06)70373-8. PMID: 16488379.
[2] Litvan I, Aarsland D, Adler CH, Goldman JG, Kulisevsky J, Mollenhauer B, Rodriguez-Oroz MC, Tröster AI, Weintraub D. MDS Task Force on mild cognitive impairment in Parkinson's disease: critical review of PD-MCI. Mov Disord. 2011 Aug 15;26(10):1814-24. doi: 10.1002/mds.23823. Epub 2011 Jun 9. PMID: 21661055; PMCID: PMC3181006.
[3] Hely MA, Reid WG, Adena MA, Halliday GM, Morris JG. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Mov Disord. 2008 Apr 30;23(6):837-44. doi: 10.1002/mds.21956. PMID: 18307261.

Evaluation of autonomic, imaging and genetic biomarkers for dementia in Parkinson's disease: a cohort description

P13

Comparing essential and dystonic tremor: the TITAN study

Cristiano Sorrentino[1], G. Lazzeri[2], C. Terranova[3], G. Paparella[4,5], A.F. Gigante[6], R. De Micco[7], L. Magistrelli[8,9], F. Di Biasio[10], F. Valentino[11], V. Moschella[12], A. Pilotto[13], M. Esposito[14], E. Olivola[5], M.C. Malaguti[15], R. Ceravolo[16], C. Dallocchio[17], F. Spagnolo[18], A. Nicoletti[19], A. De Rosa[20], R. Di Giacopo[21], A. Padovani[13], M.C. Altavista[12], C. Pacchetti[11], R. Marchese[10], E. Contaldi[8], A. Tessitore[7], S. Misceo[6], M. Bologna[4,5], V. Rizzo[3], G. Franco[2], P. Barone[1], R. Erro[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi (SA), Italy
[2]Neurology Unit, Department of Neuroscience, Dino Ferrari Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[4]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[5]Neuromed Institute IRCCS, Pozzilli (IS), Italy
[6]Neurosensory Department, Neurology Unit, San Paolo Hospital, ASL Bari, Italy
[7]Department of Advanced Medical and Surgical Sciences, Università della Campania "Luigi Vanvitelli", Napoli, Italy
[8]Department of Translational Medicine, Section of Neurology, University of Piemonte Orientale, Novara, Italy
[9]"Maggiore della Carità" University Hospital, Novara, Italy
[10]IRCCS Ospedale Policlinico San Martino, Genova, Italy
[11]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[12]Neurology Unit, San Filippo Neri Hospital ASL Roma1, Rome, Italy
[13]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[14]Clinical Neurophysiology Unit, AORN Cardarelli, Napoli, Italy
[15]Clinical Unit of Neurology, Department of Emergency, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[16]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[17]Neurology Unit, Department of Medical Specialist Area, ASST Pavia, Italy
[18]Department of Neurology, Antonio Perrino's Hospital, Brindisi, Italy
[19]University of Catania, Department "G.F. Ingrassia", Section of Neurosciences, Catania, Italy
[20]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[21]Neurology Unit, Rovereto Hospital, APSS Trento, Italy

Introduction: Tremor disorders remain as clinical diagnoses and the rate of misdiagnosis between the commonest non-parkinsonian tremors is relatively high.

Objectives: To compare the clinical features of Essential Tremor (ET), ET plus soft dystonic signs (ET+DS), and tremor combined with dystonia (TwD).

Methods: We compared the clinical features of patients with ET, ET+DS, and TwD enrolled The ITAlian tremor Network (TITAN). Linear regression models were performed to determine factors associated with health status and quality of life.

Results: Three-hundred-eighty-three patients were included. Sex distribution was significantly different between the groups with males being more represented in ET (≈55%) and females in TwD

(≈ 60%). The initial site of tremor was different between the groups with about 40% of TwD having head tremor and ET+DS unilateral upper limb tremor at onset. This pattern mirrored the distribution of overt dystonia and soft dystonic signs at examination. Sensory trick, task-specificity, and positiondependence were more common, but not exclusive, to TwD. ET patients showed the lowest degree of alcohol responsiveness and ET+DS the highest (median: 3/10 vs 5.5/10, respectively). Midline tremor was more commonly encountered and more severe in TwD than in the other groups. Regression analyses demonstrated that tremor severity, sex, age, and to a lesser degree the variable "group" independently predicted health status and quality of life ($F=10.85$; $p<0.001$), suggesting the existence of other determinants beyond tremor.

Conclusions: Although there are some demographic and clinical differences that might aid the differential diagnosis. ET and TwD manifest with a phenotypic overlap that calls for the identification of diagnostic biomarkers. Soft signs in ET+DS colocalized with tremor as it was observed in TwD, suggesting they might represent dystonic features. However, ET+DS shared features with both syndromes, suggesting intra-group heterogeneity.

References:

[1] A. M. Smith et al., "Mitochondrial dysfunction and increased glycolysis in prodromal and early Parkinson's blood cells," Mov. Disord. , vol. 33, no. 10, pp. 1580–1590, Oct. 2018, doi: 10.1002/mds.104.
[2] C. Milanese et al., "Peripheral mitochondrial function correlates with clinical severity in idiopathic Parkinson's disease," Mov. Disord. , vol. 34, no. 8, pp. 1192–1202, 2019, doi: 10.1002/mds.27723.

P14

Mobile health technology postural and turning assessment in progressive supranuclear palsy and Parkinson's disease: a multicenter study using mobile health technology analyses

Tiziana Comunale[1-3] and A. Pilotto[1-3], A. Rizzardi[1-3], C. Zatti[1-3], M.C. Rizzetti[4], A. Lombardi[1], C. Hansen[5], R. Romijnders[5], B. Borroni[1], W. Maetzler[5], A. Padovani[1-3]

[1]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Italy
[2]Department of Continuity of Care and Frailty, Neurology Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[3]Laboratory of Digital Neurology and Biosensors, University of Brescia, Italy
[4]Parkinson's Disease Rehabilitation unit, FERB Onlus Trescore Balneario, Bergamo, Italy
[5]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany

Introduction: Progressive supranuclear palsy (PSP) is a neurodegenerative disease clinically characterized by symmetric parkinsonism associated with earlier postural instability and falls compared to Parkinson's disease (PD).

Objectives: To evaluate differences in postural and turning performances between patients with PSP and PD (fallers and no fallers) using Mobile Health Technology (MHT).

Methods: 250 subjects entered the study, namely 27 participants with PSP, 44 with PD who have experienced at least 1 fall in the last year, 63 with PD who have not experienced any fall in the last year, and 116 healthy subjects performed static sway and turning tests. Static balance was evaluated with instrumented (lower back accelerometer, Rehagait®, Hasomed, Germany) 30-s trials in side by side, semitandem and tandem positions. Turning was evaluated with instrumented Timed Up and Go test. Data were analysed to determine what balance and turning parameters discriminate PSP from PD and HC and to detect the correlation of these technological measures with clinical assessment.

Results: Compared to HC and PD, PSP and PD fallers showed similar static parameters in different conditions, whereas PSP exhibited lower volume of perturbation compared to PD with falls. Turning parameters significantly differed between HC, PD without falls and PD fallers as well as PSP, with no differences between the latest groups.

Conclusions: PSP patients exhibit a similar postural instability pattern compared to PD with falls but lower perturbation volume. Different pathophysiology and compensations mechanism are thus probably related to postural instability in these patients. Turning parameters instead seem to be more sensitive in the detection of fallers and further studies are needed to determine if they could be used as markers of risk of falls or early markers of disease progression.

P15

Quantitative gait biomarkers in patients with functional gait disorders: beyond gait speed

Giulia Bonardi, M. Gandolfi, C. Bonetto, F. Salaorni, A. Sandri, C. Geroin, Z. Menaspà, N. Smania, M. Fiorio, M. Tinazzi

Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Functional gait disorders (FGDs) are disabling symptoms of Functional Motor Disorders. Clinical observations show gait improvement with distraction suggesting an association with higher-level control mechanisms. Dual tasking is a valuable tool for exploring the interplay between gait and cognition.

Objectives: To identify measures of quantitative spatio-temporal gait parameters while walking and dual tasking in FGDs that best discriminate performance from healthy controls.

Methods: This cross-sectional observational study analyzed spatial-temporal gait parameters of 87 patients with FGDs (79.3% female, age 41.9 ± 14.7 years) and 48 healthy controls (60.4% female, age 41.9 ± 15.7 years). Participants underwent spatiotemporal gait analysis during a single task (ST) and while performing motor, cognitive, and visual-fixation dual tasks (DT) [1,2]. We evaluated high-level gait control outcomes, their standard deviations (SDs), and the Dual-task Effect (DTE) [3]. The Area Under Curves (AUC) determined the objective measures that differentiated FGDs from healthy controls (HCs). A two-way repeated measures ANOVA investigated DT interference on ST gait measures.

Results: Significant group x task interactions were observed for swing time SD and stride time during cognitive dual tasks ($p<0.035$). Positive correlations were noted between motor and cognitive DTE and gait performance and steadiness ($p<0.003$). Negative correlations were found with visual DT ($p<0.041$).

Conclusions: FGDs reported poorer gait performance and less automaticity and steadiness than HCs. However, gait performance but not automaticity and steadiness were affected by DT, unlike different neurological diseases. Our findings shed light on higher-level gait control mechanisms in FGDs and suggest stride time and swing time variability as potential diagnostic biomarkers.

References:

[1] Gandolfi et al., 2021; Motor dual task with eyes closed improves postural control in patients with functional motor disorders: A posturographic study; Gait Posture.
[2] Gandolfi et al., 2023; Dual tasking affects gait performance but not automaticity in functional gait disorders: A new diagnostic biomarker Park Relat Disord.
[3] Geroin et al., 2018; Does dual-task training improve spatiotemporal gait parameters in Parkinson's disease?; Park Relat Disord.

P16

Postganglionic autonomic dysfunction and cutaneous alpha-synuclein deposits in multiple system atrophy: role as candidate biomarkers for disease severity and physiopathological implications

Roberta Telese[1,2], F. Cencini[1], A.E. Elia[1], R. Cilia[1], V. Leta[1], F. Colucci[1], A. Braccia[1], N. Golfrè Andreasi[1], L.M. Romito[1], G. Gaudiano[1], S. Rinaldo[1], R. Eleopra[1], G. Devigili[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[2]Departement of Neuroscience, University of Milano Bicocca, Milan, Italy

Introduction: Multiple system atrophy (MSA) is a progressive neurodegenerative disease clinically characterized by parkinsonism (MSA-P) and/or cerebellar dysfunction (MSA-C) associated with autonomic failure, whereas the pathological hallmark is the abnormal accumulation of alpha-synuclein in glial cells. Autonomic dysfunction is considered to be preganglionic because of the preserved cardiac sympathetic innervation seen on meta-iodobenzylguanidine (MIBG) cardiac scintigraphy in most patients [1].
Growing evidence supports the presence of postganglionic autonomic involvement in MSA. Postganglionic sudomotor dysfunction on Dynamic Sweat Test (DST) has been reported in up to 90% of patients [2]. The presence of abnormal phosphorylated alphasynuclein (p-syn) deposition within cutaneous autonomic nerve fibers on skin biopsies has been reported by several studies [3].

Objective: Peripheral autonomic involvement in MSA was explored through the evaluation of: (1) postganglionic sudomotor function, (2) cardiovascular autonomic indexes and (3) p-syn skin deposits, in order to establish their role as possible disease biomarkers.

Methods: A cross-sectional study on patients with “clinically established” MSA diagnosis [1] was performed. Complete clinical workup, MIBG cardiac scintigraphy, cardiovascular autonomic tests, DST, skin biopsies for psyn quantitation at three body sites were performed.

Results: 31 patients (21 MSA-P, 10 MSA-C) were enrolled. No difference in clinical, demographic features and clinical scales scores was found. DST was impaired in all tested patients. Cutaneous p-syn deposits were found in 81% of patients, with a topographic distribution following a distal-proximal gradient and no difference between clinical subtypes. P-syn deposits were found in both somatic and autonomic fiber, with greater prevalence in the former. The presence of widespread skin nerve p-syn deposits was associated with higher UMSARS Part II scores and with orthostatic hypotension. Neither p-syn deposition nor sudomotor dysfunction correlated with disease duration.

Conclusion: This study highlights the presence of functional abnormalities of postganglionic sudomotor pathway in MSA and provides a preliminary support for the use of cutaneous p-syn quantitation as a prognostic biomarker in MSA in clinical practice and research studies.

References:

[1] Wenning GK, Stankovic I, Vignatelli L, Fanciulli A, Calandra-Buonaura G, Seppi K, Palma JA, Meissner WG, Krismer F, Berg D, Cortelli P, Freeman R, Halliday G, Höglinger G, Lang A, Ling H, Litvan I, Low P, Miki Y, Panicker J, Pellecchia MT, Quinn N, Sakakibara R, Stamelou M, Tolosa E, Tsuji S, Warner T, Poewe W, Kaufmann H. The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Mov Disord. 2022 Jun;37(6):1131-1148. doi: 10.1002/mds.29005. Epub 2022 Apr 21. PMID: 35445419; PMCID: PMC9321158.
[2] Provitera V, Iodice V, Manganelli F, Mozzillo S, Caporaso G, Stancanelli A, Borreca I, Esposito M, Dubbioso R, Iodice R, Vitale F, Koay S, Vichayanrat E, Valerio F, Santoro L, Nolano M. Postganglionic Sudomotor Assessment in Early Stage of Multiple System Atrophy and Parkinson Disease: A Morpho-functional Study. Neurology. 2022 Mar

22;98(12):e1282-e1291. doi: 10.1212/WNL.0000000000013300. Epub 2022 Jan 11. PMID: 35017309; PMCID: PMC8967330.
[3] Gibbons C, Wang N, Rajan S, Kern D, Palma JA, Kaufmann H, Freeman R. Cutaneous α-Synuclein Signatures in Patients With Multiple System Atrophy and Parkinson Disease. Neurology. 2023 Apr 11;100(15):e1529-e1539. doi: 10.1212/WNL.0000000000206772. Epub 2023 Jan 19. Erratum in: Neurology. 2023 Oct 10;101(15):684.
PMID: 36657992; PMCID: PMC10103107.

P17

Hemichorea associated with CASPR2 antibody: a case report

Claudio Verderosa[1], P. Nigro[1], A. Mechelli[1], N. Tambasco[1], L. Parnetti[1,2]

[1]Neurology Section, Department of Medicine and Surgery, University of Perugia, Perugia, Italy
[2]Neurology Clinic, University Hospital of Perugia, Perugia, Italy

Introduction: Contactin-associated protein-like 2 (CASPR2) is a membrane protein expressed both in central and peripheral nervous system. It is essential for proper localization of voltage-gated potassium channels (VGKC) [1]. CASPR2 Antibody associated disease is an autoimmune encephalitis with a progressive course. The clinical spectrum of CASPR2 antibody disease consists of Morvan's syndrome, epilepsy, or pain syndromes, in particular painful peripheral neuropathy [2]. Other rare clinical manifestations also include cognitive disturbance and movement disorders, such like hemichorea [3], therefore diagnosis could be challenging.

Case report: A 72-years-old man presented a progressive 10-years history of sensitive and painful disturbance at inferior limbs. Physical examination and neuropsychological assessments showed right hemisome chorea-like movements, gait disturbance with severe postural instability associated with multi-domain mild cognitive impairment with compromission of subcortical functions and memory and neuropsichiatric alterations (mood deflession, anxiety). His medical history was relevant for structural epilepsy due to right hemispheric dermoid cyst, after removed, and chronic ischemic heart disease. Brain MRI, molecular analysis of IT-15 gene, peripheral blood film, autoimmune, metabolic, and paraneoplastic blood screening (determination of ANA, ANCA, ENA, anti-nDNA, aPL, Hb1Ac, cupremia, blood ceruloplasmin, vit. B12, folate, electrolytes, CEA, CA125, CA19.9) were unremarkable. Tetrabenazine was administered with poor improvement. On the following year, patient underwent on mielic fracture at D8-D9 due to a fall, requiring surgical treatment and intensive care. CSF analysis for paraneoplastic autoantibodies detected CASPR2 antibodies by indirect immunofluorescence test (titer IgM 1:10; Euroimmun, Lübeck, Germany). Tests for the remainder of the autoantibodies (anti-Hu, -Ri, -Yo, -CV2, -Ma, -Ta, -PCA2, -ANNA, -NMDA, -AMPA-1, and -AMPA-2) were negative. As a paraneoplastic process was suspected, total body computed tomography (CT) was performed and no significative alterations were found. Patient was treated with IV MP 500 mg daily (half dose due to high fragility of the patient) for three days. Unfortunately, treatment was stopped due to CVC-related sepsis. IV immunoglobulin treatment was contraindicated due to recent ischemic heart attack.

Conclusions: Chorea is a complex and rare syndrome, also associated with paraneoplastic diseases; early comprehension of the pathogenesis is crucial for a suitable treatment.

References:

[1] van Sonderen A, Ariño H, Petit-Pedrol M, Leypoldt F, Körtvélyessy P, Wandinger KP, Lancaster E, Wirtz PW, Schreurs MW, Sillevis Smitt PA, Graus F, Dalmau J, Titulaer MJ. The clinical spectrum of Caspr2 antibody-associated disease. Neurology. 2016 Aug 2;87(5):521-8. doi: 10.1212/WNL.0000000000002917. Epub 2016 Jul 1. PMID: 27371488; PMCID: PMC4970662.
[2] Binks S, Uy C, Honnorat J, et al. Pract Neurol 2022;22:19–31.
[3] Vynogradova I, Savitski V, Heckmann JG. Hemichorea associated with CASPR2 antibody. Tremor Other Hyperkinet Mov 2014; 4. doi: 10.7916/D8VM49C5.

P18

A case of SCA17 presentation in a young woman from Sri Lanka

Elena Benevento[1], J. Pasquini[1], G. Palermo[1], R. Ceravolo[1,2]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Center for Neurodegenerative Diseases, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Introduction: Spinocerebellar ataxias (SCAs) represent a group of rare, autosomal dominantly inherited neurodegenerative disorders. Currently, almost 50 subtypes have been identified with a worldwide prevalence about 2.7 cases per 100.000 [1]. A majority of the SCA patients is of Asian origin and/or inhabitant of the Asian continent [2]. A recent systematic review [3] showed that only one study investigated the prevalence of the most common SCAs in Sri Lanka. That study showed that 60% of subjects were identified as SCA1, one patient as SCA2 and 12 others remained unidentified [4]. No SCA17 cases have been previously identified in Sri Lanka. Spinocerebellar ataxia type 17 (SCA17) is caused by a trinucleotide repeat (TNR) expansion in the transcription factor TATA-binding protein (TBP) gene. It was first reported in a patient with sporadic ataxia who also presented with pyramidal signs and intellectual deterioration.

Objectives: The aim of this report is to present a clinical case of a 31- year-old woman born in Sri-Lanka. She has one brother in good health. She developed the first motor difficulties since age eighteen: she failed the driving license exam for "slowness and uncoordinated legs movements", also she used to be "too slow" in performing complex tasks (e.g., cooking). She worked as a nurse for two years (2018-2020). No story of epilepsy, cardiovascular or cerebrovascular disease, muscle-related symptoms, celiac disease. She has children and she reports one abortion. After the second pregnancy at age 28 she noticed progressive worsening of walking, weakness/loss of balance, and falls became more evident. She also developed progressive difficulty in distal movements (writing, buttoning her clothes, putting on her earrings), severe dysarthria and dysphagia for liquids. At the time of her last examination a wheelchair was needed. No cognitive decline was reported.

Methods: Diagnostic investigations included: brain 3TMRI; nerve conduction studies and electromyography of inferior limbs, somatosensory evoked potentials (SSEP); blood panels including Vitamin E and coeliac disease autoantibodies; ENT consultation and fiberoptic endoscopic evaluation of swallowing (FEES); EEG; and genetic testing for: FRAXA, SCA 1, 2, 3, 6, 7, 8, 12, 17, DRPLA.

Results: Neurological examination found spastic dysarthria, global ideo-motor slowing. Oculomotor examination revelaed divergent strabismus in the left eye, fragmented pursuit, hypometric saccades with and increased latency. Limbs ataxia and spasticity, greater on left side, were observed. Wrists and fingers showed mild dystonic features in extension. Strength was slightly diminished in the proximal upper limbs. Hyperreflexia and a positive Babinski sign were found on the left limbs. She was not able to perform Luria test. No ideomotor limbs apraxia. Romberg sign was positive. Gait was ataxic, she could walk on her own only for few meters. Brain 3T-MRI showed marked atrophy of the vermis and cerebellar hemispheres, as well as in the upper and prerolandic parietal regions of both hemispheres. Lower limbs somatosensory evoked potentials, EEG, Vit E dosage were all normal. FEES showed "closing delay of the right vocal cord" with indication to dietary adjustments for dysphagia. The genetic examination was positive for repeated triplets in TBP gene (CAG allele 1: 37 triplets, CAG allele 2: 51 triplets). Diagnosis of SCA type 17 was made.

Conclusions: We describe a case of SCA17 in a young woman from Sri Lanka. This mutation is thought to be rare in Sri Lanka based on previous epidemiological studies; nonetheless, our case warrants further investigations that may unmask more cases. The patient phenotype was predominantly spino-cerebellar with cognitive decline and only mild dystonic features.

References:

[1] M. Huang, D.S. Verbeek. Why do so many genetic insults lead to Purkinje Cell degeneration and spinocerebellar ataxia? Neurosci. (2019).
[2] L. Ruano, et al. The global epidemiology of hereditary ataxia and spastic paraplegia: a systematic review of prevalence studies. Neuroepidemiology. (2014).
[3] Van Prooije T, Ibrahim NM, Azmin S, van de Warrenburg B. Spinocerebellar ataxias in Asia: Prevalence, phenotypes and management. Parkinsonism Relat Disord. (2021).
[4] Sumathipala, D.S., Abeysekera, G.S., Jayasekara, R.W. et al. Autosomal dominant hereditary ataxia in Sri Lanka. BMC Neurol 13, 39. (2013).

P19

Conventional instrumental investigations in patients with functional motor disorders

Tommaso Ercoli[1], C. Geroin[2], E. Marcuzzo[2], R. Erro[3], S. Cuoco[3], R. Ceravolo[4], S. Mazzucchi[4], A. Pilotto[5,6], A. Padovani[5], L.M. Romito[7], R. Eleopra[7], M. Zappia[8], A. Nicoletti[8], C. Dallocchio[9], C. Arbasino[9], F. Bono[10], G. Spano[10], B. Demartini[11], O. Gambini[11], N. Modugno[12], E. Olivola[12], L. Bonanni[13], A. Albanese[14], G. Ferrazzano[15], A. Tessitore[16], L. Lopiano[17], G. Calandra Buonaura[18,19], M. Petracca[20], F. Morgante[21,22], M. Esposito[23], A. Pisani[24,25], P. Manganotti[26], L. Tesolin[27], F. Teatini[27], F. Stocchi[28], P. Solla[1], G. Defazio[29], M. Tinazzi[2]

[1]Neurological Unit, AOU Sassari, University of Sassari, Sassari, Italy
[2]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry - Scuola Medica Salernitana, University of Salerno, Baronissi (SA), Italy
[4]Center for NeuroDegenerative Diseases Parkinson and Movement Disorders, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[5]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[6]FERB Onlus, Ospedale S. Isidoro, Trescore Balneario, Bergamo, Italy
[7]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[8]Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[9]Department of Medical Area, Neurology Unit, ASST Pavia, Italy
[10]Botulinum Toxin Center, Neurology Unit A.O.U. Mater Domini, Catanzaro, Italy
[11]Aldo Ravelli Research Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[12]IRCCS Neuromed, Pozzilli, Italy
[13]Department of Neuroscience, Imaging and Clinical Sciences, University G. d'Annunzio, Chieti-Pescara, Italy
[14]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[15]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[16]Department of Advanced Medical and Surgery Sciences, University of Campania - Luigi Vanvitelli, Naples, Italy
[17]Department of Neuroscience - Rita Levi Montalcini, University of Turin, Turin, Italy
[18]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[19]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italia
[20]Movement Disorder Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[21]Neurosciences Research Centre, Molecular and Clinical Sciences Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[22]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy
[23]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[24]IRCCS Mondino Foundation, Pavia, Italy
[25]Department of Brain and Behavioral Sciences, University of Pavia, Italy
[26]Clinical Neurology Unit, Department of Medical, Surgical and Health Services, University of Trieste, Trieste, Italy
[27]Functional Movement Disorders Outpt. Clinic, Clinical Neurology and Stroke Unit Dep., Central Country Hospital, Bolzano, Italy
[28]University and Institute of Research and Medical Care San Raffaele Roma, Rome, Italy

[29]Department of Translational Biomedicine and Neurosciences, University of Bari "Aldo Moro", Bari, Italy

Introduction: The diagnosis of Functional Motor Disorders (FMD) primarily relies on clinical evaluation, and only a few tests are validated as biomarkers for the disease and FMD identification [1].

Objective: The aim of this study is to assess the frequency of use of conventional instrumental investigations (i.e., MRI, CT, Datscan, EEG, neurophysiological tests, and others) in patients with FMD and to identify clinical and demographic features that may influence exam planning.

Methods: Data were obtained from the Italian Registry of Functional Motor Disorders (IRFMD) [2]. We assessed conventional diagnostic tests conducted on the entire registry. Utilizing a logistic regression model, we examined the clinical and demographic variables significantly linked to conventional investigations for patients registered in the database (dependent variable).

Results: Among the 410 patients included in IRFMD, we identified 24 patients (5.9%) who did not undergo any conventional exams, 120 patients (29.2%) who performed only one investigation, and 266 patients (64.9%) who underwent two or more exams. Patients who did not undergo investigations were younger than patients who underwent conventional exams (39.5 + 17.8 vs. 47.8 + 15.56, p=0.023), and tremor phenotype was more represented in the first group (16/24 vs. 151/386, p=0.008). Logistic regression analysis confirmed these findings for both age (OR: 1.04, 95% CI 1.006-1.074; p=0.019), and tremor phenotype (OR: 0.255, 95% CI 0.094-0.689; p=0.007).

Conclusions: Our study provides novel information about the tendency to plan conventional investigations in patients with FMD. Patients with functional tremor were less prone to undergo exams, while investigations were more likely to be performed in older FMD patients.

References:

[1] Gilmour GS, Lidstone SC. Moving Beyond Movement: Diagnosing Functional Movement Disorder. Semin Neurol. 2023.
[2] Tinazzi M, Morgante F, Marcuzzo E, et al. Clinical Correlates of Functional Motor Disorders: An Italian Multicenter Study. Mov Disord Clin Pract. 2020;7(8):920-929.

P20

Exploring the spectrum of saccadic intrusions in essential tremor

Claudio Terravecchia[1], G. Mostile[1,2], A. Rufa[3], R. Terranova[1], C.G. Chisari[1], A. Salerno[1], A. Luca[1], G. Donzuso[1], C.E. Cicero[1], M. Zappia[1], A. Nicoletti[1]

[1]Department of Medical and Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, Catania, Italy
[2]Oasi Research Institute-IRCCS, Troina, Italy
[3] Eye Tracking and Visual Application Lab (EVA Lab), Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Ital

Introduction: Saccadic intrusions (SI) are involuntary conjugate saccadic eye movements interrupting fixation, reflecting a saccadic inhibitory deficit linked to impaired cerebellar-brainstem-basal ganglia networks functioning. To date, SI have been poorly explored in Essential Tremor (ET) and the spectrum of SI different subtypes has never been assessed.

Objective: To explore the spectrum of SI in ET in order to assess possible clinical-instrumental correlations as well as its potential role in ET phenotypization.

Methods: Total SI rate and different SI subtypes were evaluated during primary position fixation task among healthy controls (HCs), pure ET and ET-plus patients through Eyelink 1000-Plus. Monophasic Square Wave Jerks (MSWJs), Biphasic SWJs (BSWJs), Staircase SWJs (SSWJs) were qualitatively and quantitatively assessed and compared among study groups.

*Results***:** Thirty patients [9 pure ET (30%) and 21 ET-plus (70%)] and 16 HCs were enrolled. After adjusting by age, significantly higher prevalence of BSWJs was found in pure ET but not in ET-plus compared to HCs. A new pattern of “Triphasic” SWJs (TSWJ) as well as SSWJs were firstly found in pure ET and ET-plus but not in HCs. Higher total SI, BSWJ and TSWJ rate was found in pure ET as compared to ET-plus. A positive correlation was found between MSJW percentage/total SI and TETRAS motor scores for head, face, voice and limb action tremor. On the contrary, a negative correlation between BSWJ/MSWJ ratio and TETRAS-motor scores for head, face and limb action tremor was shown.

Conclusion: Different patterns of SI were found in ET patients with clinical-instrumental correlates, showing the possible usefulness of fixation quantitative analysis for ET phenotypization.

P21

Gait analysis in GLUT1 deficiency syndrome: a clinical and instrumental approach

Francescantonio Cammarota[1,2], M. Corrado[1,2], R. De Icco[1,2], V. Grillo[1,2], E. Mazzotta[1,2], V. De Giorgis[1,3], V. Vacchini[3], C. Varesio[1,3], M. Celario[1,3], D. Trabassi[4], S.F. Castiglia[1,4], M. Serrao[4], C. Tassorelli[1,2]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]Movement Analysis Research Unit, IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Child Neurology and Psychiatry, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Medical and Surgical Sciences and Biotechnologies, "Sapienza" University of Rome, Polo Pontino, Latina, Italy

Background: Gait disturbances and movement disorders are frequent in patients with GLUT-1 deficiency, mostly represented by pyramidal, cerebellar, and extrapyramidal dysfunction [1].

Objective: This study aimed to assess the ability of a set of trunk acceleration-derived gait indexes to identify gait unbalance in subjects with GLUT-1 deficiency, and to detect potential correlations with clinical and biochemical parameters.

Methods: We recorded a 30-meter gait of 10 subjects with GLUT-1 deficiency and of 10 age-, sex- and gait speed-matched healthy subjects (HS). Gait analysis was performed via an inertial measurement unit (IMU) placed at the lower back. Based on trunk acceleration patterns in the antero-posterior (AP), medio-lateral (ML), and vertical (V) directions, we calculated: spatio-temporal gait parameters, pelvic kinematics, harmonic ratios (HR), recurrence quantification analysis (RQA), stride length coefficient of variation (CV), the longest short term Lyapunov's exponent (sLLE), and the log dimensionless jerk score (LDLJ).

Results: When compared to the HS group, the GLUT-1 subjects showed lower values of HR AP, HR ML, single support (SS) phase, and cadence. Moreover, they showed higher values of CV, LDLJ AP, LLE AP, and double support (DS) phase duration. In the GLUT-1 group, HR AP negatively correlated with a positive history of recurrent falls ($r = -0.88$, $p = 0.03$), while CV negatively correlated with ketonemia ($r = -0.64$, $p = 0.04$).

Conclusions: Subjects with GLUT-1 deficiency exhibited multiple alterations in the trunk acceleration-derived gait indexes. Interestingly some of these alterations correlated with clinical/biochemical features, such as history of falls and ketonemia.

References:

[1] Pons R, et al. Movement disorders 2010;25(3):275-81.

P22

Determinants of caregiver burden in a spectrum of neurodegenerative diseases

Immacolata Carotenuto, S. Cuoco, R. Bisogno, A. Cappiello, R. Erro, M. Amboni, M.T. Pellecchia, P. Barone, M. Picillo

Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Italy

Introduction: The role of caregiver is paramount in the management of a number of neurodegenerative diseases.

Objectives: We investigated the determinants of the caregiver's burden in a cohort of patients affected by a variety of neurodegenerative diseases consecutively recruited in an outpatient setting.

Methods: Between January 2022 and January 2023, one hundred and nine patients, and their caregivers were consecutively enrolled from the Center for Neurodegenerative diseases (CEMAND) at the University of Salerno. Specifically, 23 with Alzheimer's Disease, 39 with Parkinson's disease, 15 with Supranuclear Progressive Palsy, 18 with Frontotemporal Dementia, 14 with Multiple System Atrophy diagnosed according to published clinical criteria underwent a clinical interview and evaluations. Carers completed scales regarding burden, depression and quality of life. The ANOVA and MANCOVA tests were used to compare variables between diagnostic categories. Linear regression was used to explore determinants of caregiver burden.

Results: Although patients presented different cognitive and motor status in relation to their diagnosis. we failed to detect differences between caregivers in terms of burden rated with the Zarit Burden Inventory (ZBI). Care time was the only significant variable affecting the burden, irrespective of the specific diagnosis disease ($p=0.015$). In detail, there was a linear relationship between caring time and caregiver's burden. Only caregivers' resilience ($B = - 0.685$, $p= 0.005$) significantly affected the ZBI score ($F = 9.51$, $p = 0.005$) explaining 25,4% of the variance.

Conclusions: Care time is the major determinant of caregiver's burden. The caregivers' resilience is the major protective factor for the caregiver's burden. Our data suggest that caregiver's burden can be reduced by modulating care time and increasing the resilience in a variety of neurodegenerative diseases.

P23

Precision medicine in degenerative parkinsonisms: a metabolomicsbased Ensemble Machine Learning approach

Annamaria Landolfi[1], J. Troisi[1,2,3], M. Lombardi[2,3], M.T. Pellecchia[1], M. Picillo[1], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Baronissi, Salerno, Italy
[2]Theoreo srl, spinoff company of the University of Salerno, Montecorvino Pugliano, Salerno, Italy
[3]European Institute of Metabolomics Foundation (EIM), Baronissi, Salerno, Italy

Introduction: Diagnosing Parkinsonian syndromes remains a challenge, due to significant symptom overlap within this group of disorders. The interplay of genetic and environmental factors adds to the complexity of achieving precise diagnoses. Metabolomics emerges as a promising avenue for unraveling the intricate biochemical signatures that differentiate these conditions [1].

Objectives: To find metabolomic perturbations connected to neurodegenerative parkinsonisms, in order to build a machinelearning-based diagnostic algorithm to support an early differential diagnosis

Methods: We employed a serum untargeted metabolomic profiling approach to discern variations among individuals affected from Parkinson's disease (n=87), Progressive Supranuclear Palsy (n=22), and Multiple System Atrophy (n=25). A cohort of 132 healthy subjects served as controls for comparative analysis. The metabolomic analyses were conducted using Gas Chromatography–Mass Spectrometry, a robust analytical technique capable of capturing a diverse range of metabolites. The resulting data were utilized to train three distinct ensemble machine learning algorithms, enabling the development of a predictive model for syndrome discrimination.

Results: The classification performance of the algorithms demonstrated remarkable accuracy, ranging from 100% to 87.5%. Notably, three distinct groups of metabolites exhibited significant differences, forming the basis for effective discrimination among the studied conditions. The first group featured elevated levels of glucose, fructose, and propanoic acid. In the second group, sugars (ribose, ribitol, and xylose), organic acids (2-hydroxy butyrate and glucunate), and glutathione played defining roles. The third group comprised variations in organic acids, fatty acids, amino acids, and phosphate levels.

Conclusions: The identified metabolomic signatures underscore the potential of metabolomics in elucidating the biochemical landscape associated with Parkinsonian syndromes. The discriminative power of the trained models, coupled with the distinctive metabolic patterns, holds promise for enhancing diagnostic precision in these disorders. This integrative approach not only contributes to our understanding of the underlying pathophysiological mechanisms but also offers a practical and efficient means to support diagnosis [2].

References:

[1] Dunn, W.B.; Broadhurst, D.I.; Atherton, H.J.; Goodacre, R.; Griffin, J.L. Systems Level Studies of Mammalian Metabolomes: The Roles of Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy. Chem. Soc. Rev. 2011, 40, 387–426, doi:10.1039/B906712B.
[2] Troisi, J., Landolfi, A., Vitale, C., Longo, K., Cozzolino, A., Squillante, M., Savanelli, M. C., Barone, P., & Amboni, M. (2019). A metabolomic signature of treated and drug-naïve patients with Parkinson's disease: a pilot study. Metabolomics : Official journal of the Metabolomic Society , 15(6), 90. https://doi.org/10.1007/s11306-019-1554-x.

P24

Survey on restless legs syndrome: perspectives and practices among Italian neurologists

Gloria Pompea Mingolla[1], E. Antelmi[2,3], F. Morgante[4], A. Conte[5], L. Ferini-Strambi[6], R. Ferri[7], G. Plazzi[8], G. Lanza[9], P. Mogavero[10], C. Bonetto[1], A. Berardelli[11], M. Tinazzi[1,2]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neurology Unit, Parkinson Disease and Movement Disorders Division, AOUI, Verona, Italy
[3]Department of Engineering for Innovation Medicine, University of Verona, Verona, Italy
[4]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's, University of London, London, UK
[5]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[6]Department of Clinical Neurosciences, Neurology Sleep Disorders Centre, RCCS San Raffaele Scientific Institute, Milan, Italy
[7]Clinical Neurophysiology Research Unit, Oasi Research Institute- IRCCS, Troina, Italy
[8]IRCCS Istituto delle Scienze Neurologiche di Bologna (ISNB), Bologna, Italy; Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[9]Department of Surgery and Medical-Surgical Specialties, University of Catania, Catania, Italy
[10]Istituti Clinici Scientifici Maugeri, IRCCS, Scientific Institute of Pavia, Pavia, Italy.
[11]IRCCS Neuromed, Pozzilli, Italy; Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

Introduction: Restless Legs Syndrome (RLS) affects approximately 10% of the general population, yet it remains poorly characterized and investigated. Despite advancements in the management of RLS in recent years, the disorder still suffers from low recognition, unanimous definition, and inconsistent therapeutic approaches.

Objectives: The study aims to gather insights into the knowledge and clinical experiences of Italian neurologists in diagnosing, managing, and treating RLS, examining the approaches among movement disorder specialists, sleep experts, and general neurologists.

Methods: Members of the Italian Society of Neurology, Italian Society Parkinson and Movement Disorders, and the Italian Association of Sleep Medicine were invited via email to participate in a 21-question online survey.

Results: A total of 343 neurologists completed the survey. In defining RLS, neurologists predominantly categorized it as a "sleep-related movement disorder". Most neurologists reported managing between 5-15 RLS patients annually, with sleep specialists generally managing the highest patient volume among specialists. Diagnostic approaches showed that about 34% strictly followed all five essential diagnostic criteria, with 84% conducting blood tests after diagnosis. Sleep specialists were more likely to use polysomnography. Monotherapy emerged as the preferred treatment modality, specifically dopamine agonists (69%). Treatment preferences significantly varied among specialists: movement disorder experts predominantly opted for dopamine agonists, while sleep specialists were more inclined towards iron supplementation. Regular screening for iron levels was common, primarily supplementing based on serum iron alterations. When initial treatments proved ineffective, increasing dopamine agonist dosage was the preferred strategy (40%).
Conclusions: Overall, the results reflect a lack of a clear conceptualization of RLS, with a prevalent misconception of RLS as a movement disorder influencing treatment approaches. Different

conceptualization and management of RLS emerged among sleep experts, experts in movement disorders and general neurologists. This points to the need for better diagnostic clarity and guideline adherence in RLS management.

P25

Phenotypical and treatment response heterogeneity in a cohort of normal pressure hydrocephalus patients

Alessandro Di Maio[1,2], G. Lazzeri[1,2], F. Arienti[1,2], F. Ruggiero[3], F. Mameli[3], A.B. Di Fonzo[1,2], G. Franco[1,2]

[1]Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Neurology Unit, Milano, Italy, [2]Dino Ferrari Centre, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[3]Neuropsychology and Psychology Service for Movement Disorders, Department of Neurophysiopathology, Ospedale Maggiore Policlinico, Milano, Italy

Introduction: NPH is a potentially reversible neurological syndrome characterized by cerebral ventricles enlargement associated with motor, urinary, and cognitive symptoms that lead to serious disability such as gait disturbances, complete urinary incontinence, and severe dementia [1].

Objectives: To clinically characterize a cohort of patients with normal pressure hydrocephalus (NPH) to identify possible clinical and humoral biomarkers that can predict the response to the treatment.

Methods: 57 patients with a diagnosis of idiopathic NPH that underwent tap-test (TT) procedure were retrospectively enrolled at the Neurology Department of Policlinico Hospital in Milan from 2012 to 2021.

Results: The mean age of enrolled patients was 72,5 years. 74% of them displayed motor symptoms at onset, 30% postural instability and falls, 37% urinary dysfunctions, and 56% cognitive impairment. Evans' Index was > 0.3 in 86% of them. The median volume of collected CSF was 37.5 ml and 49 (86.0%) patients improved after TT (responders); the improvement was observed in motor (85%), urinary (20%), and cognitive function (38%). The mean CSF beta-amyloid level was 562.5 pg/ml. 20 patients (35%) underwent VP surgery, and 89% of them showed an improvement in motor, 44% in urinary, and 46% in cognitive symptoms. Responders showed an earlier age of onset compared to non-responders, in addition to lower instability prevalence at onset, higher CSF collected volume, and a lower CSF beta-amyloid value. Patients who did not undergo VP shunt surgery showed lower scores at Mini-Mental State Examination (MMSE).

Conclusions: This study supports the evidence of a great clinical and therapeutical response heterogeneity and highlights some key aspects that may help clinicians during the diagnostic process, such as TT standardization, evaluation of CSF beta-amyloid levels, and alternative diagnoses exclusion.

References:

[1] R. D. Adams, C. M. Fisher, S. Hakim, R. G. Ojemann, W. H. Sweet, "Symptomatic occult hydrocephalus with 'normal' cerebrospinal-fluid pressure. A treatable syndrome.", N Engl J Med., vol. 15, pp. 117-26, Jul. 1965.

P26

Use of wearable accelerometers in patients with Friedreich's Ataxia: results of 1 year longitudinal study monitoring real-life activity

Mario Fichera[1], L. Nanetti[1], A. Mongelli[1], A. Castaldo[1], G. Marchini[1], M. Neri[2], X. Vukaj[3], M. Marzorati[3], S. Porcelli[2], C. Mariotti[1]

[1]Unit of Medical Genetics and Neurogenetics, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[3]Institute of Biomedical Technologies, National Research Council, Segrate, Italy

Introduction: Remote monitoring with wearable sensors can be used to collect digital measures related to the motor activity of the patient in a real-life setting outside clinical visits. Quantitative motor outcome measures may complement neurological evaluation and provide additional information regarding the effect of therapeutical interventions on patients' daily life.

Objectives: To assess the performances of wearables sensors to detect changes in physical activity over one year in patients with Friedreich ataxia (FRDA).

Methods: We recruited 26 patients with FRDA and 13 age-sex matched healthy controls. All patients were ambulatory at baseline. Participants were asked to wear two wearable sensors, at nondominant wrist and at waist, for 7 days. Clinical evaluation with ataxia rating scales and functional tests were performed at baseline and at 1-year follow-up. Measures extracted from accelerometers included: percentage of sedentary time, time of light and moderate-vigorous (MVPA) physical activities, number of activity bouts, Vector Magnitude on the 3 axes (VM3), and average number of steps/min.

Results: Activity monitoring was well tolerated. At baseline, all the activity monitoring variables differentiated patients from Controls, with patients being significantly more sedentary (81.5% vs. 67.4% of time, $p<0.01$). Accelerometer-based measures were highly correlated ith clinical scales and disease duration in FRDA and showed good eliability. After 1-year interval, activity levels were unchanged in controls, while in FRDA all variables indicated reduced physical activity. Statistically significant changes were observed for: (i) VM3; (ii) percentage of sedentary and light activity, and (iii) percentage of MVPA. Reduction in physical activity correlated with worsening in gait score of the Ataxia Rating Scale (SARA).

Conclusions: Our results indicate that activity monitoring is a well tolerated and sensitive tool for assessing disease severity and functional impairment in individuals with FRDA, thus supporting the usefulness of these measures as complementary tools for future clinical trials.

P27

Social cognition, behavioural and affective alterations in functional movement disorders

Paola Zinzi[1,2], S. Di Tella[3], I. Anzuino[3], M. Petracca[1], M.R. Lo Monaco[4,5], S. Fragapane[6,7], P. Calabresi[1,6], A.R. Bentivoglio[1,6], M.C. Silveri[3,4]

[1]Movement Disorders Unit, Fondazione Policlinico Universitario 'Agostino Gemelli' IRCCS, Rome, Italy
[2]Clinical Psychology Unit, Fondazione Policlinico Universitario 'Agostino Gemelli' IRCCS, Rome, Italy
[3]Università Cattolica del Sacro Cuore, Department of Psychology, Milan, Italy
[4]Center for the Medicine of Aging, Fondazione Policlinico Universitario 'Agostino Gemelli' IRCSS, Rome, Italy
[5]Università Cattolica del Sacro Cuore, Institute of Internal Medicine and Geriatrics, Rome, Italy
[6]Università Cattolica del Sacro Cuore, Institute of Neurology, Rome, Italy
[7]Department of Human Sciences and Quality of Life Promotion, San Raffaele University, Rome, Italy

Introduction and aim: Functional Movement Disorders (FMD) are a heterogeneous group of motor manifestations not attributable to known medical conditions [1]. Psychosocial and affective factors play a role in the origin of FMD. Silveri et al. reported disorders in social cognition in the domain of Theory of Mind (ToM) in FMD [2]. The aims of this study were confirming whether FMD might be related to ToM disorders and exploring the relationship between ToM abilities and psychobehavioral dimensions.

Methods: Twenty-two FMD subjects (19F, 3M, mean age 43±11.2y) underwent computerized Yoni task to assess affective and cognitive dimensions of ToM, at different complexity levels, 1 st or 2nd order [3]. Yoni also includes control items (physical dimension). Participants were cognitively screened with MoCA and Cognitive Estimation Task (bizarreness score). Their psychobehavioural status was evaluated with DES-II (dissociation), BAI (anxiety), BDI-II (depression), TAS-20 (alexithymia), BPI (pain), SF-12 (health-related quality of life), and MFI-20 (fatigue).

Results: No differences emerged in the Yoni accuracy between 1st order cognitive, affective, and physical items ($p>0.1$). A significant difference emerged on 2nd order items ($p<0.001$); in particular, FMD scored worse on cognitive and affective than control items ($ps\leq0.001$). Accuracy on cognitive 2nd order items was negatively correlated with anxiety ($p=0.024$), TAS-20 difficulty describing feelings ($p=0.013$), global fatigue ($p=0.029$) and bizarreness ($p=0.029$). When considering affective 2nd order items, significant correlations emerged with anxiety ($p=0.001$), global alexithymia ($p=0.036$) and mental fatigue ($p=0.042$). Interestingly, affective 1st items resulted also correlated with anxiety ($p=0.014$) and global alexithymia ($p=0.034$).

Conclusions: The results are consistent with the hypothesis that a ToM disorder might underlie FMD. The Yoni task highlighted the decay of the more complex ToM inferences both cognitive and affective second-order levels of reasoning. Moreover, these data contribute to highlight the relationship between disorders of social cognition, such as ToM, and emotion regulation.

References:

[1] Baizabal-Carvallo JF, Hallett M, Jankovic J. Pathogenesis and pathophysiology of functional (psychogenic) movement disorders. Neurobiology of Disease . 2019; 127:32-44.
[2] Silveri MC, Di Tella S, Lo Monaco MR, Petracca M, Tondinelli A, Antonucci G, Pozzi G, Di Lazzaro G, Calabresi P, Bentivoglio AR. Theory of mind: A clue for the interpretation of functional movement disorders. Acta Neurologica Scandinavica. 2022 May;145(5):571-578.

[3] Rossetto F, Castelli I, Baglio F, Massaro D, Alberoni M, Nemni R, Shamay-Tsoory S, Marchetti A. Cognitive and Affective Theory of Mind in Mild Cognitive Impairment and Parkinson's Disease: Preliminary Evidence from the Italian Version of the Yoni Task. Developmental Neuropsychology. 2018;43(8):764-780.

P28

Role of rest tremor pattern and REM behaviour disorder in the diagnosis of tremulous disorders

Jolanda Buonocore[1], A. Quattrone[1], R. Nisticò[2], M. Morelli[1], G. Arabia[1], M. Crasà[2], M. De Maria[2], P.P. Arcuri[3], P. Zoleo[1], B. Vescio[4], G.L. Cascini[5], A. Quattrone[2]

[1]Institute of Neurology, Department of Medical and Surgical Sciences, Magna Graecia University, Catanzaro, Italy
[2]Neuroscience Research Centre, Department of Medical and Surgical Sciences, Magna Graecia University, Catanzaro, Italy
[3]Institute of Radiology, Azienda Ospedaliera Dulbecco, Catanzaro, Italy
[4]Biotecnomed S.C.aR.L. Catanzaro, Italy
[5]Institute of Nuclear Medicine, University "Magna Graecia", Catanzaro, Italy

Introduction: The differential diagnosis of rest tremor (RT) disorders is challenging, often requiring single photon emission computed tomography with ^{123}I-ioflupane [1].

Objective: To investigate the performance of RT pattern [2-3] and RBD Single-Question-Screen (RBD1Q) [4] in distinguishing RT patients with and without striatal dopaminergic deficit.

Methods: We enrolled 181 consecutive patients presenting with RT. All patients underwent neurological examination, surface electromyography, RBD1Q and ^{123}I-ioflupane. The RT pattern was visually assessed by two expert raters and confirmed by quantitative phase calculation in all patients. We investigated the performance of RT pattern evaluated together with RBD1Q into a simple decision tree in predicting the ^{123}I-ioflupane result.

Results: Our cohort included 103 RT patients with alternating pattern (48.5% with positive RBD1Q [RBD+] and 51.5% with negative RBD1Q [RBD+]) and 78 patients with synchronous pattern (24.4% RBD+ and 75.6% RBD-) The combination of RT pattern with RBD1Q showed a better performance than these two single features used separately. The association of alternating RT pattern and RBD1Q+ had the best PPV value (94%) whereas the synchronous RT pattern associated with RBD1Q- showed the highest NPV 86.4% value in predicting ^{123}I-ioflupane result.

Conclusions: The combined use of RT pattern and RBD1Q may represent a quick, low-cost and available first-level test which may be used as surrogate biomarker of ^{123}I-ioflupane in patients with RT, especially in healthcare centres with limited resources and access to dopamine imaging diagnostic procedures.

References:

[1] Scherfler C, Schwarz J, Antonini A, et al. Role of DAT-SPECT in the diagnostic work up of parkinsonism. Mov Disord. 2007 ; 22(9):1229-38. doi: 10.1002/mds.21505.
[2] Nisticò R, Pirritano D, Salsone M, et al. Synchronous pattern distinguishes resting tremor associated with essential tremor from rest tremor of Parkinson's disease. Parkinson- ism Relat Disord 2011;17(1):30–33. https://doi.org/10.1016/j.parkreldis.2010.10.006.
[3] Quattrone A, Nisticò R, Morelli M, Arabia G, Crasà M, Vescio B, Mechelli A, Cascini GL, Quattrone A. Rest Tremor Pattern Predicts DaTscan (123 I-Ioflupane) Result in Tremulous Disorders. Mov Disord. 2021; 36: 2964-2966. doi: 10.1002/mds.28797.
[4] Postuma RB, Arnulf I, Hogl B, et al. A single-question screen for rapid eye movement sleep behavior disorder: a multicenter validation study. Mov Disord. 2012; 27: 913-6. doi: 10.1002/mds.25037.

P29

Moving Ear Syndrome: a rare but treatable phenomenon

Vidal Yahya[1,2], R.C. Chavez[1,2], L. Campiglio[1,2], M. Zardoni[1,2], A. Priori[1,2]

[1]Aldo Ravelli Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Neurology Unit, ASST Santi Paolo e Carlo, San Paolo University Hospital, Milan, Italy

Introduction: The external ear muscles are vestigial muscles innervated by the facial nerve that only 1 in 5 people can voluntarily contract. Ear dyskinesia, namely Moving Ear Syndrome (MES), is a phenomenologically rare disorder consisting in a rhythmic/semirhythmic contraction of external ear muscles, typically disappearing with sleep and voluntary face movements, and causing pain or discomfort [1–4]. Ear dyskinesia has no clear etiology yet, however it has been repeatedly associated with neuroactive drugs (e.g., SSRIs, neuroleptics, methylphenidate) [4–6]. Besides pharmacological approaches (clonazepam, pregabalin, propranolol) and the anecdotal use of pallidothalamic tractotomy, botulinum toxin injection seems to be the most effective therapy [5–10].

Objectives: To integrate clinical, neurophysiological, and therapeutical features of a patient with Moving Ear Syndrome.

Methods: A patient with MES has been clinically evaluated and underwent EMG-US-guided botulinum toxin injection.

Results: A 55-year-old man presented with involuntary repetitive backwards twitching of the right ear associated with discomfort and inner tension, that could not be suppressed and persisted during sleep, in absence of other movement disorders. The movements started 4 months prior to the evaluation and progressively worsened in frequency and amplitude, occurring several times per day and lasting for few minutes. The patient had a history of severe traumatic brain injury with left temporal encephalomalacia, followed by involuntary left ear wiggling partially resolved with transitory administration of phenobarbital. A pharmacological attempt with clonazepam was ineffective on right ear dyskinesia. Needle-EMG revealed rhythmic 400-500 ms bursts from the right auricularis posterior muscle, thus 10 units of onabotulimtoxin A were injected with EMG-US guide, with a significative reduction in frequency of the twitching after two weeks.

Conclusions: Whereas MES' etiology and pathophysiology are poorly understood, botulinum toxin injection with EMG and US guidance represents a safe and effective therapeutical option for this rare condition.

References:

[1] Keshavan MS. The ear wigglers: tics of the ear in 10 patients. Am J Psychiatry. 1988;145(11):1462-1463. doi:10.1176/ajp.145.11.1462.
[2] Kirk A, Heilman KM. Auricular Myoclonus. Can J Neurol Sci / J Can des Sci Neurol. 1991;18(4):503-504. doi:10.1017/S0317167100032236.
[3] Caviness JN, Gabellini A, Kneebone CS, Thompson PD, Lees AJ, Marsden CD. Unusual focal dyskinesias: the ears, the shoulders, the back, and the abdomen. Mov Disord. 1994;9(5):531-538. doi:10.1002/mds.870090505.
[4] Carluer L. Ear dyskinesia. J Neurol Neurosurg Psychiatry. 2006;77(6):802-803. doi:10.1136/jnnp.2004.058511. Sekeff-Sallem F, Pedroso J, Barsottini O. Moving ear syndrome secondary to bromopride and response to botulinum toxin. Mov Disord. 2019;34(1): S599-S600.
https://www.embase.com/search/resultssubaction=viewrecord&id=L631397497&from=export
[6] Naguy A, Alrashidi F, Elsori DH. Methylphenidate-induced "Moving Ear Syndrome" in a child with ADHD responding favorably to add-on propranolol. Asia-Pacific Psychiatry. 2019;11(1). doi:10.1111/appy.12347.

[7] Srirompotong S, Saeseow P, Kharmwan S, Srirompotong S. Ear wiggling tics: Treatment with botulinum toxin injection. Eur Arch Oto-Rhino-Laryngology. 2007;264(4):385-387. doi:10.1007/s00405-006-0200-1.
[8] Godeiro-Junior C, Felicio AC, Felix EPV, et al. Moving ear syndrome: The role of botulinum toxin. Mov Disord. 2008;23(1):122-124. doi:10.1002/mds.21773.
[9] Jabbour CE, Sawaya RA, Zaytoun GM. Auricular Myoclonus: A Case Report and Literature Review. J Int Adv Otol. 2021;17(6):581-583. doi:10.5152/iao.2021.21064.
[10] Kim K, Horisawa S, Kohara K, Nonaka T, Kawamata T, Taira T. Successful treatment of auricular dystonia by unilateral pallidothalamic tractotomy. Tremor and Other Hyperkinetic Movements. 2021;11(1):1-5. doi:10.5334/tohm.579.

P30

Bilateral chorea in a patient with idiopatic erythrocythosis: a rare manifestation of polycythemia vera

Marco Domenico Scanni[1,2], F. Bellizzi[1,2], G. Ermanis[1,2], C. Del Regno[1,2], A. Bernardini[2], E. Belgrado[3], F. Janes[2], G. Pellitteri[2], M. Valente[1,2]

[1]Department of Medicine (DAME), University of Udine, Udine, Italy
[2]Clinical Neurology Unit, Presidio Ospedaliero Santa Maria della Misericordia, Azienda Sanitaria Santa Maria Misericordia, Udine, Italy
[3]Neurology Unit, Presidio Ospedaliero Santa Maria della Misericordia, Azienda Sanitaria Santa Maria Misericordia, Udine, Italy

Introduction: Polycythemia Vera is a haematological disorder characterised by haemoglobin/hematocrit level above 16.5 g/dL/49% in males and 16 g/dL/48% in females, associated with positivity for JAK2 mutations [1]. The most common neurological complication of Polycythemia Vera is ischemic stroke; less common manifestations include headache, weakness, dizziness and movement disorders [2]. Here we describe a rare presentation of bilateral chorea in a 83-year-old female: the patient initially exhibited a hyperkinetic syndrome characterised by involuntary choreiform movements in the left upper limb, then radiating to the left lower limb, and finally involving the right limbs, with progressive limitations in ambulation and levels of autonomy in daily activities; haematological abnormalities consistent with polycythemia were found at blood tests, prompting further investigation into the diagnosis and neurological implications of the haematological disorder.

Objectives: To delineate the clinical course, diagnostic work-up, and management of choreic manifestations in the context of a JAK2-mutated Polycythemia Vera patient.

Methods: Comprehensive haematological, neurological, and imaging assessments were conducted to elucidate the underlying aetiology of bilateral chorea in the patient. Treatment strategies included antidopaminergic medications and phlebotomy.

Results: The patient's initial haematological findings revealed marked polycythemia. Neurological evaluation and imaging ruled out structural lesions, data confirmed also by 18-FDG PET imaging. Suspecting Polycythemia Vera, a JAK2 mutation was searched and turned out to be positive. Other plausible causes of chorea were excluded. Our patient underwent optimal haematologic management with consecutive phlebotomies; targeted therapy resulted in clear improvement of choreiform movements.

Conclusions: This case highlights an uncommon manifestation of JAK2- mutated Polycythemia Vera resulting in bilateral chorea. The findings underscore the necessity for a multidisciplinary approach in managing complex cases involving myeloproliferative neoplasms and neurological manifestations. Further research is essential to clarify the underlying pathophysiological mechanisms and optimise therapeutic interventions.

References:

[1] Tefferi A, Vannucchi AM, Barbui T. Polycythemia vera: historical oversights, diagnostic details, and therapeutic views. Leukemia. 2021;35(12):3339-3351. doi:10.1038/s41375-021-01401-3.
[2] Marvi MM, Lew MF. Polycythemia and chorea. Handb Clin Neurol. 011;100:271-6. doi: 10.1016/B978-0-444-52014-2.00019-7.

P31

Cognitive improvement after endoscopic third ventriculostomy surgery in long-standing overt ventriculomegaly in adults

Enrico Belgrado[5], F. Campanella[1], D. Piccolo[1,2,3], G. Sebastianutto[1,4], F. Marotta[1,2], M. Skrap[1], F. Tuniz[1], M. Valente[6]

[1]Neurosurgery Unit, Udine University Hospital, Udine, Italy
[2]Department of Neuroscience, University of Padua, Padova, Italy
[3]Department of Clinical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy
[4]Department of General Psychology, University of Padua, Padua, Italy
[5]Neurologic Unit, Udine University Hospital, Udine, Italy
[6]Department of Medicine (DAME) Neurologic Clinic, University of Udine, Udine, Italy

Introduction: Long-standing overt ventriculomegaly in adults (LOVA) is a chronic form of hydrocephalus that may lead to cognitive decline. This study aimed to evaluate the cognitive outcomes of endoscopic third ventriculostomy (ETV) surgery in patients with LOVA hydrocephalus.

Methods: Twenty consecutive patients with LOVA hydrocephalus underwent ETV surgery, and their cognitive status was assessed before surgery, immediately after surgery, and at four months follow-up. Cognitive function was assessed using a neuropsychological battery that measured six cognitive domains: general cognitive status, attention/executive function, language, visuospatial ability, short-term memory, and long-term memory (LTM). Cognitive reserve was also measured using the Italian version of the National Adult Reading Test (NART).

Results: LTM was the only cognitive domain that was significantly impaired in patients with LOVA hydrocephalus, and immediate postoperative improvement was observed. The amount of immediate improvement in LTM was directly correlated with cognitive reserve, as measured by the NART. Improvement in LTM was maintained at the 4-month follow-up evaluation.

Conclusions: ETV surgery may lead to immediate improvement in LTM in patients with LOVA hydrocephalus. These findings suggest that ETV surgery may be an effective treatment for LOVA hydrocephalus, and that cognitive reserve may be an important factor in predicting outcomes after surgery. Further studies with larger sample sizes are needed to confirm these findings and to determine the long-term effects of ETV surgery on cognitive function in patients with LOVA hydrocephalus.

P32

The mitigating effect of coffee

Lorenzo Bresciani[1], G. Bonato, M. Carecchio[1,2]

[1]Parkinson and Movement Disorders Unit, Centre for Rare Neurological Diseases (ERN-RND), Department of Neuroscience, University of Padova, Padova, Italy
[2]Center for Neurodegenerative Disease Research (CESNE), University of Padova, Padova, Italy

Introduction: ADCY5 mutations are a rare genetic cause of early-onset hyperkinetic movement disorders, characterized by psychomotor developmental delay, axial hypotonia and generalized chorea and dystonia that often worsen upon awakening and before falling asleep. The disease course is variable, with paroxysmal exacerbations considered a red flag for the disease. [1, 2].

Objectives: To describe the improvement of ADCY5-related movement disorders in a pediatric patient following combination of DBS and caffeine.

Methods: Video recording, genetic analysis.

Results: This 14 year-old girl had a history of delayed psychomotor milestones, axial hypotonia and generalized choreo-dystonic movements also involving the facial muscles since age 10 months, with a non-progressive course but recurrent exacerbation upon awakening. At the age of 10 years, bilateral GPi Deep Brain Stimulation (DBS) was performed, with overall improvement of hyperkinetic movements. Neurological examination at age 14 showed cervical hypotonia, speech dysarthria and saliva drooling. Gait was independent but unsteady and generalized chorea also involving perioral muscles, exacerbated by motor or cognitive tasks, was observed. Dystonic posturing of upper limbs was present, with mild difficulty in performing fine motor tasks. Motor impersistence was present on tongue prolonged protrusion, as well as bilateral mild ptosis with partial limitation of upgaze.
An ADCY5 de novo mutation (p. Arg418Trp) was found by genetic analysis (NGS panel). At the age of eleven, she was started on caffeine, followed by further amelioration of chorea; the effect of caffeine started about 20 minutes after intake and lasted for few hours, with a documented wearing-off in between doses.

Conclusions: ADCY5-related movement disorders can benefit from pallidal DBS associated with regular caffeine intake, that can significantly reduce the burden of disability in mutation carriers.

References:

[1] Carecchio, M., et al., ADCY5-related movement disorders: Frequency, disease course and phenotypic variability in a cohort of paediatric patients. Parkinsonism Relat Disord, 2017. 41: p. 37-43.
[2] Ferrini, A., et al., An Update on the Phenotype, Genotype and Neurobiology of ADCY5-Related Disease. Movement Disorders, 2021. 36.

P33

Left upper limb paralysis and ballismus in non-ketotic hyperglycemia

Lorenzo Bresciani[1], B. Savini[1], P. Santurelli[1], G. Bonato[1,2], M. Carecchio[1,2]

[1]Parkinson and Movement Disorders Unit, Centre for Rare Neurological Diseases (ERN-RND), Department of Neuroscience, University of Padova, Italy
[2]Center for Neurodegenerative Disease Research (CESNE), University of Padova, Italy

Introduction: Non-ketotic hyperglycemia (NKH) is associated with a wide range of neurological presentations and it is a frequently a misdiagnosed cause of hemichorea/hemiballismus [1-3].

Methods: We report the case of an elderly woman who developed iatrogenic hyperglycemia and focal loss of power in the left upper limb, with superimposed ballistic movements.

Results: This 76 y.o. woman complained of rapid onset of complete loss of power in the left upper limb, with superimposed involuntary movements that developed within hours two days prior our neurological evaluation. The patient had a history of pancreatic adenocarcinoma surgically removed and she was on active chemotherapy (gemcitabine-abraxane). A brain CT scan did not document acute brain lesions. On neurological examination, complete loss of power (0/5 on MRC scale) and reduced muscular tone were observed in the left upper limb, with superimposed hyperkinetic subcontinuous involuntary movements with wide and irregular amplitude. No other neurological abnormality were found. The electroencephalogram did not show epileptiform discharges timelocked with the involuntary movements. Brain MRI was unremarkable, without lesions in the right motor pathways. On admission, the blood exams were performed and plasma glucose levels turned out to be elevated (31.5 mmol/L -567 mg/dL). Subsequent progressive normalization of blood glucose via continuous insulin infusion pump was associated with the progressive disappearance of ballistic movements and full recovery of muscular strength in the left upper limb within two days.

Conclusions: To our knowledge this is the first documented case of NKH presenting with concomitant positive and negative symptoms. It has been postulated that the dyskinesia may be related to neuronal depletion of gamma-aminobutyric acid, secondary to Kreb's cycle disruption, whereas the complete paralysis may result from the local hypoperfusion due to the hyperosmolar state [1, 3].

References:

[1] Arecco, A., et al., Diabetic striatopathy: an updated overview of current knowledge and future perspectives. J Endocrinol Invest, 2023.
[2] Chua, C.B., et al., "Diabetic striatopathy": clinical presentations, controversy, pathogenesis, treatments, and outcomes. Sci Rep, 2020. 10(1): p. 1594.
[3] Rossi, S., et al., Acute stroke-like deficits associated with nonketotic hyperglycemic hyperosmolar state: an illustrative case and systematic review of literature. Neurol Sci, 2022. 43(8): p. 4671-4683.

P34

VPS16-related dystonia: the phenotypic spectrum widens

Edoardo Monfrini[1], L. Avanzino[2,3], G. Palermo[4], G. Bonato[5], G. Brescia[1,6], R. Ceravolo[4], G. Cantarella[7,8], P. Mandich[3,9], H. Prokisch[10,11], K. Storm van's Gravesande[12], G. Straccia[13], A.E. Elia[13], C. Reale[13], C. Panteghini[13], G. Zorzi[15], R. Eleopra[13], R. Erro[16], F. Blandini[1], M. Carecchio[4], B. Garavaglia[14], M. Zech[10,11,17], L.M. Romito[13], A.B. Di Fonzo[1]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy
[2]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy
[3]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[4]Center for Neurodegenerative Diseases, Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[5]Parkinson and Movement Disorders Unit, Centre for Rare Neurological Diseases (ERN-RND), Department of Neuroscience University of Padua, Padua Italy
[6]Medical Genetics Laboratory, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[7]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy
[8]Department of Otolaryngology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[9]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal, and Child Health, University of Genoa, Genoa, Italy
[10]Institute of Neurogenomics, Helmholtz Munich, Neuherberg, Germany
[11]Institute of Human Genetics, Technical University of Munich, School of Medicine, Munich, Germany
[12]Department of Pediatrics, Child and Adolescent Psychosomatics, Technical University Munich, Munich and Department of Pediatric Neurology, University Children's Hospital Freiburg, Freiburg, Germany
[13]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[14]Medical Genetics and Neurogenetics Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[15]Department of Pediatric Neuroscience, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[16]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Salerno, Italy
[17]Institute for Advanced Study, Technical University of Munich, Garching, Germany

Background: VPS16 pathogenic variants have been recently associated with inherited dystonia and they appear to be a relatively common cause of monogenic dystonia. Most patients affected by dominant VPS16-related disease display early-onset isolated dystonia with prominent oromandibular, bulbar, cervical, and upper limb involvement, followed by slowly progressive generalization.

Cases: We describe six newly reported dystonic patients carrying VPS16 mutations collected in a multicenter study displaying unusual phenotypic features in addition to dystonia, such as myoclonus, choreoathetosis, pharyngospasm and freezing of gait, not associated to adult onset VPS16-dystonia so far. Five novel pathogenic variants will be reported. DBS-GPi was effective in managing dystonia in three patients.

Conclusions: This multicentric case series expands the genetic and clinical spectrum of VPS16-related disease, prompting movement disorder specialists to suspect mutations of this gene not only in patients with isolated dystonia. The findings have relevance in the diagnostic process and help in the decision of the best therapeutic option for these patients.

References:

[1] Steel D, Zech M, Zhao C, Barwick KES, Burke D, Demailly D, Kumar KR, Zorzi G, Nardocci N, Kaiyrzhanov R, Wagner M, Iuso A, Berutti R, Škorvánek M, Necpál J, Davis R, Wiethoff S, Mankad K, Sudhakar S, Ferrini A, Sharma S, Kamsteeg EJ, Tijssen MA, Verschuuren C, van Egmond ME, Flowers JM, McEntagart M, Tucci A, Coubes P, Bustos BI, Gonzalez-Latapi P, Tisch S, Darveniza P, Gorman KM, Peall KJ, Bötzel K, Koch JC, Kmieć T, Plecko B, Boesch S, Haslinger B, Jech R, Garavaglia B, Wood N, Houlden H, Gissen P, Lubbe SJ, Sue CM, Cif L, Mencacci NE, Anderson G, Kurian MA, Winkelmann J; Genomics England Research Consortium. Loss-of-Function Variants in HOPS Complex Genes VPS16 and VPS41 Cause Early Onset Dystonia Associated with Lysosomal Abnormalities. Ann Neurol. 2020 Nov;88(5):867-877. doi: 10.1002/ana.25879. Epub 2020 Sep 21. PMID: 32808683.

[2] Monfrini E, Zech M, Steel D, Kurian MA, Winkelmann J, Di Fonzo A. HOPS-associated neurological disorders (HOPSANDs): linking endolysosomal dysfunction to the pathogenesis of dystonia. Brain. 2021 Oct 22;144(9):2610-2615. doi: 10.1093/brain/awab161. PMID: 33871597.

[3] Monfrini, Edoardo, et al. "Dominant VPS16 pathogenic variants: not only isolated dystonia." Movement Disorders Clinical Practice. Accepted Manuscript.

P35

Phenotype's evolution of Cervical Dystonia (CD) in patients treated with Botulinum toxin

Assunta Trinchillo[1,2], N. Cuomo[1], F. Habetswallner[3], M. Esposito[3]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, "Federico II" University, Naples, Italy
[2]Neuroscience and Cell Biology Institute, Neuromodulation and Motor Control Section, St George's University of London, London, United Kingdom
[3]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy

*Background***:** Cervical dystonia (CD) is an intricate neurological condition whose phenotypes and kinds of muscles involved may change over the years. Objective of the study is to evaluate how postural alterations of the head and neck can evolve over the years in patients with CD regularly treated with botulinum toxin (BoNT). In patients presenting a pattern's switch, we aim to identify the time period within those changes may occur, the most predisposed CD phenotypes and possible predisposing factors [1,2,3,4,5].

Methods: We divided idiopathic CD patients into two groups – switch YES and NO, collecting general clinical and demographic variables. We added to general clinical variables the duration of BoNT treatment, Tsui total scores and rotation, tilt and antero/retroversion subscores – assessed at T0 - before BoNT start - and at T1 - switch time in the YES group or last visit in the NO group. The risk of switch was assessed by Kaplan Meyer curves and Cox regression analysis. Finally, Multivariate linear regressions were employed to assess if Tsui severity correlated with the switch.

Results: Among 100 patients (60 women) aged 47.9 years (SD 15.3) at CD onset, 37 experienced a phenotype switch, mostly in the first five years of BoNT treatment, YES and NO groups were comparable.
Multivariate Cox Regression revealed the presence of laterocollis or rotatocollis at T0 as predictors of switch (respectively P=0.01, HR=3.5; P=0.03, HR=1.5). Multivariate linear regressions revealed that high Tsui subscores for the tilt and low Tsui total scores were risk factors for the switch (respectively P=0.002, OR=6; P=0.03, OR=0.8).

*Discussion***:** Latero and Rotatocollis are the CD phenotypes most predisposed to switch. CD characterized by neck tilt are more likely to change phenotype following treatment. Dystonias with a low degree of severity improve after treatment with botulinum toxin, changing to a different and even simpler phenotype [6,7].

References:

[1] Tatu L, Jost WH. Anatomy and cervical dystonia : "Dysfunction follows form". J Neural Transm (Vienna). 2017 Feb;124(2):237-243. doi: 10.1007/s00702-016-1621-7. Epub 2016 Sep 13. PMID: 27624726.
[2] Mink JW. Basal ganglia mechanisms in action selection, plasticity, and dystonia. Eur J Paediatr Neurol. 2018 Mar;22(2):225-229. doi: 10.1016/j.ejpn.2018.01.005. Epub 2018 Jan 17. PMID: 29396175;
PMCID: PMC5815934.
[3] Maia FM, Kanashiro AK, Chien HF, Gonçalves LR, Barbosa ER. Clinical changes of cervical dystonia pattern in long-term botulinum toxin treated patients. Parkinsonism Relat Disord. 2010 Jan;16(1):8-11. doi: 10.1016/j.parkreldis.2009.06.004. Epub 2009 Jul 8. PMID: 19589716.
[4] Kojovic M, Caronni A, Bologna M, Rothwell JC, Bhatia KP, Edwards MJ. Botulinum toxin injections reduce associative plasticity in patients with primary dystonia. Mov Disord. 2011 Jun;26(7):1282-9. doi:
10.1002/mds.23681. Epub 2011 Apr 5. PMID: 21469207; PMCID: PMC4235250.
[5] Nevrlý M, Hluštík P, Hok P, Otruba P, Tüdös Z, Kaňovský P. Changes in sensorimotor network activation after botulinum toxin type A injections in patients with cervical dystonia: a functional MRI study. Exp Brain Res. 2018 Oct;236(10):2627-2637. doi: 10.1007/s00221- 018-5322-3. Epub 2018 Jul 3. PMID: 29971454; PMCID: PMC6153868.

[6]. Röijezon U, Jull G, Djupsjöbacka M, Salomoni SE, Hodges PW. Deep and superficial cervical muscles respond differently to unstable motor skill tasks. Hum Mov Sci. 2021 Dec;80:102893. doi: 10.1016/j.humov.2021.102893. Epub 2021 Nov 9. PMID: 34763288.
[7] Elgueta-Cancino E, Marinovic W, Jull G, Hodges PW. Motor cortex representation of deep and superficial neck flexor muscles in individuals with and without neck pain. Hum Brain Mapp. 2019 Jun 15;40(9):2759-2770. doi: 10.1002/hbm.24558. Epub 2019 Mar 5. PMID: 30835902; PMCID: PMC6865448.

P36

Does thyroid diseases contribute to the natural history of idiopathic adult-onset dystonia? Data from the Italian Dystonia Registry

Sarah Idrissi[1], V. Velucci[1], M. Esposito[2], A. Trinchillo[3,29], F. Habetswallner[2], D. Belvisi[4,30], G. Fabbrini[4,30], G. Ferrazzano[4], V. Rizzo[5], C. Terranova[5], P. Girlanda[5], R. Pellicciari[1], L. Avanzino[6,7], F. Di Biasio[7], R. Marchese[7], F. Bono[8], G. Idone[8], V. Laterza[8], C. Lettieri[9], S. Rinaldo[10], R. Eleopra[10], A. Castagna[11], M.C. Altavista[12], V. Moschella[12], R. Erro[13], P. Barone[13], P. Barbero[14], R. Ceravolo[15], S. Mazzucchi[15], M.M. Mascia[16], T. Ercoli[16], A. Muroni[16], M. Zibetti[17], L. Lopiano[17], C.L.M. Scaglione[18], A.R. Bentivoglio[19], M. Petracca[19], L. Magistrelli[20], M.S. Cotelli[21], G. Cossu[22], G. Squintani[23], T. De Santis[24], T. Schirinzi[25], S. Misceo[26], A. Pisani[27,28], A. Berardelli[4,30], G. Defazio[1]

[1]Department of Translational Biomedicine and Neuroscience (DiBraiN), "Aldo Moro" University of Bari, Bari, Italy
[2]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[3]Department of Neurosciences, Reproductive Sciences and Odontostomatology, “Federico II” University, Naples, Italy
[4]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[5] Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[6] Department of Experimental Medicine (DIMES), University of Genoa, Genoa, Italy
[7] IRCCS, Ospedale Policlinico San Martino, Genoa, Italy
[8] Centre for Botulinum Toxin Therapy, Neurologic Unit, A.O.U. Mater Domini, Catanzaro, Italy
[9] Clinical Neurology Unit, "S. Maria della Misericordia" University- Hospital, Udine, Italy
[10] Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[11] IRCCS, Don Carlo Gnocchi Foundation Onlus, Milan, Italy
[12] Neurology Unit San Filippo Neri Hospital ASL Rome, Rome, Italy
[13] Department of Medicine, Surgery and Dentistry “Scuola Medica Salernitana”, University of Salerno, Salerno, Italy
[14] Neurology Unit, Mauriziano Umberto I Hospital, Turin, Italy
[15] Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[16] Neurology Unit, University Hospital of Cagliari, Cagliari, Italy
[17] Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[18] IRCCS Institute of Neurological Sciences, Bologna, Italy
[19] Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[20] Department of Translational Medicine, Movement Disorders Centre, Neurology Unit, University of Eastern Piedmont, Novara, Italy
[21] Neurology Unit, ASST Valcamonica, Esine (Brescia), Italy
[22] Neurology Service and Stroke Unit, Department of Neuroscience, AO Brotzu, Cagliari, Italy
[23] Neurology Unit, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[24] Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano (Milan), Italy
[25] Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[26] Section of Neurology, San Paolo Hospital, Bari, Italy
[27] Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[28] IRCCS Mondino Foundation, Pavia, Italy
[29] Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George’s University of London, London, UK
[30] IRCCS Neuromed Institute, Pozzilli, Italy

Background: A few earlier observations and recent controlled studies pointed to the possible contribution of thyroid diseases in idiopathic adult-onset dystonia (IAOD) [1-7].

Objective: To investigate the association between thyroid status and clinical characteristics of IAOD, focusing on dystonia localization, spread, and associated features such as tremors and sensory tricks.

Methods: Patients were identified from those included in the Italian Dystonia Registry, a multicentre dataset of patients with adult-onset dystonia. The study population included 1518 IAOD patients. Patients with hypothyroidism and hyperthyroidism were compared with those without any thyroid disease.

Results: In the 1518 IAOD patients, 167 patients (11%; 95% CI, 9.5% - 12.6%) were diagnosed with hypothyroidism and 42 (2.8 %; 95% CI, 1.99 - 3.74) with hyperthyroidism. The three groups were comparable in age at dystonia onset, but there were more women than men in the groups with thyroid disease. Analysing the anatomical distribution of dystonia, more patients with blepharospasm were present in the hyperthyroidism group, but the difference did not reach statistical significance after the Bonferroni correction. The remaining dystonia-affected body sites were similarly distributed in the three groups, as did dystonia-associated features and spread.

Conclusion: Our findings provided novel information indicating that thyroid disease has substantially no influence on the most relevant features of IAOD, including age at onset, body localization, several motor and sensory dystonia-associated features, and a tendency to spread. The lack of phenotypic differences among the three groups does not support a direct link between thyroid disorders and IAOD.

References:

[1] Lang AE. Familial Meige syndrome and thyroid dysfunction. Neurology 1985; 35:138.
[2] Miranda M, Bustamante ML, Campero M, et al., Movement disorders in non- encephalopathic Hashimoto's thyroiditis, Park. Relat. Disord. 55 (2018) 141–142.
[3] Loh LM, Hum AY, Teoh HL, Lim EC. Graves' disease associated with spasmodic truncal flexion. Parkinsonism Relat Disord 2005;11:117–119.
[4] Tan EK, Chan LL. Movement disorders associated with hyperthyroidism: expanding the phenotype. Mov Disord 2006;21:1054–1055.
[5] Asirvatham AR, Balachandran K, Mahadevan S, Balasubramanian S. Lingual dyskinesia in hyperthyroidism. BMJ Case Rep. 2017 Dec 7;2017:bcr2017223226. doi: 10.1136/bcr-2017-223226. PMID: 29222211; PMCID: PMC5728249.
[6] Kilic-Berkmen G, Scorr LM, Rosen A, Wu E, Freeman A, Silver M, Hanfelt J, Jinnah HA. Thyroid disease in cervical dystonia. Parkinsonism Relat Disord. 2023 Feb;107:105274. doi: 10.1016/j.parkreldis.2022.105274. Epub 2022 Dec 30.
[7] Defazio G, Berardelli A, Abbruzzese G, et al. Possible risk factors for primary adult onset dystonia: a case-control investigation by the Italian Movement Disorders Study Group. J Neurol Neurosurg Psychiatry. 1998 Jan;64(1):25-32. doi: 10.1136/jnnp.64.1.25.

P37

Does botulinum toxin affect psycho-social aspect in dystonia?

Angelica Marfoli[1], F. Ruggiero[2], F. Mameli[2], D. Mellace[1], A. De Sandi[2], A. Tomaselli[2], E. Zirone[2], S. Barbieri[2], A. Priori[3,4], R. Ferrucci[1,2]

[1]Dipartimento di Oncologia ed Emato-Oncologia, Università degli Studi di Milano, Milan, Italy
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan, Italy
[4]ASST-Santi Paolo e Carlo, S.C. di Neurologia

Introduction: Dystonia is a movement disorder in which sustained muscle contractions give rise to abnormal postures or involuntary movements [1]. It is a disabling and disfiguring disorder that affects activities of daily living and can give people with this disorder a bizarre appearance that is associated with embarrassment and can lead to psychological morbidity, social avoidance and isolation [2]. Intramuscular injection of botulinum toxin (BoNT) is the most effective treatment for motor symptoms in focal dystonia, but little is known about its impact on psychological well-being.

Objectives: The aim was to evaluate psycho-social changes in patients with focal dystonia after starting BoNT treatment using selfreported scales.

Methods: The visual analogue scale (VAS) assessing body selfimage, self-reported depression, self-distress, satisfaction with physical aspects and social avoidance was completed by 11 patients with dystonia and 12 patients with hyperhidrosis as a control group, before botulinum toxin therapy (T0) and after four weeks (T1).

Results: Our results showed that only self-distress improved in patients with dystonia at T1 (ρ=0.01), while in hyperhidrosis group we found that body self-image (ρ=0.05), self-reported depression (ρ=0.02), self-distress (ρ=0.001) and satisfaction with physical aspects (ρ=0.03) improved after treatment with BoNT.

Conclusions: In summary, according to the literature, the treatment of dystonia with BoNT has an effective impact on the motor symptoms and thus has an influence on the psychological distress associated with the disease. Individuals with hyperhidrosis experienced poorer psychological well-being and also suffered from higher levels of distress compared to dystonic patients. This suggests that individuals with this condition are more vulnerable to social aspects than dystonic patients.

References:

[1] Albanese et al., 2013. Mov Disord; 28:863–873.
[2] Anderson et al., 2005. Behavioural Neurology of Movement Disorders; 2nd Edition.

P38

Transcranial alternating current stimulation of the cerebellum in cervical dystonia

Davide Costa[1], D. Birreci[1], M. Passaretti[1], A. Cannavacciuolo[1,2], D. Colella[1], L. Angelini[1], G. Paparella[1,2], A. Guerra[3], A. Berardelli[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy
[3]Parkinson and Movement Disorder Unit, Study Center on Neurodegeneration (CESNE), Department of Neuroscience, University of Padua, Padua, Italy

Introduction: Cervical dystonia (CD) stands as a challenging movement disorder characterized by a complex pathophysiology, including the role of cerebellar abnormalities [1]. Transcranial Alternating Current Stimulation (tACS) is a non-invasive neurophysiological tool capable of entraining brain oscillations in humans. When applied to the primary motor cortex (M1) or cerebellum, tACS exhibits the ability to transiently modulate neuronal activity by synchronizing neural rhythms.

Objective: To explore the effects of cerebellar tACS in CD patients, and to assess its potential in ameliorating motor abnormalities.

Methods: Twelve CD patients, predominantly exhibiting the torticollis phenotype, were included, each matched with age- and gender-matched healthy controls (HC). Objective assessments of fast voluntary neck movements were conducted using a motion system analysis [2]. Peak angular velocity (degree/sec) and movement amplitude (degrees) for both pro- and anti-dystonic movements were measured. Cerebellar stimulation was applied at theta, beta, and gamma frequencies, along with sham stimulation, while patients performed fast voluntary neck movements. The assessments were conducted at least three months post-botulinum toxin injection.

Results: As expected, CD patients performed slower and less ample neck movements compared to HC. Cerebellar tACS had no significant effects on neck movement kinematics in CD patients, irrespective of the stimulation frequency. However, correlation analysis unveiled that cerebellar theta-tACS tended to improve movement velocity, particularly in more severe CD cases ($r = -0.77$; $P < 0.05$).

Conclusions: This study provides novel information into the potential impact of cerebellar tACS on CD. Although overall effects on movement kinematics were negligible, the relationship with severity scores suggests a nuanced therapeutic potential for cerebellar theta-tACS in addressing more severe CD cases. The effects of cerebellar tACS in CD will need to be further investigated through a more in-depth kinematic analysis on a larger number of patients.

References:

[1] Bologna M, Berardelli A. Cerebellum: An explanation for dystonia? Cerebellum Ataxias. 2017 May 12;4:6. doi: 10.1186/s40673-017-0064-8.
[2] Gregori B, Agostino R, Bologna M, Dinapoli L, Colosimo C, Accornero N, Berardelli A. Fast voluntary neck movements in patients with cervical dystonia: a kinematic study before and after therapy with botulinum toxin type A. Clin Neurophysiol. 2008 Feb;119(2):273-80.

P39

The role of poly-electromyography under pharmacological sedation in distinguishing functional from idiopathic dystonia: a pilot study

Fabio Paio[1,3], S. Rinaldo[1], C. Carozzi[2], O. Amanda[2], G. Devigili[1], L.M. Romito[1], R. Cilia[1], N. Golfrè Andreasi[1], M. Corradi[1], A.E. Elia[1], F. Colucci[1], A. Braccia[1], R. Telese[1], M. Tinazzi[3], G. Marco[2], R. Eleopra[1]

[1]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Department of Anaesthesia, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[3]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Functional dystonia (FD) is the most challenging functional movement disorders. Phenomenological signs lack the specificity to distinguish it from idiopathic dystonia (ID) [1]. Most of the clinical-anamnestic details considered key clues for FD may be also observed in ID. Although some neurophysiological differences have been postulated [2], accurate tests and biomarkers for differential diagnosis are still missing.

Objectives: To assess any differences in muscle activity between ID and FD patients at the poly-electromyography (poly-EMG) performed under propofol sedation and its recovery.

Methods: We consequently enrolled 10 patients with clinically definite FD and 17 with ID according to the current criteria [3,4]. Propofol 1% was administered through a peripheral vein until loss of consciousness. Sedation level was monitored continuously by EEG and bispectral index and stratified according to the Observer's Assessment of Alertness/Sedation Scale. Poly-EMG from symptomatic and non-symptomatic muscles was carried out under five scenarios: alertness, mild and deep sedation and, once propofol suspended, partial and full recovery of consciousness.

Results: At the alertness evaluation, co-contractions and prolonged bursts were found without differences in both groups but a subjective greater variability of muscular activity was noted in FD patient ($p=0,001$). During mild sedation, EMG activity persisted in all patients (FD and ID) except one with FD. During deep sedation, EMG activity was not recorded in any FD patient but was found in 53% of ID ($p=0.01$). During partial recovery of consciousness EMG activity was recorded in only one FD patient but in all ID patients ($p<0.0001$). At the end, only 30% of subject with FD compared to 94% of ID presented the same muscular pattern found at the baseline evaluation ($p=0.001$).

Conclusions: The “electrical silence” during deep sedation and especially during partial recovery of consciousness is the strongest neurophysiological marker of “functionality”. A different “dystonic” recruitment at the end may represent a neurophysiological clue for functional incongruence and inconsistency.

References:

[1]. Newby R et al., Mov Disord. 2016; 31(12): 1777-1784. doi:10.1002/mds.26805Dsds.
[2] Quartarone A et al., Brain. 2009; 132(10): 2871-2877. doi:10.1093/brain/awp213Dsd.
[3] Gupta A et al., Curr Opin Neurol. 2009; 22(4): 430-436. doi:10.1097/WCO.0b013e32832dc169.
[4] Albanese A et al., Mov Disord. 2013; 28(7): 863-873. doi:10.1002/mds.25475.

P40

Does sex influence the natural history of idiopathic adult-onset dystonia?

Vittorio Velucci[1], S. Idrissi[1], R. Pellicciari[1], M. Esposito[2], A. Trinchillo[3,4], D. Belvisi[5,6], G. Fabbrini[5,6], G. Ferrazzano[5], C. Terranova[7], P. Girlanda[7], G. Majorana[7], V. Rizzo[7], F. Bono[8], G. Idone[8], V. Laterza[8], L. Avanzino[9,10], F. Di Biasio[10], R. Marchese[10], A. Castagna[11], M. Ramella[11], C. Lettieri[12], S. Rinaldo[13], M.C. Altavista[14], L. Polidori[14], L. Bertolasi[15], M.C. Tozzi[15], R. Erro[16], P. Barone[16], P. Barbero[17], R. Ceravolo[18], M.M. Mascia[19], T. Ercoli[20], A. Muroni[19], C.A. Artusi[21], M. Zibetti[21], C.L.M. Scaglione[22], A.R. Bentivoglio[23], M.S. Cotelli[24], L. Magistrelli[25], G. Cossu[26], A. Albanese[27], G. Squintani[28], T. Schirinzi[29], A.F. Gigante[30], L. Maderna[31], R. Eleopra[13], A. Pisani[32], D. Cassano[33], M. Romano[34], M. Rizzo[34], A. Berardelli[5,6], G. Defazio[1]

[1]Department of Translational Biomedicine and Neuroscience, University of Bari Aldo Moro, Bari, Italy
[2]Clinical Neurophysiology Unit, Antonio Cardarelli Hospital, Naples, Italy
[3]Department of Neurosciences, Reproductive Sciences and Odontostomatology, Federico II University Hospital, Naples, Italy
[4]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[5]Department of Human Neurosciences, University of Rome La Sapienza, Rome, Italy
[6]IRCCS Neuromed Institute, Pozzilli, Italy
[7]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[8]Center for Botulinum Toxin Therapy, Neurologic Unit, Mater Domini University Hospital, Catanzaro, Italy
[9]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[10]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[11]IRCCS Don Gnocchi Foundation, Milan, Italy
[12]Clinical Neurology Unit, Santa Maria della Misericordia University Hospital, Udine, Italy
[13]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[14]Neurology Unit, Presidio Ospedaliero San Filippo Neri, Rome, Italy
[15]Neurologic Unit, Integrated University Hospital of Verona, Verona, Italy
[16]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[17]Neurology Unit, Ospedale Umberto I di Torino, Turin, Italy
[18]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[19]University Hospital of Cagliari, Cagliari, Italy
[20]Sassari University Hospital, Sassari, Italy
[21]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[22]IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy
[23]Institute of Neurology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[24]Neurology Unit, ASST della Valcamonica, Esine, Italy
[25]Department of Translational Medicine, Movement Disorders Centre, Neurology Unit, University of Eastern Piedmont, Novara, Italy
[26]Department of Neuroscience, Neurology Service and Stroke Unit, AO Brotzu, Cagliari, Italy
[27]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Italy
[28]Department of Neurosciences, Biomedicine and Movement Sciences, Neurology Unit, University of Verona, Verona, Italy
[29]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

[30]Section of Neurology, San Paolo Hospital, Bari, Italy
[31]Department of Neurology and Laboratory of Neuroscience, Istituto Auxologico Italiano Istituto di Ricovero e Cura a Carattere Scientifico, Milan, Italy
[32]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[33]Unit of Neurology, Maria Vittoria Hospital, Turin, Italy
[34]Neurology Unit, Villa Sofia Cervello United Hospitals, Palermo, Italy

Introduction: Several earlier studies showed a female predominance in idiopathic adult-onset dystonia (IAOD) affecting the cranial-cervical area and a male preponderance in limb dystonia [1-4]. However, sex related differences may result from bias inherent to study design. Moreover, information is lacking on whether sex-related differences exist in expressing other dystonia-associated features and dystonia spread.

Objective: To provide accurate information on the relationship between sex differences, motor phenomenology, dystonia-associated features, and the natural history of IAOD.

Methods: Data of 1701 IAOD patients from the Italian Dystonia Registry [5] were analysed.

Results: Women predominate over men in blepharospasm, oromandibular, laryngeal and cervical dystonia; the sex ratio was reversed in task-specific upper limb dystonia, and no clear sex difference emerged in non-task-specific upper limb dystonia and lower limb dystonia. This pattern was present at disease onset and the last examination. Women and men did not significantly differ for several dystonia-associated features and tendency to spread. In women and men, the absolute number of individuals who developed dystonia tends to increase from 20 to 60 years and then decline. However, when we stratified by site of dystonia onset, different patterns of female-to-male ratio over time could be observed in the various forms of dystonia.

Conclusions: Our findings provide novel evidence on sex as a key mediator of IAOD phenotype at disease onset. Age-related sexual dimorphism may result from the varying exposures to specific ageand sex-related environmental risk factors interacting in a complex manner with biological factors such as hormonal sex factors.

References:

[1] Soland VL, Bhatia KP, Marsden CD. Sex prevalence of focal dystonias. J Neurol Neurosurg Psychiatry. 1996;60:204-5.
[2] Sex-related influences on the frequency and age of onset of primary dystonia. Epidemiologic Study of Dystonia in Europe (ESDE) Collaborative Group. Neurology. 1999;53:1871-3.
[3] Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. Lancet Neurol. 2004;3:673-8.
[4] LeDoux MS, Vemula SR, Xiao J, Thompson MM, Perlmutter JS, Wright LJ, Jinnah HA, Rosen AR, Hedera P, Comella CL, Weissbach A, Junker J, Jankovic J, Barbano RL, Reich SG, Rodriguez RL, Berman BD, Chouinard S, Severt L, Agarwal P, Stover NP. Clinical and genetic features of cervical dystonia in a large multicenter cohort. Neurol Genet. 2016;2:e69.
[5] Defazio G, Esposito M, Abbruzzese G, Scaglione CL, Fabbrini G, Ferrazzano G, Peluso S, Pellicciari R, Gigante AF, Cossu G, Arca R, Avanzino L, Bono F, Mazza MR, Bertolasi L, Bacchin R, Eleopra R, Lettieri C, Morgante F, Altavista MC, Polidori L, Liguori R, Misceo S, Squintani G, Tinazzi M, Ceravolo R, Unti E, Magistrelli L, Coletti Moja M, Modugno N, Petracca M, Tambasco N, Cotelli MS, Aguggia M, Pisani A, Romano M, Zibetti M, Bentivoglio AR, Albanese A, Girlanda P, Berardelli A. The Italian Dystonia Registry: rationale, design and preliminary findings. Neurol Sci. 2017 May;38(5):819-825.

P41

Occupation as a risk factor for idiopathic dystonias

Vittorio Velucci[1], L. Di Lorenzo[2], I.M. Di Somma[2], M. Esposito[3], S. Idrissi[1], R. Pellicciari[1], L. Avanzino[4,5], G. Fabbrini[6,7], D. Belvisi[6,7], A. Castagna[8], C. Terranova[9], F. Bono[10], M.C. Altavista[11], C. Lettieri[12], C.L.M. Scaglione[13], M. Zibetti[14], P. Barbero[15], R. Erro[16], A.R. Bentivoglio[17], R. Ceravolo[18], L. Magistrelli[19], T. Schirinzi[20], G. Cossu[21], G. Squintani[22], A.F. Gigante[23], M.M. Mascia[24], A. Berardelli[6,7], G. Defazio[1]

[1]Department of Translational Biomedicine and Neuroscience, University of Bari Aldo Moro, Bari, Italy
[2]Department of Interdisciplinary Medicine, Section of Occupational Medicine, University of Bari Aldo Moro, Bari, Italy
[3]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[4]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[5]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[6]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[7]IRCCS Neuromed Institute, Pozzilli, Italy
[8]Don Gnocchi Foundation, Milan, Italy
[9]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[10]Centre for Botulinum Toxin Therapy, Neurologic Unit, A.O.U. Mater Domini, Catanzaro, Italy
[11]Neurology Unit, San Filippo Neri Hospital, Rome, Italy
[12]Clinical Neurology Unit, University-Hospital of Udine, Udine, Italy
[13]IRCCS Institute of Neurological Sciences, Bologna, Italy
[14]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[15]Neurology Unit, Mauriziano Umberto I Hospital, Turin, Italy
[16]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[17]Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[18]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[19]Department of Translational Medicine, Movement Disorders Centre, Neurology Unit, University of Eastern Piedmont, Novara, Italy
[20]Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[21]Department of Neuroscience, Neurology Service and Stroke Unit, AO Brotzu, Cagliari, Italy
[22]Department of Neurosciences, Biomedicine and Movement Sciences, Neurology Unit, University of Verona, Verona, Italy
[23]Section of Neurology, San Paolo Hospital, Bari, Italy
[24]University Hospital of Cagliari, Cagliari, Italy

Introduction: Different body locations of idiopathic adult-onset dystonia (IAOD) are associated with specific demographic and clinical characteristics [1-4], as well as with specific risk factors [5,6]. This suggests that, even if there might be an underlying common pathogenic mechanism, divergent pathogenic processes - in which occupation may play a role - could underlie the various forms of dystonia.

Objectives: To investigate the association between main lifetime occupation and specific forms of idiopathic dystonia at onset, namely blepharospasm, laryngeal dystonia, cervical dystonia, and upper limb dystonia.

Methods: Data on 940 IAOD patients from the Italian Dystonia Registry [7] were analysed. Each patient was assigned to the corresponding occupational category by specialists in occupational medicine according to the ISTAT classification [8]. Logistic regression models (adjusted for sex, year of birth, age at dystonia onset, education, and Italian geographical areas) were computed to compare patients with a specific dystonia at onset to patients with all other forms of dystonia.

Results: Compared to other professions, skilled workers exhibited an increased risk for blepharospasm at onset (OR = 2.0, 95% CI 1.2-3.3), cleaning staff for cervical dystonia (OR = 3.6, 95% CI 1.2-10.3), and musicians for task-specific upper limb dystonia (OR = 24.0, 95% CI 7.4-78.0). No statistically significant association emerged between occupation and laryngeal dystonia. In examining dystonia-associated features, sensory trick was found to be less frequent in musicians, along with a lower frequency of dystonic tremor; conversely, agricultural workers and unskilled professions experienced a higher frequency of dystonic tremor. Finally, homemakers had a greater tendency to spread, while dystonia remained focal in all musicians over 8.8 ± 8.5 years.

Conclusions: Our findings provide novel evidence on occupation as a key mediator of IAOD phenotype at disease onset and on its natural history.

References:

[1] Sex-related influences on the frequency and age of onset of primary dystonia. Epidemiologic Study of Dystonia in Europe (ESDE) Collaborative Group. Neurology. 1999;53:1871-3.

[2] Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. Lancet Neurol. 2004;3:673-8.

[3] LeDoux MS, Vemula SR, Xiao J, Thompson MM, Perlmutter JS, Wright LJ, Jinnah HA, Rosen AR, Hedera P, Comella CL, Weissbach A, Junker J, Jankovic J, Barbano RL, Reich SG, Rodriguez RL, Berman BD, Chouinard S, Severt L, Agarwal P, Stover NP. Clinical and genetic features of cervical dystonia in a large multicenter cohort. Neurol Genet. 2016;2:e69.

[4] Berman BD, Groth CL, Sillau SH, Pirio Richardson S, Norris SA, Junker J, Brüggemann N, Agarwal P, Barbano RL, Espay AJ, Vizcarra JA, Klein C, Bäumer T, Loens S, Reich SG, Vidailhet M, Bonnet C, Roze E, Jinnah HA, Perlmutter JS. Risk of spread in adult-onset isolated focal dystonia: a prospective international cohort study. J Neurol Neurosurg Psychiatry. 2020 Mar;91(3):314-320.

[5] Defazio G, Abbruzzese G, Girlanda P, Buccafusca M, Currà A, Marchese R, Martino D, Masi G, Mazzella L, Vacca L, Livrea P, Berardelli A. Primary cervical dystonia and scoliosis: a multicenter case-control study. Neurology. 2003;60:1012-5.

[6] Defazio G, Abbruzzese G, Aniello MS, Bloise M, Crisci C, Eleopra R, Fabbrini G, Girlanda P, Liguori R, Macerollo A, Marinelli L, Martino D, Morgante F, Santoro L, Tinazzi M, Berardelli A. Environmental risk factors and clinical phenotype in familial and sporadic primary blepharospasm. Neurology. 2011;77:631-7.

[7] Defazio G, Esposito M, Abbruzzese G, Scaglione CL, Fabbrini G, Ferrazzano G, Peluso S, Pellicciari R, Gigante AF, Cossu G, Arca R, Avanzino L, Bono F, Mazza MR, Bertolasi L, Bacchin R, Eleopra R, Lettieri C, Morgante F, Altavista MC, Polidori L, Liguori R, Misceo S, Squintani G, Tinazzi M, Ceravolo R, Unti E, Magistrelli L, Coletti Moja M, Modugno N, Petracca M, Tambasco N, Cotelli MS, Aguggia M, Pisani A, Romano M, Zibetti M, Bentivoglio AR, Albanese A, Girlanda P, Berardelli A. The Italian Dystonia Registry: rationale, design and preliminary findings. Neurol Sci. 2017 May;38(5):819-825.

[8] Italian National Institute of Statistics (ISTAT). Classification of occupation 2021 (CP2021). Available from: https://professioni.istat.it/sistemainformativoprofessioni/cp2011/? db=2021.

P42

Lower limb dystonia only during down the stairs: a rare task-specific dystonia

Elena Benevento[1], G. Palermo[1], E. Unti[1], R. Ceravolo[1,2]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Center for Neurodegenerative Diseases, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Introduction: Focal task-specific dystonias represent a rare condition and usually affect the upper limbs or craniocervical regions (e.g., writer's cramp, musician's hand dystonia, or embouchure dystonia). Lower extremity dystonias is thought to be rare in adults and when it does occur it tends to be non-task specific and often associated with parkinsonism, trauma, stroke, or psychogenic behavior. However, focal task-specific dystonias in the lower limb or foot have been described during walking, running, hiking or cycling. More recently, a task-specific lower limb movement disorder triggered only by walking down stairs has been reported in few cases. [1,2,3]

Case description: We report the case of 54 years-old woman presenting with task-specific dystonia manifested only when going down the stairs. She presented with a history of non-progressive right lower limb symptoms manifested only when going down stairs that she came to notice about 2 years earlier. She explained that, when she went down stairs, she was unable to control her right leg coming down. These symptoms were not reproducible when she walked down stairs backward or climbing stairs. Walking on horizontal ground was normal. There was no history of trauma, psychiatric, or other medical problems, nor a family history of movement disorders. Her neurological examination was entirely normal, and there were no orthopedic abnormalities. There was no distractibility and inconsistency. Brain magnetic resonance imaging and electromyography studies of the lower limb were normal. The patient did not want any treatment.

Discussion: Down the stairs dystonia is a novel, rare, adult-onset, task-specific focal isolated syndrome of lower limbs. To date, only 9 other cases describing task-specific lower limb dystonia while going down stairs have been published. As in our case, most patients are females with unremarkable medical and family histories, all with normal neurological examination and lack of progression or significant functional impairment.

References:

[1] https://doi.org/10.1002/mdc3.12371.
[2] McKeon A, Matsumoto JY, Bower JH, et al. The spectrum of disorders presenting as adult-onset focal lower extremity dystonia. Parkinsonism Relat Disord. 2008.
[3] Ramdhani RA, Frucht SJ. Adult-onset Idiopathic Focal Lower Extremity Dystonia: A Rare Task-Specific Dystonia. Tremor Other Hyperkinet Mov (N Y). 2013.

P43

Early onset cervical dystonia associated with mutation in CACNA1A gene

Valentina Floris[1], F. Pinna[1], C. Frau[2], S. Othmani[1], P. Solla[2], C.F. Bagella[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Unit of Neurology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Introduction: Mutations in CACNA1A have been associated with several autosomal dominant neurologic disorders, including familial hemiplegic migraine type 1, episodic ataxia type 2, and spinocerebellar ataxia type 6 [2].

Objectives: We describe a case of CACNA1A mutation, childhood onset of segmental dystonia [1].

Methods: Herein we describe a caucasian 60-year-old female, second child of non-consanguineous healthy parents, presented with a history of abnormal neck posture since early childhood. No progression of these sign occurred. She denied any illnesses, exposures or trauma around this time. There was no family history of similar symptoms. The patient's physical examination revealed craniocervical dystonia showing blepharospasm, antero-Collis, head tremor, decreased right arm swing and she exhibit some bradykinesia, but these issues did not inhibit her actions significantly. There were no signs of dysmetria or ataxia on exam. MRI of the brain and spinal cord was unremarkable as well as the striatal uptake of the dopamine transporter ligand FP-CIT with SPECT. During the hospitalization, given the possibility of it being dopamine-responsive dystonia, the patient was trialed on carbidopa/levodopa without improvement. She also was receiving regular botulinum toxin injections for her cervical dystonia, with some improvement.

Results: A dystonia panel was sent, and it showed a new nonsense variant c.6a63c>T; p. Arg2155Cys* in the CACNA1A gene to be a possible cause of dystonia. To the best of our knowledge, p.Arg2155Cys* in CACNA1A has not been described in the literature to date.

Conclusions: Dystonia can be an aspect of the clinical phenotype of CACNA1A [3]. The report of other patient with cervical dystonia and a mutation in CACNA1A supports the idea that our patient's childhood-onset dystonia is due to her mutation in CACNA1A [4]. Unlike other case-report reported in literature, our patient did not have manifested any cerebellar signs. So, an important issue remains the coexistence of marked phenotypic variability across different mutation types.

References:

[1] Focal Dystonic Tremor as a Prominent Feature in a Child with a CACNA1A-Related Disorder Marta Mercati, MD,1 Federica Graziola, MD, PhD,2,* Laura Canafoglia, MD, PhD,3 Davide Caputo, MD,2 Federica Rachele Danti, MD, PhD,2 Chiara Reale, MSc,4 and Giovanna Zorzi, MD2 .
[2] From Genotype to Phenotype: Expanding the Clinical Spectrum of CACNA1A Variants in the Era of Next Generation Sequencing Elisabetta Indelicato and Sylvia Boesch*.
[3] CACNA1A MUTATION PRESENTING WITH FOCAL DYSTONIA 1,2Jason Gu*, 1,3,4Kishore R Kumar, 1,3Carolyn M Sue. 1 Department of Neurology, Royal North Shore Hospital, St Leonards, NSW, Australia; 2 Neurology, The Wollongong Hospital, Wollongong, NSW, Australia; 3 University of Sydney, Camperdown, NSW, Australia; 4 Kinghorn Centre of Clinical Genomics, Garvan Institute of Medical Research, Sydney, NSW, Australia 10.1136/jnnp-2017-316074.99.
[4] Novel Mutation in CACNA1A Associated with Activity-Induced Dystonia, Cervical Dystonia, and Mild Ataxia Benjamin Stampfl and Dominic Fee, Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA.

P44

Could artificial intelligence predict GBA1-mutated genotype in Parkinson's Disease patients?

Giulia Di Rauso[1,2], A. Ghibellini[3], S. Grisanti[2], F. Cavallieri[1], V. Fioravanti[1], E. Monfrini[4,5], G. Toschi[1], G. Portaro[1], R. Bacchin[6], J. Rossi[1,2], R. Sabadini[1], V. Ferrari[1], A. Melpignano[7], F. Pacillo[7], M. Scarano[8], A. Groppi[1], L. Gherardini[9], C. Lucchi[10], G. Biagini[10], M.C. Malaguti[6], L. Bononi[3], M. Gabbrielli[3], A.B. Di Fonzo[4], A. Scaglioni[11], F. Valzania[1]

[1]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[3]Department of Computer Science and Engineering, Alma Mater Studiorum - University of Bologna, Italy
[4]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[5]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[6]Neurology Unit, Santa Chiara Hospital, Trento, Italy
[7]Presidio Ospedaliero Fidenza AUSL Parma, Fidenza, Italy
[8]Dipartimento di Cure Primarie, Azienda Unità Sanitaria Locale (AUSL) Modena, Modena, Italy
[9]Sano Centre for Computational Personalised Medicine, Personal Health Data Science Team, Krakow, Poland
[10]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[11]Centro S. Maria ai Servi, Fondazione Don Gnocchi, Parma, Italy

Introduction: GBA1 is the major genetic risk factor for PD [1].

Objective: To assess whether artificial intelligence could predict GBA1-mutated genotype in Parkinson's Disease (GBA1-PD) considering the different impact of significant clinical features.

Methods: A consecutive cohort of GBA1-PD patients has been paired for age, sex, disease duration, Hoehn & Yahr stage, and comorbidities (Charlson Comorbidity Index) with a cohort of consecutive non-mutated PD (NM-PD) patients. Clinical assessment included the MDS-UPDRS total scores and subscores, and the Montreal Cognitive Assessment (MoCA). The pre-processing phase consisted in categorizing patients based on a binary target (GBA1-PD or NM-PD). To address missing values and inconsistencies in the data, we compared two imputation techniques: K-Nearest Neighbors and Iterative Imputer. We applied the Chi-square and Mann-Whitney test to identify features that significantly differ between the two groups. For predictive modeling, we explored a variety of algorithms, such as Support Vector Machines, Logistic Regression, Random Forest, Stochastic Gradient Descent Classifier, and Decision Tree. Each model was rigorously evaluated to determine its effectiveness in accurately categorizing patients. By examining the contribution of individual features in the predictive models, we were able to identify the most significant factors influencing the genetic categorization.

Results: The dataset comprised 116 patients: 58 GBA1-PD (males: 31; age: 64.47 years; disease duration: 7.95 years, MDS-UPDRS III: 28.95; CCI: 2.48) and 58 NM-PD (age: 64.64 years; disease duration: 7.67 years, MDS-UPDRS III: 35.98; CCI: 2.67). For each patient 124 distinct features were recorded. Among these features, 16 had been used by the model to identify mutated or nonmutated

GBA1 genotype with an accuracy between 60-70%. These variables included family history, score and subscores for motor impairment (e.g., MDS-UPDRS III total score, rigidity, bradykinesia and PIGD subscores) and cognitive impairment.

Conclusions: Selected models, using 16 significant variables, could predict GBA1 genotype with an accuracy between 60-70%.

References:

[1] V. Yahya, A. Di Fonzo, and E. Monfrini, 'Genetic Evidence for Endolysosomal Dysfunction in Parkinson's Disease: A Critical Overview', Int. J. Mol. Sci., vol. 24, no. 7, p. 6338, Mar. 2023, doi: 10.3390/ijms24076338

P45

The role of the "unfolded protein response" and the perk Pathway in Parkinson's disease: study of genetic Polymorphisms

Marika Alborghetti[1], N. Palomba[2], E. Bianchini[1], D. Rinaldi[1], C. Strafella[3], V. Caputo[3], E. Giardina[3], F. Nicoletti[2], T. Esposito[4], F. Pontieri[1]

[1]Sapienza, University of Rome, Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Rome, Italy
[2]IRCSS Neuromed, Pozzilli, Isernia, Italy
[3]IRCCS Fondazione Santa Lucia, Rome, Rome, Italy
[4]Institute of Genetics and Biophysics CNR, Biomedicine, Napoli, Italy

Introduction: The accumulation of α -synuclein in Parkinson's disease (PD) leads to the stress of endoplasmic reticulum (ER) [1-3]. The resulting cellular response is called "Unfolded Protein Responce" (UPR). UPR is activated with the aim of reducing protein synthesis and simultaneously stimulate the prodyction of proteins that mediate apoptosis to reduce protein aggregation. PERK (PKR-like ER kinase) and the transcription factor EIF2A are the main mediator of the UPR.

Objectives: To study a possible association between polymorphisms of the genes coding for proteins involved in the UPR and the development of PD or PD motor and nonmotor symptoms.

Methods: The study sample included a total sample size of 1666 subjects with 960 PD patients and 506 age/gender-matched healthy controls. The analysis focused on the genetic variants (SNV) of genes coding for proteins involved in the UPR (EIF2AK3, LRRK2, ATF4, ATF6, XBP1, BCL2, EIF2A, ERN1). The DNA was extracted from the blood samples and the Open Array ™ technology allowed a massive and simultaneous genotyping of all the samples under examination.

Results: We find 51 SNVs concern EIF2AK3 coding for PERK and EIF2A coding for eIF2α, with a statistically significant association with susceptibility to PD.

Conclusion: Our study confirms the involvement of UPR and in particular of the PERK pathway in the development of PD. The PERK pathway represents a potential target for the development of new therapeutic strategies for both neuroprotective and symptomatologic purposes [4].

References:

[1] Ghemrawi R, Khair M. Endoplasmic Reticulum Stress and Unfolded Protein Response in Neurodegenerative Diseases. Int J Mol Sci. 2020 Aug 25;21(17):6127.
[2] Toyofuku T, Okamoto Y, Ishikawa T, Sasawatari S, Kumanogoh A. LRRK2 regulates endoplasmic reticulum-mitochondrial tethering through the PERK-mediated ubiquitination pathway. EMBO J. 2020 Jan 15;39(2):e100875.
[3] Xiang C, Wang Y, Zhang H, Han F. The role of endoplasmic reticulum stress in neurodegenerative disease. Apoptosis. 2017 Jan;22(1):1-26.
[4] Halliday M, Radford H, Zents KAM, Molloy C, Moreno JA, Verity NC, Smith E, Ortori CA, Barrett DA, Bushell M, Mallucci GR. Repurposed drugs targeting eIF2α-P-mediated translational repression prevent neurodegeneration in mice. Brain. 2017 Jun 1;140(6):1768-1783.

P46

Combined assessment of blood gcase activity and α-synuclein levels in GBA mutation arriers: a novel potential biomarker?

Chiara Pasquini[1], M. Avenali[1,2], S.P. Caminiti[2], S. Cerri[1], G. Ongari[1], M. Gegg[3], M. Toffoli[3], D. Hughes[4], C. Cerami[5], C. Crespi[5], E.M. Valente[6], A.H. Schapira[5], F. Blandini[2,7]

[1]IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK
[4]Lysosomal Storage Disorders Unit, Royal Free Hospital and Department of Haematology, UCL, London, UK
[5]Scuola Universitaria Superiore IUSS Pavia, Pavia, Italy
[6]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[7]Ca' Granda IRCCS Foundation, Ospedale Maggiore Policlinico, Milan, Italy

Introduction: Glucocerebrosidase (GBA) mutations are the most frequent genetic risk factor for Parkinson Disease (PD). Decreased glucocerebrosidase activity (GCase) and increased α-synuclein (α-syn) levels are both considered promising biomarkers for GBA-PD. However, the role of combined blood GCase/α-synuclein is still poorly investigated.

Objectives: The present study investigates whether combined evaluation of blood GCase and α-synuclein can predict disease severity in GBA-PD and prodromal features in asymptomatic GBAcarriers (GBA-nonPD).

Methods: 98 subjects (30 GBA-nonPD, 29 GBA-PD and 39 healthy controls) underwent a detailed clinical assessment, as well as measurement of GCase activity and α-syn levels in peripheral blood mononuclear cells (PBMCs). A two-step clustering analysis was performed to split the subjects into distinct clusters based on their combined GCase/α-syn biochemical profile. Motor and non-motor scores of GBA-PD and GBA-nonPD were analyzed among clusters.

Results: Combined blood GCase/α-syn showed high accuracy to discriminate subjects into two clusters: 1) benign (high GCase/mid-low α-syn); 2) malignant (low GCase/high α-syn). All healthy controls belonged to the benign cluster, while 59% of GBA-PD and 47% of GBA-nonPD fell in the malignant cluster. GBA-PD within the malignant cluster showed motor and non-motor features similar to those in the benign cluster, while cognitive performance was significantly worse (lower MoCA scores). GBA-nonPD within the malignant cluster had a higher prevalence of sleep disorders and depressive symptoms, while their motor scores did not differ significantly from those within the benign cluster.

Conclusions: We report for the first time that combined blood GCase/α-syn assessment defines a distinctive biochemical profile able to identify a more severe cognitive phenotype in GBA-PD and more pronounced prodromal non-motor features in GBA-nonPD. Longitudinal studies are needed to confirm the accuracy of this potential biomarker.

P47

Next-Generation Sequencing study of a cohort of Italian patients affected by Parkinson's Disease. A discussion about importance for positive family history for extrapyramidal signs

Caterina Del Regno[1,2], G. Ermanis[1,2], F. Janes[1], C. Qehaja[1], A. Bernardini[1], G. Pellitteri[1], D. De Monte[1,2], M.D. Scanni[1,2], E. Belgrado[3], M. Mucchiut[3], E. Betto[4], I. Lonigro[5], G.L. Gigli[1,2], M. Valente[1,2]

[1]Clinical Neurology Unit, Santa Maria della Misericordia University Hospital, Udine, Italy
[2]Department of Medical Area, University of Udine, Udine, Italy
[3]Neurology Unit, Santa Maria della Misericordia University Hospital, Udine, Italy
[4]Institute of Medical Genetics, Azienda Sanitaria Friuli Centrale (ASUFC), Udine, Italy
[5]Lab. Genetica Medica, Istituto per le Malattie Rare "Mauro Baschirotto" B.I.R.D. Foundation, Costozza di Longare (VI), Italy

Introduction: Parkinson's disease (PD) is a complex neurodegenerative disorder, widely regarded as a multifactorial disease where either genetic and environmental factors play a role in risk of onset, clinical phenotype, and trajectory of progression [1]. Meta-analysis showed that having a family history of PD is a strong risk factor for later diagnosis of PD, with a 3–4x increase in odds [1]. Truly monogenic forms of Parkinson's account only for about 5-10% of PD patients [2], whereas Genome-Wide Associations Studies (GWAS) have contributed to delineate single alleles with a small but additive effect in increasing risk of PD development [1].

Objectives: To describe the genetic background in a cohort of PD patients and to evaluate the association between the presence of risk variants associated with PD and a positive family history.

Methods: We recruited 97 individuals with a clinical diagnosis of PD, with age at motor symptoms onset ≤ 60 years and/or a family history of PD or extrapyramidal signs, and we analyzed their DNA samples with a Next-Generation Sequencing panel.

Results: Our population had an average age at symptoms onset of 52,99 years. 32/97 had a positive family history for movement disorders. 62/97 had a positive test revealing 22 different gene's mutations (GBA, A2M, and LRRK2 being the most frequent). There were no significant associations between patients tested positive and: i. a family history of parkinsonism; ii. clinical features such as tremor dominant/bradykinetic phenotype, dystonia, cognitive impairment, and poor levodopa response.

Conclusions: The absence of a positive family history for movement disorders should not prevent PD patients from genetic testing. Since GWAS can account only for 16-36% of PD heritability [3], further efforts in evaluating genetic background of PD patients are still needed, also to clarify the relationship between specific mutations and clinical phenotype.

References:

[1] Day JO, Mullin S. The Genetics of Parkinson's Disease and Implications for Clinical Practice. Genes (Basel). 2021 Jun 30;12(7):1006. doi: 10.3390/genes12071006. PMID: 34208795; PMCID: PMC8304082.
[2] Jia F, Fellner A, Kumar KR. Monogenic Parkinson's Disease: Genotype, Phenotype, Pathophysiology, and Genetic Testing. Genes (Basel). 2022 Mar 7;13(3):471. doi: 10.3390/genes13030471. PMID: 35328025; PMCID: PMC8950888.
[3] Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, Tan M, Kia DA, Noyce AJ, Xue A, Bras J, Young E, von Coelln R, Simón-Sánchez J, Schulte C, Sharma M, Krohn L, Pihlstrøm L, Siitonen A, Iwaki H,

Leonard H, Faghri F, Gibbs JR, Hernandez DG, Scholz SW, Botia JA, Martinez M, Corvol JC, Lesage S, Jankovic J, Shulman LM, Sutherland M, Tienari P, Majamaa K, Toft M, Andreassen OA, Bangale T, Brice A, Yang J, Gan-Or Z, Gasser T, Heutink P, Shulman JM, Wood NW, Hinds DA, Hardy JA, Morris HR, Gratten J, Visscher PM, Graham RR, Singleton AB; 23andMe Research Team; System Genomics of Parkinson's Disease Consortium; International Parkinson's Disease Genomics Consortium. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. Lancet Neurol. 2019 Dec;18(12):1091-1102. doi: 10.1016/S1474-4422(19)30320-5. PMID: 31701892; PMCID: PMC8422160.

P48

Genetica della distonia: uno studio di prevalenza in un gruppo di pazienti seguiti presso il Policlinico Gemelli di Roma

Pasquale Sanginario[1], A.T. Cimmino[1], F. Musso[1], M. Petracca[2], D. Tiziano[1,2], A.R. Bentivoglio[1,2], P. Calabresi[1,2], G. Di Lazzaro[2]

[1]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Introduction: Dystonia represents the manifestation of several pathogenetic entities and can occur isolated or combined [1]. TOR1A (DYT1) variants were firstly recognized as the hereditary cause of primary dystonia. However, the recent optimization of gene sequencing procedures allowed to identify many other genes involved in the pathogenesis of dystonic syndromes [2].

Objectives: Our aim is to analyze the prevalence of genetic variants associated with dystonic syndromes in a group of selected patients and define their clinical phenotype.

Methods: We analyzed Next Generation Sequencing (NGS) panels of 63 patients presenting with a primary dystonic syndrome.

Results: NGS panels of 25 of these patients (40%) were negative. In 38 patients (60%) variants were detected. A total of 61 variants were reported, among which 13 were classified as pathogenetic/likely pathogenetic, and 48 as variants of unknown significance (VUS). Four patients received a genetic diagnosis (ATM, PRRT2, TH and GNAL). Five patients presented VUS in ANO3, CIZ1, TOR1A, GLB1, SGCE and had clinical signs and a segregation of the variants compatible with the related clinical phenotype. The remaining twenty-nine patients had inconclusive results.

Conclusions: In our case series, a definite genetic diagnosis was made in 6% of the tested patients. A genetic diagnosis was probable in 8% of patients. Even though the diagnostic yield was quite low, it allowed to make diagnosis in patients with atypical phenotypes of genetic syndromes, in which a genetic counseling is mandatory. However, the most frequently reported variants are VUS, which imply some difficulties in the interpretation and pose some challenges for the family counseling. In conclusion, the wide availability of NGS panels can help redefining diagnostic accuracy in patients which could benefit from a genetic diagnosis in both terms of treatment and counseling. However, a correct counseling to patients in view of possible inconclusive results should be made.

References:

[1] Grütz, Karen, and Christine Klein. "Dystonia updates: definition, nomenclature, clinical classification, and etiology." Journal of Neural Transmission 128 (2021): 395-404.
[2] Fuchs, Tania, and Laurie J. Ozelius. "Genetics in dystonia: an update." Current neurology and neuroscience reports 13 (2013): 1-8.

P49

Parkinson's disease as an isolated presentation of THAP1 deletion: a case report

Rita Cancilla[1], E. Ambrosini[2], A. Percesepe[2], J. Paul[3], A. Negrotti[1]

[1]Neurology Unit, Department of Medicine and Surgery, University of Parma, Parma, Italy
[2]Medical Genetics, Department of Medicine and Surgery, University of Parma, Parma, Italy
[3]CENTOGENE GmbH, Rostock, Germany

Introduction: Parkinson's disease and dystonia exhibit clinical overlaps, with specific gene variants contributing to both conditions: dystonia is notable in PD variants associated with PRKN, PINK1, DJ-1, and PLA2G6, while parkinsonism is observed in dystonia related variants of GCH1, TH, TAF1, ATP1A3, and PRKRA [1]. An isolated form, DYT-THAP1, presents as an autosomal dominant subtype, marked by focal and segmental dystonia [2].

Objective: No reports of parkinsonism in THAP1 deletion were documented until now. However, we present a case of parkinsonism in a patient with a THAP1 mutation (c.70_71+8del).

Methods: A 61-year-old woman was referred to Movement Disorders outpatient for resting tremor of the right upper limb for five months. Right lower limb tremor began two years earlier and hyposmia twenty years prior. She has a history of type II diabetes mellitus, obesity (BMI 50 kg/m2) and autoimmune hypothyroidism. She has a positive paternal family history (father and aunt) for tremor. Neurological examination revealed bradykinesia, right upper and lower limbs resting tremor, reduced swing and mild hypomimia. Brain MRI showed chronic vasculopathy and Dopamine Transporter imaging (SPECT with ^{123}I-Ioflupane) revealed left nigrostriatal dopaminergic pathway impairment. Levodopa/carbidopa alleviated symptoms initially, and ropinirole was added due to persistent tremor and bradykinesia. Given the diagnosis of idiopathic Parkinson’s disease, the patient was involved in the ROPAD (Rostock International Parkinson's Disease) study, aiming to better understand the genetic contribution to PD [3].

Results: A custom NGS panel (CENTOGENE) identified a heterozygous mutation in THAP1 (c.70_71+8del), confirmed by an Italian center and classified as probably pathogenic (class 4 according to ACMG Guidelines).

Conclusions: Literature associates THAP1 mutations with varied dystonic symptoms and ages of onset. Given the reduced penetrance of THAP1 mutations, with only 50-65% exhibiting dystonic phenotypes: is the parkinsonism a phenotypic expansion or is it an incidental THAP1 mutation unrelated to the clinical presentation?

References:

[1] Wang Y, Zhao Y, Pan H, Zeng Q, Zhou X, Xiang Y, Zhou Z, Xu Q, Sun Q, Tan J, Yan X, Li J, Guo J, Tang B, Yu Q, Liu Z. Genetic analysis of dystonia-related genes in Parkinson's disease. Front Aging Neurosci. 2023 May 26;15:1207114.
[2] Gervais V, Campagne S, Durand J, Muller I, Milon A. NMR studies of a new family of DNA binding proteins: the THAP proteins. J Biomol NMR. 2013 May;56(1):3-15.
[3] Skrahina V, Gaber H, Vollstedt EJ, Förster TM, Usnich T, Curado F, Brüggemann N, Paul J, Bogdanovic X, Zülbahar S, Olmedillas M, Skobalj S, Ameziane N, Bauer P, Csoti I, Koleva-Alazeh N, Grittner U, Westenberger A, Kasten M, Beetz C, Klein C, Rolfs A; ROPAD Study Group. The Rostock International Parkinson's Disease (ROPAD) Study: Protocol and Initial Findings. Mov Disord. 2021 Apr;36(4):1005-1010.

P50

Comorbidities in genetic Parkinson's disease patients: comparison between LRRK2, GBA1, and idiopathic PD

Giulia Di Rauso[1,2,3], F. Pirone[2,4], G. Franco[2], F. Arienti[2], I. Trezzi[2], E. Frattini[2], F. Cavallieri[3], V. Rispoli[5], F. Valzania[3], E. Monfrini[2,4], A.B. Di Fonzo[2]

[1]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[2]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[3]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[4]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[5]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

Introduction: Pathogenic variants in LRRK2 gene are the most common monogenic cause of Parkinson disease (PD), while GBA1 is the major genetic risk factor for PD [1].

Objective: To evaluate the occurrence of medical comorbidities associated with PD genes (GBA1-PD and LRRK2-PD) compared to a cohort of idiopathic PD (iPD), focusing on early detectable or treatable diseases.

Methods: This retrospective observational study included PD patients carrying pathogenetic variant in LRRK2 or GBA1 genes, and patients non-mutated in PD associated genes (iPD) as control group. We evaluated demographic data and the following personal comorbidities (presence/absence): cardiological, oncological, cerebrovascular, kidney, endocrinological, autoimmune and immuno-mediated diseases, aneurysms or arteriovenous malformations, type 2 Diabetes Mellitus (T2-DM) and dyslipidemia. Categorical variables were reported as percentages, while continuous variables as medians and interquartile range. Prevalence of comorbidities between groups were compared through the Fisher exact test.

Results: 165 PD patients were included: 73 GBA1-PD (male: 52; age: 69 years; disease duration: 10.5 years), 23 LRRK2-PD (male: 12; age: 63 years; disease duration:10 years) and 69 iPD (male: 44; age: 64 years; disease duration: 8 years). LRRK2-PD patients had a significantly higher prevalence of oncological disorders, compared to iPD (39.13% vs 11.59%, p=0.01), but not compared to GBA1-PD (39.13% vs 20.55%, p=0.10). More than half of LRRK2-PD patients with malignancies had ≥ 2 tumors in their lifetime and had at least one family member with cancer. The most prevalent malingnancies in our LRRK2-PD coohort were cutaneous melanomas, hematological malignancies, uterine and breast cancers. The frequency of patients affected by T2-DM was significantly higher in LRRK2-PD (28.57%) patients than in iPD (5.88%, p= 0.01) and GBA1-PD (8.33%, p= 0.02).

Conclusions: This study highlighted that LRRK2-related PD are likely to be more susceptible to T2-DM and to specific malinganceis compared to GBA1-PD and iPD.

References:

[1] V. Yahya, A. Di Fonzo, and E. Monfrini, 'Genetic Evidence for Endolysosomal Dysfunction in Parkinson's Disease: A Critical Overview', Int. J. Mol. Sci., vol. 24, no. 7, p. 6338, Mar. 2023, doi: 10.3390/ijms24076338.

P51

Relative frequency and phenotypic spectrum of GAA-FGF14 ataxia (SCA27B) patients: an Italian multicenter cohort study

Sara Satolli[1], S. Rossi[2], G. Bruno[3], E. Capacci[4], C. Casali[5], R. Ceravolo[6], S. Cotti Piccinelli[7], C. Criscuolo[8], R. De Micco[9], G. De Michele[8], R. Fancellu[10], C. Ferrari[4], A. Filla[8], N. Fini[11], A. Govoni[12], D. Lopergolo[13], A. Malandrini[13], A. Mignarri[13], O. Musumeci[14], M.T. Pellecchia[15], A. Perna[16], A. Petrucci[16], R. Ravenni[17], I. Ricca[1], A. Rufa[13], G. Silvestri[2,18], A. Tessitore[9], D. Pellerin[19], B. Brais[19], F.M. Santorelli[1]

[1]Molecular Medicine for Neurodegenerative and Neuromuscular Diseases Unit, IRCCS Fondazione Stella Maris, Pisa, Italy
[2]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[3]Department of Neurosciences, Division of Pediatric Neurology, "Santobono-Pausilipon" Children's Hospital, Naples, Italy
[4]Department of Neuroscience, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence, Florence, Italy
[5]Department of Medical and Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy
[6]Department of Clinical and Experimental Medicine, Center for Neurodegenerative Diseases-Parkinson's Disease and Movement Disorders, University of Pisa, Pisa, Italy
[7]Department of Clinical and Experimental Sciences, NeMO-Brescia Clinical Center for Neuromuscular Diseases, University of Brescia, Brescia, Italy
[8]Department of Neurosciences Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[9]Department of Advanced Medical and Surgical Sciences, University of Campania “Luigi Vanvitelli”, Napoli, Italy
[10]UO Neurologia, IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[11]Neurology Unit, Department of Neurosciences, AOU di Modena, Modena, Italy
[12]Neuromuscular-Skeletal and Sensory Organs Department, AOU Careggi, Florence, Italy
[13]Department of Medicine, Surgery and Neurosciences, Unit of Neurology and Neurometabolic Disorders, AOU Senese, Università di Siena
[14]Unit of Neurology and Neuromuscular Disorders, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[15]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Salerno, Italy
[16]Center for Neuromuscular and Neurological Rare Diseases, San Camillo Forlanini Hospital, Rome, Italy
[17]Unità Operativa Complessa di Neurologia e Neuroriabilitazione, Presidio Ospedaliero di Abano Terme - Azienda ULSS 6 Euganea, Padova, Italy
[18]UOC Neurologia Fondazione Policlinico Gemelli IRCCS, Rome, Italy
[19]Departments of Neurology and Neurosurgery, Montreal Neurological Hospital and Institute, McGill University, Montreal, Canada

Introduction: Autosomal dominant spinocerebellar ataxia due to intronic GAA repeat expansion (RE) in the FGF14 gene (GAA-FGF14 ataxia; SCA27B) is a recently identified, relatively common, form of late onset ataxia.

Objective: Here, we aimed to: investigate relative frequency of GAA-FGF14 in different clinical-defined disease subgroups and characterize the clinical phenotype of GAA-FGF14 patients collected in an Italian multicenter cohort study.

Methods: First, we screened a total of 406 clinically diagnosed late onset cerebellar ataxia (LOCA), subdivided in sporadic adult-onset cerebellar ataxia (SAOA), autosomal dominant cerebellar ataxia (ADCA) and multisystem atrophy - cerebellar variant (MSAC).
Then, we analyzed the clinical, genetic and neuroradiological features of 52 index cases carrying a heterozygous GAA-FGF14 RE. At the end, we compared Italian cohort with already reported GAA-FGF14 cohorts of various ethnic backgrounds.

*Results***:** The estimated prevalence of SCA27B was 13.5% among LOCA patients, 8% among SAOA patients, 38.5% in ADCA, 2% among MSA-C patients. Fifty out of 52 Italian GAA-FGF14 patients consistently presented as late-onset (60.5±13) cerebellar syndrome. All symptomatic individuals showed evidence of impaired balance and gait cerebellar oculomotor signs (saccadic intrusion, nystagmus, slowing saccades) wer also frequent (80%). Episodic manifestations at onset occurred in 36% of patients Dysautonomia and cognitive impairment were infrequent. Peripheral neuropathy was reported in 23.5% of patients. Brain magnetic resonance imaging showed cerebellar atrophy in most cases (81%). Longitudinal assessments indicated slow progression of ataxia (0.33 SARA points/year) and minimal functional impairment (55% of patients are still fully ambulant after 10 years of disease duration). We found no correlation between RE, age at onset, longitudinal SARA scores or disease duration.

Conclusion: Relative frequency of SCA27B among ADCA patients is very high. Consistent with all the cohorts described to date, GAA-FGF14 patients present as an adult-onset, slowly progressive cerebellar ataxia with predominant axial involvement and frequent cerebellar oculomotor signs.

P52

Lysosomal-PD and mitochondrial-PD: implication of dysfunctional cellular pathways

Giulia Di Rauso[1,2,3], F. Pirone[2,4], G. Franco[2], F. Arienti[2], E. Frattini[2], I. Trezzi[2], F. Cavallieri[3], F. Valzania[3], E. Monfrini[2,4], A.B. Di Fonzo[2]

[1]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[2]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[3]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[4]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Introduction: The pathogenesis of Parkinson's Disease (PD) has been related to many dysfunctional cellular pathways, including lysosomal and mitochondrial dysfunction [1].

Objective: To evaluate phenotypic differences between mutated-PD patients on the basis of the dysfunctional cellular pathway underlying the disease, namely the mitochondrial (mito-PD) or endolysosomal (lyso-PD) pathways.

Methods: This retrospective observational study included PD patients carryng pathogenetic variant in LRRK2, GBA1, PRKN, PINK1, DJ-1, RAB39B, POLG, TWNK, OPA1 and mtDNA. We collected data about demographic features, presence of motor/nonmotor symptoms, levodopa-induced dyskinesias (LID) and motor fluctuation (MF), and Total Levodopa Equivalent Daily Dose (LEDD) at disease onset, 5- and 10-years followup. Patients were divided into mito-PD (PRKN, PINK1, DJ-1, TWNK, POLG, OPA1, mtDNA) or lyso-PD (LRRK2, RAB39B, GBA1) groups according to the cell pathway in which the mutated gene is most involved. Categorical variables were reported as percentages and compared through the Fisher exact test, while continuous variables were reported as medians and interquartile range and compared through Wilcoxon or Kruskal-Wallis tests.

Results: 135 PD patients were included: 99 Lyso-PD (male: 65, age at onset: 55 years; disease duration: 10 years; GBA1, LRRK2, RAB39B), and 36 mito-PD (male: 19, age at onset: 41 years; disease duration: 10 years; PINK1, PRKN, DJ-1, POLG, TWNK, OPA1, mtDNA). Non-motor symptoms (dysautonomia, hyposmia, cognitive impairment, hallucinations, urinary simptoms, sciallorhea) were more frequent in lyso-PD, except for psychiatric and sleep disorders, as well as the prevalence of MF and LID. Lyso-PD were more frequently hypokinetic and rigid, while mito-PD had higher prevalence of dystonia. LEDD was lower in mito-PD (5y: 358 mg; 10y: 480 mg) than lyso-PD (5y: 500 mg; 10y: 645 mg) at 5- ($p=0.05$) and 10- years ($p=0.06$) follow-up.

Conclusions: This study highlighted that lyso-PD had more frequently non-motor symptoms, MF and LID, while mito-PD had sustained response to low doses of levodopa.

References:

[1] V. Yahya, A. Di Fonzo, and E. Monfrini, 'Genetic Evidence for Endolysosomal Dysfunction in Parkinson's Disease: A Critical Overview', Int. J. Mol. Sci., vol. 24, no. 7, p. 6338, Mar. 2023, doi: 10.3390/ijms24076338.

P53

Effects of loading, tapping performance, and ballistic movements on postural tremor features in patients with essential tremor

Daniele Birreci[1], D. Costa[1], L. Angelini[1], A. Cannavacciuolo[1,2], M. Passaretti[1], A. Martini[1], A.S. Grandolfo[1], M. De Riggi[1], G. Paparella[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: In recent years, a comprehensive set of neurophysiological tests, including the loading test, tapping performance analysis, and the evaluation of response to ballistic movements, has been proposed to formulate laboratory-supported criteria for diagnosing functional tremor. These criteria are intended for use in both clinical practice and experimental research [1,2].

Objective: To comprehensively evaluate the effects of loading, tapping performance, and ballistic movements on major tremor features in patients with essential tremor (ET).

Methods: The enrolled ET patients were evaluated using a standardized clinical scale, the Fahn-Tolosa-Marin Tremor Rating Scale (FTM-TRS). A comprehensive tremor evaluation at baseline and during loading, finger tapping (at 1, 3, and 5 Hz), and ballistic movements was conducted using an optoelectronic system. Data were analyzed through non-parametric Friedman Analysis of Variance (ANOVA).

Results: Thirteen ET patients were included (6 females, 64.9±17.6 years), with a mean disease duration of 15.6±10.9 years and an FTMTRS score of 20.6±10.1. At baseline, postural tremor had a mean frequency of 5.98±1.42 Hz and a mean amplitude of 0.053±0.036 GRMS^2. ANOVA unveiled a difference in amplitude (Chisquare=12.24; p=0.03), with lower values during 1 Hz finger-tapping movements (0.045 GRMS^2), compared to the other conditions. Moreover, we found an inverse correlation between baseline tremor amplitude and the reduction in tremor amplitude during 1 Hz tapping (r=-0.62, p=0.021). Finally, the analysis did not reveal variations in tremor frequency across different manoeuvres (Chi-square=3.48; p=0.62).

Conclusions: Gaining insights into the impact of loading, tapping performance, and ballistic movements on postural tremor features in patients with tremor holds relevance for clinical applications, especially within the diagnostic process. Expanding the analysis to larger patient samples could contribute to a deeper understanding of how clinical factors influence the observed effects.

References:

[1] P. Schwingenschuh et al., “Moving toward ‘laboratory-supported’ criteria for psychogenic tremor,” Movement Disorders, vol. 26, no. 14, pp. 2509–2515, Dec. 2011, doi: 10.1002/mds.23922.
[2] 2 P. Schwingenschuh et al., “Validation of ‘laboratory-supported’ criteria for functional (psychogenic) tremor,” Movement Disorders, vol. 31, no. 4, pp. 555–562, Apr. 2016, doi: 10.1002/mds.26525.

P54

Neurophysiological correlates of freezing of gait in Parkinson's disease: insights from TMS-EEG targeting the occipital cortex

Angela Comanducci[1], F.L. Saibene[1], C. Derchi[1], T. Atzori[1], S. D'Ambrosio[1], P. Arcuri[1], A. Salvatore[1], S. Gobbo[1], A. Castagna[1], A.B. Di Fonzo[2], J.S. Navarro[1], M. Meloni[1,3]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[3]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy

Introduction: Parkinson's Disease (PD) is characterized by a spectrum of motor dysfunctions, including the debilitating symptom of Freezing of Gait (FOG). While the pathophysiology of FOG is multifaceted and not entirely understood, there is growing evidence suggesting the involvement of cortical changes, in addition to subcortical alterations [1,2,3]. This study employs Transcranial Magnetic Stimulation combined with Electroencephalography (TMS-EEG) targeted at the occipital cortex to probe the electrophysiological properties of this area and its relationship to FOG in PD patients.

Objectives: To investigate the neurophysiological mechanisms of FOG, with a focus on the role of the associative visual cortex (BA19). Considering BA19's crucial involvement in higher-order visual processing and spatial awareness, this study aims to determine how the localized functional dynamics within BA19, as revealed through TMS-EEG, may contribute to the development of FOG in cognitively intact PD patients.

Methods: Thirty PD patients underwent an extensive neuropsychological assessment to rule out cognitive impairment. They were then categorized into two groups based on the presence or absence of FOG. The experimental procedure involved the use of TMS to specifically perturb BA19 and high-density EEG to measure the natural frequency of evoked oscillations in this area. An integrated neuronavigation system, utilizing the individual MRI of each patient, ensured precise targeting and accurate estimation of the induced maximum electric field. In addition to the natural frequency, other key electrophysiological indicators, such as the local mean field power and the slope of TMS-evoked potentials, were computed.

Results: In FOG+ patients, we observed a significant reduction in the natural frequency of oscillation within BA19. Furthermore, we also demonstrated enhanced local mean field power and a steeper slope of TMS-evoked responses suggesting an increased local cortical excitability.

Conclusions: These findings highlight the potential impact of local neurophysiological alterations in BA19 on the development of FOG. In particular, the significant reduction in natural frequency, deviating from the physiological alpha-band oscillations typically evoked in healthy individuals, suggests early functional degeneration in the occipital cortex, even before the onset of overt cognitive impairment. Importantly, the dysfunction in BA19, crucial for spatial awareness and the integration of visual-spatial information, could directly contribute to the pathogenesis of FOG and represents a potential target for future treatment strategies.

References:

[1] Leodori G, Fabbrini A, Suppa A, Mancuso M, Tikoo S, Belvisi D, Conte A, Fabbrini G, Berardelli A. Effective connectivity abnormalities in Lewy body disease with visual hallucinations. Clin Neurophysiol. 2023 Dec;156:156-165. doi: 10.1016/j.clinph.2023.10.009. Epub 2023 Nov 3. PMID: 37952445.
[2] Casarotto S, Turco F, Comanducci A, Perretti A, Marotta G, Pezzoli G, Rosanova M, Isaias IU. Excitability of the supplementary motor area in Parkinson's disease depends on subcortical damage. Brain Stimul. 2019 Jan-Feb;12(1):152-160. doi: 10.1016/j.brs.2018.10.011. Epub 2018 Oct 23. PMID: 30416036.
[3] Leodori G, De Bartolo MI, Guerra A, Fabbrini A, Rocchi L, Latorre A, Paparella G, Belvisi D, Conte A, Bhatia KP, Rothwell JC, Berardelli A. Motor Cortical Network Excitability in Parkinson's Disease. Mov Disord. 2022 Apr;37(4):734-744. doi: 10.1002/mds.28914. Epub 2022 Jan 9. PMID: 35001420.

P55

Proactive inhibition and action preparation as a function of impulsivity traits: preliminary data from a TMS study

Fabio Giovannelli[1], V. Benedetti[1], L.M. Raglione[2], G. Gavazzi[1], M. Hezayen[2], M.P. Viggiano[1], M. Cincotta[2]

[1]Dipartimento NEUROFARBA, Università degli Studi di Firenze, Firenze, Italy
[2]SOC Neurologia Firenze, Area delle Neuroscienze, Dipartimento delle Specialistiche Mediche, Azienda USL Toscana Centro, Firenze, Italy

Introduction: Studies using transcranial magnetic stimulation (TMS) have shown specific modulations (preparatory inhibition and facilitation) of the corticospinal excitability preceding movement execution. These modulations during action preparation have also been observed in tasks used to assess inhibitory control. However, the relationship between action preparation, intentional inhibition processes and impulsive personality traits is still under investigation in healthy individuals and in Parkinson's disease (PD).

Objectives: The aim of the present study was to evaluate the temporal dynamics of corticospinal excitability modulation during action preparation in a proactive inhibition task based on the impulsivity traits. Here we present preliminary data in normal controls.

Methods: Ten right-handed healthy volunteers underwent impulsivity trait assessment (BIS-11), a Go-only choice reaction time (CRT) task and a modified version of the Go/No-go task (GNT) in which they were instructed to press a button in response to 'Go', withhold responses to 'No-go', and decide whether to press or withhold to 'Choose' stimuli. In CRT and GNT, single-pulse TMS was applied to the left M1 hand during the 'readiness' proactive period at the baseline and randomly at one of five time points (-2000, -1500, -1000, -500, and 0 ms before the Go/No-go/Choose cues).

Results: In GNT, in which proactive inhibition was required during the readiness period, the corticospinal excitability was significantly lower compared to the Go-only CRT task, regardless the experimental condition (Go/No-go/Choose). When participants were split into two groups according to the median BIS-11 score, this difference in the corticospinal excitability between the GNT and the Go-only CRT tasks was lower in subjects with higher impulsivity traits.

Conclusions: Preliminary data suggest that proactive inhibitory control exerted during action preparation modulates motor cortex excitability as a function of impulsivity traits. This paradigm appears as potential tool to investigate the relationship between proactive inhibition and impulsivity traits in PD.

P56

Quantitative EEG in Parkinson's disease: when REM sleep behavior disorder onset really matters

Calogero Edoardo Cicero[1], R. Terranova[1], R. Garofalo[1], S. Tabbì[1], A. Luca[1], G. Mostile[1,2], L. Giuliano[1], G. Donzuso[1], M. Zappia[1], A. Nicoletti[1]

[1]Department of Medical, Surgical Sciences and Advanced Technologies G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[2]Oasi Research Institute - IRCCS, Troina, Italy

Introduction: Parkinson's disease (PD) body-first subtype is characterized by prodromal autonomic symptoms and REM sleep behavior disorder (RBD), symmetric dopaminergic degeneration, and increased risk of dementia. On the other hand, the PD brain-first subtype has fewer non-motor symptoms and a milder motor phenotype. The temporal relationship between RBD onset and motor symptoms onset may differentiate these two subtypes.

Objectives: To investigate electrocortical differences between brainfirst and body-first PD patients.

Methods: PD patients with an available routinely collected EEG were retrospectively selected. RBD was diagnosed using the RBD screening questionnaire (≥6). According to the onset of RBD patients were classified into PD-RBDpre (RBD onset before motor symptoms) and PD-RBDpost (RBD onset after motor symptoms). Patients without RBD were classified as PD-RBD-. Presence of Mild Cognitive Impairment (MCI) was diagnosed according to the MDS criteria. EEG Spectral analysis was performed in resting state by computing the Power Spectral Density (PSD) of site-specific signal epochs for the common frequency bands (delta, theta, alpha, beta).

Results: Thirty-eight PD-RBD-, 14 PD-RBDpre and 31 PD-RBDpost patients were recruited. Comparing both global and site-specific absolute values, we found a significant trend toward beta band reduction going from PD-RBD-, PD-RBDpost and PD-RBDpre. No significant differences were found between PD-RBDpost and PD-RBDpatients.

Conclusions: PD-RBDpre patients may represent a different subset of patients as compared to patients without RBD, while patients with later onset have intermediate EEG spectral features. Quantitative EEG could be used as a biomarker in the differentiation of PD subtypes.

P57

Unveiling the meaning of motor cortical excitability changes in Parkinson's disease

Flavia Aiello[1], G. Leodori[1,2,*], M.I. De Bartolo[1,2,*], C. Piervincenzi[1], M. Mancuso[1], A. Ojha[1], M. Costanzo[1], G. Vivacqua[3], G. Fabbrini[1,2], A. Conte[1,2], P. Pantano[1,2], A. Berardelli[1,2], D. Belvisi[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Unit of Microscopic and Ultrastructural Anatomy, Campus Bio-Medico University of Rome, Rome, Italy

** G. Leodori and M.I. De Bartolo contributed equally to this work*

Introduction: Studies of transcranial magnetic stimulation electroencephalography (TMS-EEG) have demonstrated reduced excitability in the primary motor cortex (M1) and increased excitability in the pre-supplementary motor area (pre-SMA) in moderate and advanced Parkinson's disease (PD) patients. It is still unclear, however, whether these abnormalities are evident from the early stages of the disease, their behavioral correlates, and relationship to subcortical changes.

Objectives: Investigating the presence of motor cortical excitability changes in early-stage PD and exploring their association with bradykinesia and structural connectivity in cortico-subcortical connections.

Methods: Thirty-five early PD patients, 19 drug-naive (de novo PDDNPD) and 16 treated with levodopa (L-dopa PD-LPD), and 31 healthy controls (HCs) participated in the study. Participants underwent TMSevoked potentials (TEPs) recording from M1 and preSMA, kinematic recordings of voluntary finger tapping movements, and a 3T-MRI scan. We compared TEP P30 from M1 stimulation and N40 from pre-SMA stimulation, between patients with early PD and HCs. We also examined correlations with clinical, kinematic, and Diffusion tensor imaging (DTI) parameters.

Results: We found a significant reduction in M1 P30 amplitude in both DNPD and LPD patients compared to HCs. Conversely, an increased pre-SMA N40 amplitude was observed only in LPD patients. Notably, pre-SMA N40 amplitude correlated significantly with longer PD duration, higher levodopa equivalent daily dose, and greater motor severity. PD patients exhibited smaller amplitude and slower velocity in finger tapping movements and altered structural integrity in white matter tracts of interest, compared to HC. However, these changes did not correlate with TEP alterations.

Conclusions: M1 hypoexcitability is already present at disease onset and does not correlate with investigated clinical features, thus representing a "parkinsonian state". Conversely, pre-SMA hyperexcitability appears to reflect PD progression. The absence of correlation between TEPs and DTI abnormalities implies that M1 and pre-SMA cortical excitability alterations do not reflect corticosubcortical structural disconnections.

P58

Neurophysiological correlates of limb-kinetic apraxia in Parkinson's disease

Martina De Riggi[1], G. Paparella[1,2], A. Cannavacciuolo[1,2], D. Birreci[1], D. Costa[1], M. Passaretti[1], L. Angelini[1], D. Colella[1], A. Berardelli[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: Many neurophysiological studies have shown primary motor cortex (M1) abnormalities in Parkinson's disease (PD) and some relationship with bradykinesia, one of the cardinal motor features of the disease [2]. However, it is unclear whether there is any relationship between M1 dysfunction and manual dexterity loss, i.e., limb-kinetic apraxia, another possible, though under-investigated motor feature in PD [1].

Objectives: To investigate the potential relationships between objective assessments of limb-kinetic apraxia, through kinematic analysis, and neurophysiological measures of M1, using transcranial magnetic stimulation techniques in patients with PD.

Methods: A sample of twenty-one PD patients and an equal number of age- and gender-matched healthy controls (HC) participated in the study. Objective evaluations of limb-kinetic apraxia during a 10-sec coin rotation task were conducted through kinematic analysis. Various parameters, including the number of movements performed, mean angular velocity, and measures of movement regularity (i.e., intermovement intervals and movement units of the velocity profile), were recorded. M1 excitability was assessed through motor thresholds, analysis of the input/output curve of motor-evoked potentials (MEP), and short-interval intracortical inhibition (SICI). Patients were assessed in the OFF-medication state and tested on the most affected side of the body.

Results: PD patients exhibited slower and more irregular task performance compared to HC. Additionally, they displayed steeper input/output curves and reduced SICI in contrast to HC. Within the PD sample, objective measures of limb-kinetic apraxia correlated with the slope of the input/output MEP curve. Higher M1 excitability, i.e. steeper input-output MEP curve, was associated with decreased velocity and increased irregularity during the motor task ($r = -0.44$ and 0.62, respectively; both $Ps < 0.05$).

Conclusions: This study objectively delineates the characteristics of limb-kinetic apraxia and its neurophysiological correlates in PD, contributing further insights into the pathophysiological role of M1 in this condition.

References:

[1] Zadikoff C, Lang AE. Apraxia in movement disorders. Brain. 2005 Jul;128(Pt 7):1480-97.
[2] Bologna M, Paparella G, Fasano A, Hallett M, Berardelli A. Evolving concepts on bradykinesia. Brain. 2020 Mar 1;143(3):727-750. doi: 10.1093/brain/awz344. PMID: 31834375; PMCID: PMC8205506.

P59

Psychophysiopathological correlates of apathy in Parkinson's disease

Serena Oliveri[1,2], N.V. Maiorana[1], T. Bocci[1,2], C. Casellato[2], M. Guidetti[1], E. Scelzo[2], B. Rovetti[2], D. Dreon[2], S. Botta[2], A. Priori[1,2]

[1]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Clinical Neurology Unit, ASST Santi Paolo e Carlo, Department of Health Sciences, Polo Universitario San Paolo, University of Milan, Milan, Italy

Introduction: Apathy, often associated with impaired executive functions, is found in 19–29% of patients with Parkinson's disease (PD) [1,2].

Objectives: To assess the psychophysiological correlates and neuropsychological features of apathy in PD.

Methods: 12 patients were assessed (in ON condition) through the Montgomery-Asberg Depression Rating Scale (MADRS), Starkstein Apathy Scale (SAS), Lille Apathy Rating Scale (LARS). They underwent event-related potentials (ERPs) recording using an oddball task; two blocks of 250 stimuli each (75 dB) were presented in a random order, with 50 target (2000 Hz) and 200 non-target tones (1000 Hz), with an interstimulus interval of 1s.

Results: P3a and P3b latency of PD group significantly differed from the healthy control group ($p<0.001$). N1 and N2 were comparable. 2 patients had altered P3b latency (matched for age) and they showed significant higher impairment in Self Awareness (SA) subscale of LARS (M=0.845) compared to patients with normal P3b (M=-0.840); [$F(6,1) = 13.580$ $p = 0.010$]. A significant correlation was also found between Intellectual Curiosity (IC) LARS subscale and P3b latency [$\rho = -0.810$, $p = 0.022$]. Also, significant negative correlations were found between MADRS scores and P3a latency ($\rho = -0.731$ $p = 0.04$) and P3b latency ($\rho = -0.857$ $p = 0.01$). No altered values or significant correlations were found for other ERPs components. Ten over 12 patients had mild or moderate depression, and 6 out 12 had full-blown apathy. The severity of apathy correlated with depression [$X^2(3)=9.018$, $p=0.029$] and impairment in Intellectual Curiosity (IC LARS subscale) [$F(10,1)=5.042$, $p = 0.015$].

Conclusions: P3a and P3b latency in apathetic PD patients were associated with specific domains of apathy, IC and SA, and severity of depression, reflecting a neurophysiological abnormal pre-attentive and information processing. P300 might be a valid biomarker to discriminate depression and apathy symptoms in PD and to better characterize disease progression [3,4].

References:

[1] Ou R, Lin J, Liu K, Jiang Z, Wei Q, Hou Y, Zhang L, Cao B, Zhao B, Song W, Shang H. Evolution of Apathy in Early Parkinson's Disease: A 4-Years Prospective Cohort Study. Front Aging Neurosci. 2021 Jan 28;12:620762. doi: 10.3389/fnagi.2020.620762. PMID: 33633560;PMCID: PMC7901914.
[2] Steffens DC, Fahed M, Manning KJ, Wang L. The neurobiology of apathy in depression and neurocognitive impairment in older adults: a review of epidemiological, clinical, neuropsychological and biological research. Transl Psychiatry. 2022 Dec 26;12(1):525. doi: 10.1038/s41398-022-02292-3. PMID: 36572691; PMCID: PMC9792580.
[3] Tokic K, Titlic M, Beganovic-Petrovic A, Suljic E, Romac R, Silic S. P300 Wave Changes in Patients with Parkinson's Disease. Med Arch. 2016 Dec;70(6):453-456. doi: 10.5455/medarh.2016.70.453-456. PMID: 28210020; PMCID: PMC5292223.

[4] de Tommaso M, Betti V, Bocci T, Bolognini N, Di Russo F, Fattapposta F, Ferri R, Invitto S, Koch G, Miniussi C, Piccione F, Ragazzoni A, Sartucci F, Rossi S, Arcara G, Berchicci M, Bianco V, Delussi M, Gentile E, Giovannelli F, Mannarelli D, Marino M, Mussini E, Pauletti C, Pellicciari MC, Pisoni A, Raggi A, Valeriani M. Pearls and pitfalls in brain functional analysis by event-related potentials: a narrative review by the Italian Psychophysiology and Cognitive Neuroscience Society on methodological limits and clinical reliability-part I. Neurol Sci. 2020 Oct;41(10):2711-2735. doi: 10.1007/s10072-020-04420-7. Epub 2020 May 9. PMID: 32388645.

P60

Tic suppression in Gilles de la Tourette syndrome, a transcranial magnetic stimulation-electroencephalography study

Marco Mancuso[1], C. Cutrona[1,2], G. Leodori[1,2], G. Gallo[1], F. Marchet[1], M. Costanzo[1,2], D. Belvisi[1,2], A. Berardelli[1,2], A. Conte[1,2]

[1]Istituto Neuroscienze Umane, La Sapienza University of Rome, Rome, Italy
[2]Istituto IRCCS Neuromed, Pozzilli (IS), Italy

Introduction: In Gilles de la Tourette syndrome (GTS), tics are often preceded by a premonitory urge (PU), which can worsen during voluntary tic suppression. Previous functional MRI studies have indicated a correlation between tics and activity in the Supplementary Motor Area (SMA) and Primary Motor Cortex (M1), as well as between PU and activity in the Brodmann Area 40 (BA40) and Dorsolateral Prefrontal Cortex (DLPFC). Our study aimed to investigate the roles of these cortical areas excitability in the pathophysiology of tics and PU using transcranial magnetic stimulation coupled with EEG (TMS-EEG).

Methods: We recruited 10 healthy volunteers (HV) and 10 GTS patients. Clinical assessment included the Premonitory Urge for Tic Scale (PUTS) and to the Yale Global Tic Severity Scale (YGTSS). We administered 100 TMS stimuli at 110% of the resting motor threshold intensity to SMA, M1, BA40, and DLPFC in two conditions: free ticcing and tic suppression (avoiding blinking in HV), the latter designed to intensify PU.

Results: Early TEPs from M1 were smaller in GTS patients compared to HV during the free tics condition. Additionally, early TEPs from BA40 and SMA displayed distinct amplitude modulations in response to the suppression condition between groups. Tic suppression was associated with a strong inhibition of early BA40 TEPs and an altered modulation of SMA (no significant post-hoc) in GTS. A reduced M1 excitability in GTS might reflect altered cortical inhibitory mechanisms. The abnormal BA40 modulation during tic suppression supports the central role of this area in the PU. The abnormal SMA modulation during tic suppression might suggest its involvement in the voluntary suppression of tics at the premotor phase, potentially reflecting either a compensatory response or a disruption in normal motor control processes.

P61

Beta power circadian modulation in patients with Parkinson's disease and conventional or adaptive deep brain stimulation

Claudio Baiata[1], S. Manfroni[1], L. Caffi[1,2,3], M. Locatelli[4], A. Ampollini[4], S. Bonvegna[1], C. Palmisano[2], I.U. Isaias[1,2]

[1]Parkinson Institute Milan, ASST G.Pini-CTO, Milano, Italy
[2]University Hospital Würzburg and Julius Maximilian University of Würzburg, Würzburg, Germany
[3]The BioRobotics Institute, Scuola Superiore Sant'Anna, Pisa, Italy
[4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Introduction: Increased beta power oscillations in the subthalamic nucleus (STN) are a key feature of Parkinson's disease (PD). However, their physiological contribution to motor and non-motor tasks, such as the sleep-awake cycle, is still poorly understood, and may influence the clinical benefit of deep brain stimulation (DBS), both in conventional (cDBS) and adaptive (aDBS) modes.

Objectives: To investigate the impact of cDBS and aDBS on sleep-wake subthalamic beta power fluctuations in PD.

Methods: We acquired subthalamic local field potentials (LFP) in four patients with idiopathic PD and implanted with the AlphaDBS device. This device can operate in either cDBS, with constant stimulation parameters, or aDBS, adjusting the current amplitude linearly with respect to subthalamic beta power. Patients were recorded consecutively for 10 days in both stimulation modes, i.e. cDBS and aDBS, and with unchanged drugs doses. We calculated the amplitude of the STNLFP in a patient-specific frequency range centered around the most prominent beta peak with 1 min resolution and analyzed the distribution of the beta amplitude separately for the sleeping and waking time.

Results: One patient showed a reduction in subthalamic beta power during sleep compared to waking hours under both stimulation modes (median reduction of 15.4% in cDBS and 15.5% in aDBS). All other patients had sleep-awake beta power modulation < 5% in both stimulation modes. The stimulation modes did not affect the sleep-awake modulation of subthalamic beta power (not significant two-way ANOVA on the ranked data).

Conclusions: Our preliminary data show a variable modulation of subthalamic beta power during sleep-wake cycle in parkinsonian patients with comparable impact of cDBS and aDBS.

P62

Biomechanical and neurophysiological analysis of rigidity in Parkinson's disease: the effect of L-dopa

Marco Falletti[1], F. Asci[1], A. Zampogna[1], M. Patera[1], M. Hallett[3], J. Rothwell[4], A. Suppa[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed Institute, Pozzilli (IS), Italy
[3]Human Motor Control Section, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, USA
[4]UCL Queen Square Institute of Neurology, London, UK

Introduction: Rigidity is one of the cardinal motor signs in Parkinson's disease (PD) and typically improves after the administration of L-Dopa [1]. However clear experimental evidence of how and through which mechanisms L-Dopa improves rigidity in PD are still lacking. Recently, by using a robotic device and a specific algorithm able to discriminate the main biomechanical components of muscle tone (i.e., neural, viscous, and elastic components), we have demonstrated that parkinsonian rigidity prominently reflects the abnormal increase of neural component (NC). The concurrent investigation of spinal (short-latency stretch reflexes - SLRs) and supraspinal reflexes (long-latency stretch reflexes - LLRs) also allowed us to associate parkinsonian rigidity with an abnormal rise of LLRs in PD patients ON therapy [2].

Objectives: In this study, we aimed to assess the effect of L-Dopa on rigidity in PD, by comparing specific biomechanical components of muscle tone and concurrent neurophysiological recordings in PD patients, OFF and ON therapy.

Methods: Eighteen PD patients randomly underwent two independent experimental sessions (OFF and ON L-Dopa), each consisting of controlled wrist extensions delivered by a robot-assisted device, at different angular velocities (50, 100, 150, 200, 236, and 280°/sec). Biomechanical components of muscle tone (neural - NC, viscous - VC, and elastic component - EC) were extracted and estimated using a specific algorithm. Simultaneously, we recorded surface EMG from wrist flexors muscles to assess SLRs and LLRs.

Results: In PD patients, NC was significantly greater in OFF than ON L-Dopa when tested at angular velocities higher than 200°/sec ($p<0.01$). By contrast, VC and EC were comparable in OFF and ON state, at all the angular velocities. Also, the amplitude of LLRs was significantly higher in the OFF than ON state at 236 and 280°/sec ($p<0.05$). Starting from 200°/sec, the higher the angular velocity, the greater the NC and the amplitudes of LLRs, in both OFF and ON states.

Conclusions: L-Dopa significantly improves parkinsonian rigidity by decreasing the neural component of muscle tone and the abnormally enhanced LLRs.

References:

[1] Frequin HL, Schouten J, Verschuur CVM, et al. Levodopa Response in Patients With Early Parkinson Disease: Further Observations of the LEAP Study. Neurology. 2023;100(4):e367-e376. doi:10.1212/WNL.0000000000201448.
[2] Asci F, Falletti M, Zampogna A, et al. Rigidity in Parkinson's disease: evidence from biomechanical and neurophysiological measures. Brain. Published online April 5, 2023:awad114. doi:10.1093/brain/awad114.

P63

Neurogenic orthostatic hypotension is associated with occipital cortex connections disruption: a fMRI study

Corrado Campisi[1], V. Bertotti, F. D'Agata[1], G. Imbalzano[1], C. Ledda[1], E. Montanaro[1,2], M.M. Tangari[1], M. Laudadio[1], C.A. Artusi[1,2], M.G. Rizzone[1,2], M. Zibetti[1,2], L. Lopiano[1,2], M. Bozzali[1,2], A. Romagnolo[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy

Introduction: Neurogenic Orthostatic Hypotension (nOH) is a disabling feature of Parkinson's disease (PD), affecting 20-50% of patients. Whether nOH contributes directly to worse outcomes through hypoperfusion mechanisms, or is merely associated with them as a marker of a more aggressive PD phenotype, remains unclear. Functional MRI (fMRI) studies could help in clarifying this debated issue.

Objective: To evaluate differences in functional connectivity (FC) at fMRI scans between PD patients with nOH and without OH (non-OH).

Methods: We enrolled 49 consecutive patients with advanced PD (mean [SD] age: 60.8 [8.1] years, M/F: 40/9); 19 had OH at bedside evaluation, but 5 of them did not fulfill criteria for nOH (i.e. Δ HR/Δ systolic BP ratio £0.5) and were excluded from the analyses. All patients underwent MRI acquisition, including resting state fMRI. We run Mann-Whitney test between the two groups for demographic and clinical data. Then, we run a seed-based FC analysis.

Results: Age, sex, disease duration, dopaminergic therapy (LEDD) and motor disability (MDS-UPDRS-III) were not significantly different between the two groups, while Hoehn&Yahr stage and global cognitive performance (MMSE) were significantly lower in nOH. FC analyses showed that non-OH patients had stronger connections between the right posterior superior temporal gyrus (pSTG) and the bilateral occipital cortices (i.e., cuneus, precuneus, intracalcarine, lingual, and fusiform) than nOH. On the other hand, nOH patients had higher connectivity between posterior cerebellum and frontal orbital cortex.

Conclusions: nOH is associated with disconnection between pSTG and occipital cortices, probably through the involvement of the Middle Longitudinal Fasciculus (MdLF), which is implicated in language, visuospatial and auditory functions. Our preliminary data on resting state fMRI confirms previous studies showing the association between nOH and occipital and temporal hypoperfusion [1] and posterior cerebellum hyperconnections [2]. Moreover, they underline the need for future studies encompassing task-based fMRI paradigms.

References:

[1] Robertson AD, Messner MA, Shirzadi Z, Kleiner-Fisman G, Lee J, Hopyan J, Lang AE, Black SE, MacIntosh BJ, Masellis M. Orthostatic hypotension, cerebral hypoperfusion, and visuospatial deficits in Lewy body disorders. Parkinsonism Relat Disord. 2016 Jan;22:80-6. doi: 10.1016/j.parkreldis.2015.11.019. Epub 2015 Nov 23. PMID: 26639982.

[2] Kimmerly DS, O'Leary DD, Menon RS, Gati JS, Shoemaker JK. Cortical regions associated with autonomic cardiovascular regulation during lower body negative pressure in humans. J Physiol. 2005 Nov 15;569(Pt 1):331-45. doi: 10.1113/jphysiol.2005.091637. Epub 2005 Sep 8. PMID: 16150800; PMCID: PMC1464214.

P64

Motion analysis and MRI characteristics in patients with isolated REM sleep behavior disorder

Elisabetta Sarasso[1,8,9], A. Gardoni[1], S. Marelli[2], R. Balestrino[3,4,8], L. Zenere[1], A. Grassi[1,8], A. Castelnuovo[2], A. Tettamanti[5,8], L. Ferini-Strambi[2], M. Filippi[1,3,6,7,8], F. Agosta[1,6,8]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Division of Neuroscience, Sleep Disorders Center, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurosurgery and Gamma Knife Radiosurgery Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Department of Rehabilitation and Functional Recovery, IRCCS San Raffaele Scientific Institute, Milan, Italy
[6]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[7]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[8]Vita-Salute San Raffaele University, Milan, Italy
[9]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy

Introduction: Clinical, gait analysis, and magnetic resonance imaging (MRI) features might be biomarkers of conversion from isolated REM sleep behavioral disorder (iRBD) to parkinsonisms.

Objectives: The aim of the study was to assess gait analysis, neurological, neuropsychological and structural/functional MRI characteristics in patients with iRBD.

Methods: Thirty-eight patients with a polysomnography-confirmed iRBD and 28 age/sex-matched healthy controls were included. Subjects underwent neuropsychological assessment and motor functional evaluations including Nine-Hole Peg Test (9HPT), 5-Time Sit-To-Stand (5TSTS), Timed Up and Go test (TUG) and 4-Meter Walking Test (4MWT) with and without a cognitive dual-task (TUG-COG and 4MWT-COG). Spatio-temporal gait parameters during 4MWT(-COG) and TUG(-COG) were collected using a stereophotogrammetric system. We obtained the functional connectivity (FC) maps of the main resting-state networks using Independent Component Analysis. Brain structural alterations were assessed using whole-brain voxel-based morphometry, FIRST for deep grey matter volumes and Freesurfer for cortical thickness and brainstem volumes.

Results: IRBD patients relative to controls showed worse performance during the 9HPT and 5TSTS, greater asymmetry of arm swing amplitude during 4MWT and higher stride length variability during 4MWT-COG. Dual-task worsened the walking performance of iRBD more than controls. IRBD patients showed worse memory and abstract reasoning relative to controls. Moreover, iRBD patients showed decreased FC of pallidum and putamen within the Basal Ganglia network and of occipital and temporal areas within the Visuo-Associative network, and reduced volume of the supramarginal gyrus.

Conclusions: We found subtle motor, cognitive, and structural and functional MRI changes that may represent initial manifestations of neurodegeneration in iRBD patients. The combination of clinical, gait analysis, and MRI data might be helpful to predict the conversion from iRBD to parkinsonisms. The collection of longitudinal data in a larger sample will allow to verify this hypothesis.

*Funding***:** Italian Ministry of Health [grant number #RF-2018-12366746]

P65

Comparative analysis of supra and infratentorial atrophy in cerebellar ataxias: unveiling distinctions across different etiologies

Stefano Pisano[1,6], S. Basaia[1], O. Stojiljković[7], S. Mesaros[7], N. Dragasevic[7], M. Filippi[1,2,3,4,5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]Neurology Department, Istituto Clinico S. Anna Hospital, Gruppo San Donato, Brescia
[7]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: Patterns of supra and infratentorial brain atrophy may be useful in differentiating cerebellar ataxias (CA) due to different causes.

Objectives: This study investigates structural changes in gray matter (GM) and white matter (WM) in patients with CA arising from inherited, sporadic, and neurodegenerative causes.

Methods: Twenty-eight autosomal dominant (AD) CA patients, 17 autosomal recessive (AR) CA patients, 29 sporadic cases of CA, 8 multiple system atrophy patients (MSAc) and 20 controls were included. MRI and clinical assessment were performed; whole-brain Voxel-Based Morphometry (VBM) and cerebellar-optimized VBM (SUIT toolbox) were used to assess GM atrophy. Brainstem and superior cerebellar peduncles (SCP) volumes were estimated and compared.

Results: All CA groups showed widespread GM cerebellar atrophy compared to controls. Additionally, AD and AR groups showed distinct clusters of supratentorial GM atrophy compared to controls, mainly involving temporal and parietal regions. No supratentorial GM differences were found among CA groups. SUIT-VBM revealed more severe atrophy in the medial Crus-I and II in MSAc compared to AD, and in AR compared to AD. AD, AR, and MSAc groups exhibited reduced whole-brainstem, midbrain, and pons volumes compared to controls; AD and MSAc groups also exhibited reduced wholebrainstem and pons volumes compared to sporadic cases. AD and AR showed reduced medulla volumes compared to controls and sporadic cases. SCP volume reduction was evident in all CA groups compared to controls, with AD showing also decreased SCP volume compared to sporadic cases.

Conclusions: All CA groups showed diffuse cerebellar atrophy, additionaly AD and AR groups showed distinct supratentorial patterns of atrophy. The sporadic group showed less involvement of brainstem structures compared to other CA groups, potentially aiding in distinguishing sporadic from inherited forms. The evidence of distinct patterns of structural alterations in different CA etiologies might contribute to an improved differential diagnosis.

P66

Neural correlates of motor imagery versus action observation of gait tasks in patients with Parkinson's disease and freezing of gait: an fMRI study

Andrea Gardoni[1], E. Sarasso[1,5,6], L. Zenere[1], E. Canu[1], S. Basaia[1], E. Pelosin[6], M. Filippi[1,2,3,4,5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]NeurologyUnit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy

Introduction: Parkinson's disease (PD) patients with freezing of gait (FoG) showed an altered recruitment of the mirror neuron system (MNS) during action observation (AO) and motor imagery (MI).

Objectives: To compare the neural correlates of MI and AO in PD-FoG patients relative to healthy controls.

Methods: Twenty-four PD-FoG patients and 19 age/sex-matched healthy controls were included. The subjects underwent brain MRI including a MI/AO task. During MI, they imagined themselves performing three gait tasks exacerbating FoG (starting/stopping walking in a narrow hallway; turning around 360° in a small radius; going through a doorway) while navigating first-person videos. During AO, subjects observed third-person videos representing a person performing the same three actions.

Results: During MI relative to AO, both PD-FoG patients and healthy controls showed higher activity of lingual gyrus, while only healthy controls had a higher activity of cerebellum VI. Healthy controls also showed increased recruitment of middle/superior frontal gyri, middle cingulum, prefrontal cortex and hippocampus during AO relative to MI. PD-FoG patients relative to healthy controls showed a reduced activity of vermis VI during MI relative to AO.

Conclusions: Both healthy controls and PD-FoG subjects showed an activation of sensorimotor areas and of the MNS during both MI and AO. MI relative to AO required higher recruitment of lingual gyrus, involved in visual memory and motion perception, and, only in healthy controls, of cerebellum VI that is implicated in body representation, motor processing and attentive-executive functions.
PD-FoG patients can thus activate, at least partially, areas involved in MI. Only in healthy subjects, AO compared to MI activated more the fronto-parietal MNS that plays a role in action understanding and imitation learning. MI and AO might represent complementary approaches in PD-FoG patients to stimulate the activity of sensorimotor and MNS brain areas in a specific way.

P67

Identification of Parkinson's disease biomarkers in a multi-modal AI framework using raw MRI and clinical data

Silvia Basaia[1], F. Sciancalepore[1,6], E. Sarasso[1,5,9], R. Balestrino[3,5,8], I. Stankovic[7], A. Tomic[7], R. De Micco[10], A. Tessitore[10], M. Salvi[6], F.M. Meiburger[6], V.S. Kostic[7], F. Molinari[6], M. Filippi[1,2,3,4,5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]Biolab, PoliTo (BIO)Med Lab, Department of Electronics and Telecommunications, Politecnico di Torino, Torino, Italy
[7]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[8]Neurosurgery and Gamma Knife Radiosurgery Unit, IRCCS Ospedale San Raffaele, Milan, Italy
[9]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy
[10]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy

Introduction: Artificial intelligence may be a powerful tool to diagnose and monitor Parkinson's Disease (PD).

Objectives: The main goal of this study was to develop a 3D Convolutional Neural Network (CNN) based on multimodal MRI, clinical and demographic data to differentiate between healthy controls and PD patients and to predict the progression of PD (stable vs worsening).

Methods: Three cohorts of PD subjects and controls were selected from different studies: (i) 148 PD subjects (86 mild, 62 moderate-tosevere) and 60 controls; (ii) 56 mild-PD subjects and 20 controls from PPMI database; and (iii) 91 mild-PD subjects and 38 controls. All participants underwent a brain MRI at baseline and a clinical evaluation at baseline and after 2 years. Mild-PD subjects were classified stable or worsening using a k-means clustering based on baseline and follow-up UDPRS-III value. CNN, which are mathematical representations of the human neural architecture, were applied. No pre-processing on MRI images was performed.

Results: Considering moderate-to-severe PD patients relative to controls, the accuracy rate on the test dataset reached nearly 75%, only relying on MRI data for classification. However, considering mild-PD vs controls, the accuracy rate was around 65% on the test set, highlighting challenges in the extraction of discriminative features during the initial stages of the disease. In the differentiation between clinically stable and worsening PD, CNN reached over 70% accuracy rate on the test set by combining raw MRI and clinical data.

Conclusions: By integrating MRI data with clinical and demographic information, our CNN demonstrated promising results and offers a valuable tool for early diagnosis and personalized treatment planning for PD patients.

Supported by: Italian Ministry of Health (GR-2018-12366005, RF-2018-12366746, GR-2021-12374601).

P68

Exploring the relationship between L-dopa response and cognitive functions in advanced Parkinson's disease patients: insights from a mixed approach with inertial sensor and advanced neuroimaging analyses

Corrado Campisi[1], C.A. Artusi[1,2], L. Serra[3], F. D'Agata[1], E. Montanaro[1,2], M. Laudadio[1,2], G. Imbalzano[1], C. Ledda[1], M.G. Rizzone[1,2], M. Zibetti[1,2], A. Romagnolo[1,2], L. Lopiano[1,2], M. Bozzali[1,2,4]

[1]Neuroscience department "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy
[3]Neuroimaging Laboratory, IRCCS Santa Lucia Foundation, Rome, Italy
[4]Department of Neuroscience, Brighton and Sussex Medical School, University of Sussex, Brighton East Sussex, UK

Introduction: Inertial sensors offer more precise and quantitative motor assessment in Parkinson disease (PD). We hypothesize they can be used as a biomarker for cognitive function deficits due to common patternbetween gait and cognition.

Aim: To investigate possible relationships and common neurobiological substrates between gait response to L-dopa and cognition in PD patients analyzed with resting-state functional MRI (rs-fMRI).

Methods: We recruited 51 patients with advanced PD (mean [SD] age:60.5 [8.1] years; M/F:37/14). Gait analyses were conducted in off-medication (med-off) and in on-medication (med-on). All patients underwent a neuropsychological (NPS) examination and 3T rs-fMRI. We employed atlas PET maps of four neurotransmitter (NT) receptors (i.e., Norepinephrine, Dopamine, Serotonin and Acetylcholine). Regression analyses were first run including multi-domain NPS Z-scores and differences between med-off and med-on gait data. Rs-fMRI were processed using REACT [1] to obtain functional connectivity (FC) maps weighted for each NT. Then, we run GLM analyses to find associations between NT-FC maps and cognitive/motor parameters (P-values cluster level corrected < 0.001). Finally, we run conjunction analyses to identify areas of NT-FC associated with both motor and cognitive parameters.

Results: We found association between time up-and-go (TUG) and both executive functions and long-term memory. FC maps of every NT showed a lateralized pattern of association in which patients having the best L-dopa response based on TUG and the best scores in executive functions were hyper connected to the right postero-inferior temporal gyrus; viceversa, they were hyper-connected to the left postero-inferior temporal gyrus.

Discussion: The inferior temporal gyrus is part of the frontoparietal network which is known to be crucial for the executive functions. Regardless of the NT considered, the frontoparietal network is strictly associated with improvement or worsening of executive performance and influence the L-dopa response on TUG performance.

References:

[1] O. Dipasquale, P. Selvaggi, M. Veronese, A.S. Gabay, F. Turkheimer, M.A. Mehta, "Receptor-Enriched Analysis of functional connectivity by targets (REACT): A novel, multimodal analytical approach informed by PET to study the pharmacodynamic response of the brain under MDMA", Neuroimage 2019, 195, 252-260.

P69

DAT-imaging and clinical phenotypes of Parkinson's disease: findings and follow up at 5 years

Sara Varanese[1], N. Modugno[2], M.P. Buongarzone[1], S. Viola[1], D. Travaglini[1], L. Bonanni[3]

[1]Asl 2 Lanciano-Vasto-Chieti, Ospedale Civile San Pio, Vasto (CH), Italy
[2] IRCCS NEUROMED, Pozzilli, Italy
[3] G. d'Annunzio Univeristy of Chieti-Pescara, Medicine and Aging Department, Chieti, Italy

Introduction: An accurate diagnostic and therapeutic approach to Parkinson's disease (PD) requires understanding of the risk to develop nonmotor symptoms (i.e. cognitive and pychiatric disorders).

Objectives: To evaluate: 1. The relationship of motor and nonmotor symptoms with specific patterns of striatal dopaminergic denervation in a cohort of symptomatic PD patients with dopaminergic denervation at dopamine transporter single photon emission tomography (DAT-SPECT). 2.The prognostic value of specific dopaminergic denervation pattern on cognitive impairment.

Methods: Twenty-eight patients at PD onset, with dopaminergic denervation at DAT-SPECT[l1], were studied. Patients were divided into two groups based on the evidence of dopaminergic denervation in putamina alone (PD-p) or in putamina and caudates (PD-pc). The two groups were compared as per demographics, motor phenotypes, disease severity according to MDS-UPDRS III, psychiatric symptoms as per NPI and cognitive symptoms as per MoCA score at baseline. Cognitive assessment was repeated at 5 years follow up. Premotor symptoms were also assessed.

Results: Twelve patients were classified as PD-p (M/F=5/7; mean age=64,31±8,5years; mean disease duration 3±2.68 mean UPDRS III 20.44±5.96); 16 patients were classified as PD-pc (M/F=10/6; mean±Standard deviation (SD) age 62.33± 8.65 years; disease duration 1.76±1.09 years; UPDRS III 31.29±8.16). The two groups did not differ in terms of age, gender and disease duration. At baseline PD-pc group showed worse UPDRS scores ($p<0.0001$). Rigid phenotype was found in 66,7% of PD-pc vs. 12,5% in PD-p ($p<0.0001$); tremulous phenotype was found in 4,8% of PD-pc vs. 56,3% of PD-p ($p<0.0001$); mixed phenotype was equally found in the two groups (28.6% of PD-pc vs. 31.3% of PD-p, $p>0.05$. Premotor (present for at least 3 years before the motor onset) mood disorders (depression and anxiety) were found in 47.5% of PD-pc, and 12.5% in PD-p (P=0.001). 71.4% of PD-pc patients had psychiatric symptoms at baseline (generalized anxiety, panic attacks, phobia, obsessive-compulsive disorder, moderate to severe depression). In the PD-p group 31.3% had psychiatric symptoms at baseline (mild depression and/or anxiety). MoCA equivalent score was <17.32 (cut-off[l2]) in 32% of PD-pc group and in none of the PD-p patients at baseline. At 5 years follow up MoCA score was below cut off in 83% of PD-pc group [l3] and 9% of PD-p.

Conclusions: The evidence of early dopaminergic denervation in the caudates correlates with a more complex phenotype of PD.

P70

123I-Metaiodobenzylguanidine myocardial scintigraphy in differential diagnosis between Parkinson's disease and multiple system atrophy

Mauro Catalan[1], F. Dore[2], P. Polverino[1,3], C. Bertolotti[1,4], A. Sartori[1], L. Antonutti[1], A. Cucca[1], G. Furlanis[1], S. Capitanio[2,5], P. Manganotti[1]

[1]Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy
[2]Nuclear Medicine, Imaging Diagnostic Department, University Hospital and Health Services of Trieste, University of Trieste, Italy
[3]Neurology Department, Humanitas Research Hospital, Milan, Italy
[4]Neurology Department, Niguarda Hospital, Milan, Italy
[5]Nuclear Medicine, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Introduction: 123I-metaiodobenzylguanidine (123I-MIBG) myocardial scintigraphy provides a measure of cardiac sympathetic innervation and may be useful in differentiating Parkinson's disease (PD) from Multiple System Atrophy (MSA) [1]. In PD patients a reduction of the tracer in the myocardial muscle is detected, while in MSA the exam generally results normal [2]. 123I-MIBG myocardial scintigraphy was recently included as a supportive feature in the MDS PD and MSA diagnostic criteria [3-4]. Nevertheless, a mild reduction of 123I-MIBG uptake in MSA patients and a normal uptake in early stage of PD may sometimes occur, thus limiting the diagnostic accuracy.

Objectives: To evaluate the contribution of myocardial scintigraphy in distinguishing PD from MSA in a real-life cohort of patients.

Methods: 85 patients with parkinsonism, referred to the Movement Disorders Unit of the Neurology Department of Trieste, who underwent a 123I-MIBG myocardial scintigraphy, were screened. 23 patients, who satisfied a diagnosis of PD and 26 patients with a diagnosis of MSA, according to MDS criteria, were identified. Sensitivity, specificity, predictive positive value (PPV), and predictive negative value (PNV) were obtained, matching the clinical diagnosis with the scintigraphy's result. Mean early and delayed heart/mediastinum (H/M) ratios and washout rate (WR) were then compared between the PD and MSA groups.

Results: Impaired MIBG uptake was found in 21/23 PD patients, while normal uptake was found in 20/26 MSA patients (sensitivity 91.3%, specificity: 77.1%, PPV: 0.78, NPV: 0.91). In patients with early dysautonomia, the accuracy was higher (sensitivity 100%, specificity 85%). Mean early H/M ratio, delayed H/M ratio and WR, resulted significantly different comparing PD vs MSA groups (1.40 vs 1.69, 1.28 vs 1.68 and 48,7% vs 30%, respectively) ($p < 0.05$).

Conclusions: MIBG myocardial scintigraphy resulted highly sensitive but less specific in the differentiating PD from MSA patients. The accuracy improves considering only patients presenting early autonomic dysfunction.

References:

[1] Courbon FC, et al. 2003. Mov Disord;18:890-897.
[2] Braune S, et al. 1999. Neurology;53:1020-1025.
[3] Postuma RB, et al. 2015. Mov Disord;30:1591-1599.
[4] Wenning GK, et al. 2022. Mov Disord;37:1113-1148.

P71

Art therapy as an add on activity to intensive rehabilitation treatment in Parkinson's disease: a booster to patient's well being?

Chiara Siri, M.G. Longoni, M. Zarucchi, A. De Laurenzis, A. Carollo, A. Ranghetti, V. Cereda, M. Pellegrino, G. Manoni, M. Canesi

Department of Parkinson's Disease and Movement Disorders Rehabilitation, Moriggia Pelascini Hospital, Gravedona, Italy

Introduction: Art therapy (AT) lowers depressive symptoms and enhances the benefit of physical exercise on QoL in elderly [1]. In people with Parkinson's disease (PWPD), research on AT is still poor and mostly focused on its effects cognition [2].

Objectives: We aimed to explore the effect of group AT sessions on emotional wellbeing in PWPD.

Methods: We consecutively enrolled 39 non-demented PWPD (AT_group: age: 66.7±7.7; disease duration: 10.6±5.6; UPDRS III: 35±13.7; M=19) attending the multidisciplinary aerobic motorcognitive rehabilitation 4 weeks training at our department and participating in AT weekly sessions as add on activity. Despite being performed in small groups (3-4 PWPD), AT was tailored (material and themes choices) on each single patient. We enrolled 39 PWPD (CNTR) matched by demographic and clinical variables to the AT_group who attended one session of occupational therapy instead of AT. Profile of Mood Scale (POMS) is used to measure the impact of a treatment and can be repeated after a short time. We administered POMS to all participants at admission (T0) and discharge (T1) and the changes in the subscales (depression/dejection, tension/anxiety, anger/hostility, fatigue/indolence, confusion, and vigour) were compared within and between groups. The relation between POMS, clinical features, neuropsychological (MoCA, FAB, CDT, BDI-II, STAI I and II) and motor (UPDRSIII, 6MWT, BBS, TUG) assessments were explored.

Results: The two groups were comparable in POMS scores at baseline; in AT_group, POMS subscales scores significantly improved between T0 and T1 and delta of change was significantly higher compared to CNTR; POMS subscales correlated with BDI-II, STAI, UPDRSIII and 6MWT but the improvement in in the motor scales was independent from the change in POMS subscales.

Conclusions: AT activity during admission for intensive rehabilitative treatment significantly enhances patient's emotional wellbeing. Noteworthy, the improvement in mood states is not related to the improvement in motor symptoms.

References:

[1] Galassi F, Merizzi A, D'Amen B, Santini S. Creativity and art therapies to promote healthy aging: A scoping review. Front Psychol. 2022 Sep 26;13:906191. doi: 10.3389/fpsyg.2022.906191. PMID: 36225688; PMCID: PMC9549330.
[2] Cucca A, Di Rocco A, Acosta I, Beheshti M, Berberian M, Bertisch HC, Droby A, Ettinger T, Hudson TE, Inglese M, Jung YJ, Mania DF, Quartarone A, Rizzo JR, Sharma K, Feigin A, Biagioni MC, Ghilardi MF. Art therapy for Parkinson's disease. Parkinsonism Relat Disord. 2021 Mar;84:148-154. doi: 10.1016/j.parkreldis.2021.01.013. Epub 2021 Jan 23. PMID: 33526323.

P72

Efficacy and safety of a telerehabilitation program for the treatment of nocturnal hypokinesia in people with Parkinson's disease: a pilot study

Pietro Lombardo[1], E. Bianchini[1,2], S. Galli[1], F. Bianchini[1], F. D'Audino[1], M. Alborghetti[1], D. Rinaldi[1], L. De Carolis[1], P. Pacilio[1], F.E. Pontieri[1]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Univ. Grenoble Alpes, AGEIS, Grenoble, France

Introduction: Reduced bed mobility (i.e., nocturnal hypokinesia) is not uncommon in people with Parkinson's disease (PwPD) [1]. However, although a rationale for a potential effectiveness of rehabilitation on this symptom [2], only very few studies investigate the effectiveness of physiotherapy on nocturnal hypokinesia in PwPD [3] and no study evaluated the effectiveness of telerehabilitation on this manifestation.

Objectives: To evaluate the safety and effectiveness of a telerehabilitation program on bed mobility and sleep quality in PwPD with nocturnal hypokinesia.

Methods: Eight PwPD [females: 3 (38%); age: 65.9±10.2; disease duration: 9.8±5.7; LEDD: 727±227 mg; mHY: 2 (2-2; 2-3)] with nocturnal hypokinesia (item 2.9 of MDS-UPDRS-II≥1) underwent a 6-week telerehabilitation program consisting of 1 remote visit with a therapist and a minimum of two sessions of >30-min of selfconducted exercises per week through video tutorials. Participants were evaluated at baseline (T0) and at the end of the intervention (T1) by means of MDS Unified Parkinson's disease Rating Scale (MDSUPDRS) parts I-IV, Parkinson's disease Sleep Scale (PDSS2), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Nocturnal Hypokinesia Questionnaire (NHQ), Functional Mobility Composite Score (FMCS) and Parkinson's disease Questionnaire 39 (PDQ39). Wilcoxon test was used to compare clinical scores between T1 and T0.

Results: No patient reported adverse events during treatment. A significant reduction in MDS-UPDRS-II item 2.9 score (p=0.048, median difference: 1), PSQI (p=0.021, median difference: 3), PDSS2 (p=0.042, median difference: 6.7), ESS (p=0.041, median difference: 2) was found at T1 compared to T0. No significant difference was found for the other examined variables between T1 and T0.

Conclusions: Our results suggest that telerehabilitation could be effective and safe in treating PwPD with nocturnal hypokinesia.

References:

[1] Stack, E.L.; Ashburn, A.M. Impaired Bed Mobility and Disordered Sleep in Parkinson's Disease. Mov Disord 2006, 21, 1340–1342, doi:10.1002/mds.20944.
[2] Taniguchi, S.; D'cruz, N.; Nakagoshi, M.; Osaki, T.; Nieuwboer, A. Determinants of Impaired Bed Mobility in Parkinson's Disease: Impact of Hip Muscle Strength and Motor Symptoms. NeuroRehabilitation 2022, 50, 445–452, doi:10.3233/NRE-210301.
[3] Janssens, J.; Malfroid, K.; Nyffeler, T.; Bohlhalter, S.; Vanbellingen, T. Application of LSVT BIG Intervention to Address Gait, Balance, Bed Mobility, and Dexterity in People with Parkinson Disease: A Case Series. Phys Ther 2014, 94, 1014–1023, doi:10.2522/ptj.20130232.

P73

Classification and quantification of physical therapy interventions across multiple neurological disorders: a comparison between Parkinson disease, stroke and multiple sclerosis

Thomas Bowman[1], F.G. Mestanza Mattos[2], S. Salvalaggio[3,4], F. Marazzini[5], C. Allera Longo[6], S. Bocini[7], V. Bonci[8], M. Gennuso[8], F.G. Materazzi[9,10], E. Pelosin[11,12], M. Putzolu[13], R. Russo[6], A. Turolla[14,15], S. Mezzarobba[11,12,16,] D. Cattaneo[1,2]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy
[3]Laboratory of Computational Neuroimaging, IRCCS San Camillo Hospital, Venice, Italy
[4]Padova Neuroscience Center, Università degli Studi di Padova, Padova, Italy
[5]AIAS ETS Milano, Pantigliate, Italy
[6]Department of Rehabilitation, San Carlo Borromeo Hospital, Milan, Italy
[7]Division of Physical and Rehabilitation Medicine, Fondazione Opera San Camillo, Presidio di Torino, Turin, Italy
[8]Department of Neurological Sciences, Neurorehabilitation Clinic, AOU delle Marche, Ancona, Italy
[9]Montecatone Rehabilitation Institute, Imola, Italy
[10]Department of Biotechnological and Applied Clinical Sciences (DISCAB), University of L'Aquila, L'Aquila, Italy
[11]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[12]IRCCS Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[13]Department of Experimental Medicine (DIMES), Section of Human Physiology, University of Genoa, Genoa, Italy
[14]Department of Biomedical and Neuromotor Sciences (DIBINEM), Alma Mater Studiorum Università di Bologna, Bologna, Italy
[15]Unit of Occupational Medicine, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[16]Azienda Sanitaria Universitaria Giuliano Isontina (ASUGI), Trieste, Italy

Introduction: Despite their importance in neurorehabilitation, few researchers [1,2] have investigated the prevalence of goals and interventions of physical therapy (PT) in everyday clinical practice.

Objectives: To describe and compare the prevalence of PT goals and interventions in people with Parkinson's disease (PwPD), Stroke (PwST) and Multiple Sclerosis (PwMS).

Methods: A multicentre longitudinal observational study was conducted in six hospitals and three rehabilitation centres throughout Italy. We recruited PwPD (n = 35), PwST (n = 119) and PwMS (n = 48) who underwent PT sessions provided by the national health system. For each participant, the physiotherapist who provided the treatment completed a semi-structured interview to report the goals and interventions used. The prevalence of goals and interventions was calculated as a percentage, taking into account the number of hours devoted to each pathology.

Results: A total of 4850 hours of PT were analyzed. The most selected goal in PwPD was "walking" (34.9%) followed by "balance" (11.5%) and "outdoor mobility" (11.1%). In PwST the most selected goals was "walking" (35%), followed by "manipulation and grasping" (13.1%) and "balance" (12.6%). Similarly, in PwMS the most selected goal was "walking" (34.3%), followed by "manipulation and grasping" (17.9%) and "muscle strength" (8.4%). Considering PT interventions, the most selected in PwPD was "walking training" (20.2%), followed by "balance training" (13.1%)

and “dual-task exercises” (9.3%). In PwST “walking training” was the primary intervention followed by “balance training” (13.4%) and “proprioceptive exercises” (13.3%). In PwMS, the most selected intervention was “walking training” (16.8%), followed by “manipulation and grasping exercises” (15.3%).

Conclusions: The most relevant PT goals and interventions across neurological diseases were those related to “walking”. Activities related to “manipulation and grasping” were poorly considered in PwPD compared with others pathologies, while improving “outdoor mobility” and “dual task exercises” were most commonly used in the PD population.

References:

[1] Dijkers MP, Hart T, Tsaousides T, Whyte J, Zanca JM. Treatment taxonomy for rehabilitation: past, present, and prospects. Arch Phys Med Rehabil. 2014 Jan; 95: S6-16.
[2] Rasova K, Freeman J, Martinkova P, Pavlikova M, Cattaneo D, Jonsdottir J, Henze T, Baert I, Van Asch P, Santoyo C, Smedal T, Beiske AG, Stachowiak M, Kovalewski M, Nedeljkovic U, Bakalidou D, Guerreiro JM, Nilsagård Y, Dimitrova EN, Habek M, Armutlu K, Donzé C, Ross E, Ilie AM, Martić A, Romberg A, Feys P. The organisation of physiotherapy for people with multiple sclerosis across Europe: a multicentre questionnaire survey. BMC Health Serv Res. 2016;16:552.

P74

White matter microstructural changes following Quadrato Motor Training in Parkinson's disease: a longitudinal study

Raffaella Di Giacopo[1], D. Ottaviani[1,] , R. Franciosi[2], T.D. Ben-Soussan[3], C. Meli[4], C. Longo[5], M.C. Malaguti[5], R. Bacchin[5], B. Giometto[1,5], C.C. Quattrocchi[2]

[1]Unità Operativa di Neurologia, Ospedale di Rovereto, Rovereto (TN), Italy
[2]Unità Operativa di Radiologia, Ospedale di Rovereto Rovereto (TN), Italy
[3]Istituto di Ricerca per le Neuroscienze, l'Educazione e la Didattica (RINED), Fondazione Patrizio Paoletti (FPP), Assisi (PG), Italy
[4]Centro Interdipartimentale Mente/Cervello (CIMEC), Trento, Italy
[5]Unità Operativa di Neurologia, Ospedale di Trento, Trento, Italy

Introduction: Cognitive decline in Parkinson's disease (PD) can involve multiple domains, such as executive, attentional and visuospatial abilities [1]. MCI can be recognized from the early stage of the disease. Therefore, the motor rehabilitation treatment makes use of cognitive strategies and viceversa [2]. Recently, a new paradigm, the Quadrato Motor Training (QMT), has been developed to improve attention, coordination, ideational flexibility and spatial cognition, with significant results in healty volunteers [3].

Objectives: The aim of this case-control study was to investigate, in a cohort of PD patients, the longitudinal effects of QMT on motor and cognitive symptoms and the relationship between these and changes in white matter microstructure.

Methods: Fifty PD patients were randomized to daily perform QMT (QMT group) or sham exercise (sham group) for a period of 4 weeeks. The QMT requires standing at one corner of a square and making movements toward different corners in response to verbal instructions. During the sham exercise the movements (steps) were on a single spatial direction. To verify the exercise compliance, subjects were asked to complete a personal diary at home daily. Sleep hours were monitored daily. They also performed a complete neuropsychological evaluation of the cognitive and affective domains. At T0 and T1 the subjects underwent the UPDRS scale (part I, II, III, IV, V), the Time Up and Go test; brain MRI (including 3D volumetry, DTI and resting-state fMRI).

Results: At time T1 compared to T0, changes of FA were found in the QMT group probably related to sensorimotor effects and in agreement with previous studies. Also main associative white matter traits were involved in the circuits of spatial cognition and executive functions.

Conclusions: Improving impaired cognitive functions in PD using QMT may have significant implications for neurorehabilitation programs. Noteworthily, QMT is a relatively short workout, very easy to perform and practice in a limited space.

References:

[1] Litvan I, Goldman, G, Troster A.I et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov. Disord. 2012; 27:349–356.
[2] Ferrazzoli D, Ortelli P, Iansek R. et al. Rehabilitation in Movement Disorders: from basic mechanisms to clinical strategies. Handb Clin Neurol 2022; 184:341-55.
[3] Ben-Soussan, T. D., Berkovich-Ohana, A., Piervincenzi, C., et al. Embodied cognitive flexibility and neuroplasticity following Quadrato Motor Training. Front. Psychol. 6:1021. doi: 10.3389/fpsyg. 2015.01021.

P75

Effectiveness of an immersive virtual reality rehabilitation program in patients with functional motor disorders: a randomized controlled trial pilot

Angela Sandri[1], M. Bertozzo[1], Z. Menaspà[1], F. Bombieri[1], C. Geroin[1], D. Vidale[2], M. Pirini[2], M. Fiorio[1], M. Gandolfi[1], M. Tinazzi[1]

[1]Department of Neuroscience, Biomedicine and Movement Science, University of Verona, Verona, Italy
[2]Khymeia SRL, Padova, Italy

Introduction: Functional motor disorders (FMDs) are disabling neurological conditions manifesting involuntary learned altered movement patterns. Multidisciplinary rehabilitation reduces motor and non-motor symptoms [1,2]. Virtual Reality (VR) holds promise as a tool to address pathophysiological features like attention, sense of agency, and beliefs/expectations.

Objectives: To explore feasibility and effects on symptoms of a VR-based rehabilitation treatment against the conventional one.

Methods: Patients were randomly assigned to either Experimental (EG) or Control Group (CG) training. The five-day VR-intervention explained aims and contents, guided patients through a VR-familiarization phase, and applied experimental intervention. The VR program was developed with Khymeia (Padova – Italy). Exercises focused on patients' dynamic engagement in immersive exergames (Vive) involving motor and attentional tasks to improve postural control and balance. CG followed the conventional treatment [1,2]. Primary outcomes were the Simulator Sickness Questionnaire (SSQ) and the System Usability Scale (SUS) administered after the rehabilitation week (T1). Motor and non-motor symptoms' measures were collected before rehabilitation (T0), after it (T1), and at 3-month (T2). Non-parametric tests were used for statistical analyses. The project was funded by the Joint Research Project.

Results: 36 patients were enrolled. The final sample comprised 11 (11 females, mean age: 38.91±14.82) patients in the EG and 14 (12 females, mean age: 47±20.70) in the CG. SUS (mean: 20.57 [10-100]) and SSQ (mean: 7.4 [0-96]) confirmed usability and no adverse events. Regarding secondary outcomes, SF-12 physical score was significantly increased ($p=0.035$), and anxiety symptoms were significantly reduced ($p=0.042$) at T2 vs T0 in the EG while not in the CG. No other significant between-group differences were noted.

Conclusions: VR-based rehabilitation program is feasible for FMDs. Training effects were similar between groups for motor outcomes. However, improvement on physical quality of life and anxiety was observed. Further studies are needed to confirm the effects on symptoms' perception.

References:

[1] Nielsen et al., 2017. J Neurology, Neurosurg, Psychiatry 88(6):484-490.
[2] Gandolfi et al., 2021. NeuroRehab 48:305-314.

P76

Evaluation of the effectiveness of a rehabilitation programme for the improvement of musical performance in a sample of musicians with focal hand dystonia: a case series

Francescaroberta Panuccio[1], R. Simeon[1], O. Fedrizzi[2], D. Siviglia[1], G. Fabbrini[1], A. Berardi[1], A. Carlizza[2], G. Galeoto[1]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]UniCamillus University of Rome, Rome, Italy

Introduction: Musician's dystonia is a neurological condition characterized by the permanent loss of control of finely controlled hand movements when playing a musical instrument [1,2]. It mainly affects professional players in performing repetitive, finely controlled hand movements necessary for their musical practice [3].

Objective: The study in question aims to formulate a rehabilitation treatment protocol for patients with musician's hand dystonia, based on integrated occupational therapy and physiotherapy interventions.

Methods: The description of the treatment protocol will be shown through the presentation of three case reports. A pianist, a saxophonist, and a violinist have been enrolled in this study, attending an intervention programme based on four common steps. The outcomes measure used for the first assessment and the follow-up were the Disability of the Arm, Shoulder and Hand, the ABILHAND, the Tubiana and Chamagne Scale, the Arm Dystonia Disability Scale, and the Jebsen-Taylor Hand Function Test. The results were subjected to statistical analysis: being the sample of the study very small, the median of the results has been considered; then, the non-parametric Wilcoxon test was used to calculate statistical significance ($p < 0.05$).

Results: According to the statistical analysis of the collected results, no statistically significant results were obtained; however, clinically significant results were highlighted based on the observation of the raw scores of each musician. Every patient experienced varying degrees of improvement between the initial assessment and the follow-up and reported significant gains in motor control, motor accuracy, sensory discrimination, and musical performance.

Conclusions: The results of the study in question indicate that our rehabilitation program is an effective approach to improving the musical performance of musicians with focal hand dystonia. The combination of manual therapies, instrument-specific exercises and occupational therapy has proven effective in providing targeted solutions to this complex challenge.

References:

[1] Jabusch H, Altenmüller E. Focal dystonia in musicians: From phenomenology to therapy. Adv Cogn Psychol. 2006;2(2):207–20.
[2] Altenmüller E, Jabusch H. Focal Dystonia in Musicians. Phenomenology, Pathophysiology, Triggering Factors, and Treatment. Med Probl Perform Art. 2010;
[3] Altenmüller E. Focal dystonia: advances in brain imaging and understanding of fine motor control in musicians. Hand Clin. 2003;19(3):523–38, xi.

P77

Physiotherapy after subthalamic nucleus deep brain stimulation in patients with Parkinson's disease: a Delphi consensus study on safety and efficacy

Matteo Guidetti[1], R. Duncan[2,3], F. Lena[4], T. Bocci[1,5], A. Fasano[6,7,8,9], T. Foltynie[10], K.D. Foote[11], C. Hamani[12,13,14], J.K. Krauss[15], A. Kühn[16,17,18,19,20], P. Limousin[21], A.M. Lozano[6,7,22], N.V. Maiorana[1], N. Modugno[4], E. Moro[23], M.S. Okun[24,25], S. Oliveri[1], M. Santilli[4], A. Schnitzler[26,27], Y. Temel[28], L. Timmermann[29], V. Visser-Vandewalle[30], J. Volkmann[31], A. Priori[1,5]

[1]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Program in Physical Therapy, Washington University, School of Medicine in St Louis, St Louis, MO, USA
[3]Departments of Neurology, Washington University, School of Medicine in St Louis, St Louis, MO, USA
[4]Department of Neurology, IRCCS INM Neuromed, Pozzilli, Italy
[5]Clinical Neurology Unit, "Azienda Socio-Sanitaria Territoriale Santi Paolo E Carlo", Department of Health Sciences, University of Milan, Milan, Italy
[6]Krembil Research Institute, University Health Network, Toronto, ON, Canada
[7]CRANIA Center for Advancing Neurotechnological Innovation to Application, University of Toronto, ON, Canada
[8]KITE, University Health Network, Toronto, ON, Canada
[9]Division of Neurology, Edmond J. Safra Program in Parkinson's Disease Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada
[10]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology and the National Hospital for Neurology and Neurosurgery, London, UK
[11]Department of Neurosurgery, Norman Fixel Institute for Neurological Diseases, University of Florida, USA
[12]Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, M4N 3M5, ON, Canada
[13]Harquail Centre for Neuromodulation, 2075 Bayview Avenue, Toronto, M4N 3M5, ON, Canada
[14]Department of Surgery, University of Toronto, Toronto, M5T 1P5, ON, Canada
[15]Department of Neurosurgery, Medizinische Hochschule Hannover, Hannover, Germany
[16]Department of Neurology, Charité-Universitätsmedizin Berlin, Berlin, Germany
[17]Bernstein Center for Computational Neuroscience, Humboldt- Universität, Berlin, Germany
[18]NeuroCure, Exzellenzcluster, Charité-Universitätsmedizin Berlin, Berlin, Germany
[19]DZNE, German Center for Neurodegenerative Diseases, Berlin, Germany
[20]Berlin School of Mind and Brain, Humboldt-Universität zu Berlin, Berlin, Germany
[21]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology and the National Hospital for Neurology and Neurosurgery, London, UK
[22]Division of Neurosurgery, Department of Surgery, University of Toronto, Toronto, ON, Canada
[23]Grenoble Alpes University, Division of Neurology, Centre Hospitalier Universitaire de Grenoble, Grenoble Institute of Neuroscience, Grenoble, France
[24]Department of Neurology, Norman Fixel Institute for Neurological Diseases, University of Florida, USA
[25]Department of Neurosurgery, Norman Fixel Institute for Neurological Diseases, University of Florida, USA
[26]Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany

[27]Department of Neurology, Center for Movement Disorders and Neuromodulation, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
[28]Department of Neurosurgery, Maastricht University Medical Center, Maastricht, The Netherlands
[29]Department of Neurology, University Hospital of Marburg, Marburg, Germany
[30]Department of Stereotactic and Functional Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany
[31]Department of Neurology, University Hospital Würzburg, Würzburg, Germany

*Introduction***:** Although the motor improvements induced by deep brain stimulation of the subthalamic nucleus (STN-DBS) are wellestablished in Parkinson's Disease (PD) [1], the actual effects of the stimulation on axial symptoms (e.g., postural instability and gait impairments) are still matter of debate [2]. Physiotherapy (PT) is considered an effective treatment to improve axial symptoms in PD patients without DBS [3], but it has never been systematically assessed for PD patients with DBS.

*Objectives***:** Gather the opinions of DBS clinical and academic experts on the role of physiotherapy after DBS implant in PD patients.

*Methods***:** After performing a systematic scoping review on clinical articles studying physiotherapy treatments in PD patients with STNDBS, we created a 5-points Likert scale questionnaire that we sent to chosen DBS experts according to Delphi method process [4].

Results: Panellists (n=21) strongly agreed that PT might improve motor symptoms and quality of life in PD patients with STN-DBS, maximizing the effects of the stimulation (for all, 89% strongly agreed, median ± IQR: 5 ± 0). Also, they agreed that the physiotherapist should be part of the multidisciplinary team, with PT prescribed in the treatment guidelines both in acute and chronic phase (for all, >88% strongly agreed, median ± IQR: 5 ± 0).

Conclusion: PT might be a safe and effective complementary treatment for PD patients with STN-DBS, thus its role and effect should be further explored.

References:

[1] Limousin, P. & Foltynie, T. Nature Reviews Neurology 2019 15:4 15, 234–242 (2019).
[2] Duncan, R.P., Van Dillen, L.R., Garbutt, J.M., Earhart, G.M. & Perlmutter, J.S. Pilot and Feasibility Studies 4, 1–7 (2018).
[3] Cosentino, C. et al. Movement disorders : official journal of the Movement Disorder Society 35, 523–536 (2020).
[4] Hsu, C.-C. & Sandford, B.A. Practical assessment, research, and evaluation 12, 10 (2007).

P78

Kinematic signature of rigidity during passive upper limb mobilization in patients with Parkinson's disease

Antonio Cannavacciuolo[1], M. De Riggi[2], A. Martini[2], D. Birreci[2], D. Costa[2], L. Angelini[2], A.S. Grandolfo[2], M. Passaretti[2], G. Paparella[1,2], M. Bologna[1,2]

[1]IRCCS Neuromed, Pozzilli, IS, Italy
[2]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy

Introduction: Rigidity stands as one of the cardinal motor manifestations of Parkinson's disease (PD), and is defined as a marked but velocity-independent increase in muscle activity in response to the muscle stretch applied [1,2]. Quantitative assessments of rigidity in PD patients have been conducted using a robotic manipulandum that passively pronates and supinates the forearm. Nevertheless, additional methods for objectively measuring rigidity are needed.

Objectives: To develop an alternative method for assessing rigidity based on the kinematic analysis of passive upper limb movements in PD.

Methods: We assessed upper limb rigidity in PD patients (ON medication) both clinically and through kinematic analysis. The kinematic parameters of interest, such as peak angular velocity and movement units of the velocity profile, were recorded during passive mobilization of the upper limb. EMG activity from both the experimenter's and the patient's muscles was recorded to verify that the patients did not actively move their arm during the tests. PD patients were examined on the most affected side of the body. Finally, we explored potential correlations between clinical and kinematic data.

Results: Eleven PD patients participated in the study, including 3 females, with a mean age of 73.7±7.5 years. The average duration of the disease was 9.4±3.8 years, and the mean MDS-UPDRS (part III) score was 32.5±16.7. All patients scored ≥ 1 in the clinical assessment of upper limb rigidity. The analysis revealed a significant positive correlation between the clinical score for upper limb rigidity and the number of movement units in the velocity profile during passive arm movements ($R = 0.82$; $P = 0.002$).

Conclusions: We here propose an alternative method for the objective quantification of upper limb rigidity in PD patients. The proposed methodology is intended for use in both clinical and experimental research studies.

References:

[1] Bologna M, Paparella G. Pathophysiology of rigidity in Parkinson's disease: Another step forward. Clin Neurophysiol. 2020 Aug;131(8):1971-1972. doi: 10.1016/j.clinph.2020.05.013. Epub 2020 May 29. PMID: 32507558.
[2] Chen R, Berardelli A, Bhattacharya A, Bologna M, Chen KS, Fasano A, Helmich RC, Hutchison WD, Kamble N, Kühn AA, Macerollo A, Neumann WJ, Pal PK, Paparella G, Suppa A, Udupa K. Clinical neurophysiology of Parkinson's disease and parkinsonism. Clin Neurophysiol Pract. 2022 Jun 30;7: 201-227. doi: 10.1016/j.cnp.2022.06.002.

P79

Effects of an intensive multidisciplinary rehabilitative treatment versus an individual treatment at home in Parkinson's disease: preliminary results

Francesca Lea Saibene[1], A. Salvatore[1], S. Gobbo[1], F. Merlo[1], A. Castagna[1], E. Farina[1], M. Alberoni[1], E. Calabrese[1], T. Bowman[1], D. Anastasi[1], D. Cattaneo[1,2], C. Agliardi[1], C. Arienti[1], F.R. Guerini[1], M. Saresella[1], M. Clerici[1], J.S. Navarro[1], P. Arcuri[1], M. Meloni[3]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]University of Milan, Milan, Italy
[3]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy

Introduction: Although a beneficial effect of multidisciplinary intensive training programs on people with Parkinson's Disease (PwPD) has been documented [1, 2], results in the literature are still mixed.

Objective: The main objective of this project was that of assessing the effect of a multidisciplinary intensive treatment in an experimental group (EXP-group) compared to a control group (CTRLgroup) in two timepoints on cognition, motor symptoms, and Quality of Life. Moreover, we wanted to explore biomolecolar changes in the NDEVs-BDNF as a marker of exercise-induced neuroplasticity.

Methods: To do so, 57 PwPD (26CTRL/31EXP; 28F/29M; Age: 69,16±5.27; mH&Y: 1,5-3) underwent a complete evaluation at T0, after 6-weeks (T1) and after 3-months (T2). Assessment comprised MDS-UPDRS-III [3], MoCA test [4], mDGI, PDQ-39, and BDNF from NDEVs [5]. Between T0 and T1, the EXP-group was administered a daily intensive out-patient multidisciplinary rehabilitative program while the CTRL-group underwent a program of individual treatment at home consisting of stretching and active mobilization.

Results: Results showed that the EXP-group improved in MDSUPDRS-III scores compared to the CTRL-group at T1. In addition, a significant improvement at mDGI was observed both at T1 and at T2 only in the EXP-group. Moreover, there was a general improvement in PDQ-39 at T1 without group differences. Eventually, there was an increase in NDEVs-BDNF levels in the EXP-group compared to the CTRL-group at T2. No effects were observed in MoCA scores.

Conclusion: These results reveal a beneficial effect of a muldisciplinary treatment on motor symptoms and balance compared to a control program. Moreover, the significant increase in NDEVs-BDNF at follow-up hints at a treatment-induced plasticity in the experimental group

References:

[1] Meloni, M., Saibene, F. L., Di Tella, S., Di Cesare, M., Borgnis, F., Nemni, R., & Baglio, F. (2021). Functional and Cognitive Improvement After an Intensive Inpatient Multidisciplinary Rehabilitation Program in Mild to Severe Parkinson's Disease: A Retrospective and Observational Study. Frontiers in Neurology, 12, 626041.
[2] Ferrazzoli, D., Ortelli, P., Zivi, I., Cian, V., Urso, E., Ghilardi, M. F., ... & Frazzitta, G. (2018). Efficacy of intensive multidisciplinary rehabilitation in Parkinson's disease: a randomised controlled study. Journal of Neurology, Neurosurgery & Psychiatry, 89(8), 828- 835.
[3] Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., ... & LaPelle, N. (2008). Movement Disorder Societysponsored revision of the Unified Parkinson's Disease Rating Scale (MDSUPDRS): scale presentation and clinimetric testing results. Movement disorders: official journal of the Movement Disorder Society, 23(15), 2129-2170.
[4] Santangelo, G., Siciliano, M., Pedone, R., Vitale, C., Falco, F., Bisogno, R., ... & Trojano, L. (2015). Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36, 585-591.
[5] Agliardi, C., Meloni, M., Guerini, F. R., Zanzottera, M., Bolognesi, E., Baglio, F., & Clerici, M. (2021). Oligomeric α-Syn and SNARE complex proteins in peripheral extracellular vesicles of neural origin are biomarkers for Parkinson's disease. Neurobiology of Disease, 148, 105185.

P80

Neurofilaments and blood-derived extracellular vesicles as measurable biomarkers for the prediction of the response to the rehabilitation treatment

Alice Gualerzi[1], G. Lombardi[2,3,] S. Picciolini[1], A. Mangolini[1], V. Mangolini[1,4], F. Rodà[1,5], L. Forleo[1], R. Martino[1], S. Ramat[6], S.G. Doronzio[3,7], D. Longo[3,7], M. Baccini[3], F. Cecchi[3,7], M. Bedoni[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano, Italy
[2]Dipartimento di Neuroscienze, Psicologia, Area del Farmaco e Salute del Bambino, Università di Firenze, Firenze, Italy
[3]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Firenze, Italy
[4]Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, Brescia, Italy
[5]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[6]Parkinson Unit, Azienda Ospedaliera Universitaria Careggi, Firenze, Italy
[7]Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Italy

Introduction: The integration of virtual reality (VR) on treadmill training (TT) in Parkinson's disease (PD) rehabilitation is an extremely current topic in PD research. Large studies with a randomized controlled design are necessary to define recommendations for the use of VR and TT, isolated and in combination, in PD rehabilitation. Besides, a timely optimization of personalized rehabilitation for people with PD (pwPD) is in part limited by the lack of measurable biomarkers indicative of neuroplasticity and predictive of the response to treatment. Considering the complex processes occurring in the PD brain, Extracellular Vesicles (EVs) are considered promising candidates as they are vehicles of α-synuclein and other PD-related molecules throughout the body. Moreover, correlation was already found between the clinical profiling of pwPD and the biochemical modifications of blood EVs [1].

Objectives: This study is part of a single-center, randomized controlled single-blind trial with an active control group, the VIRTREAD-PD trial [2], whose primary objective is to compare the effects on gait
performances of the conventional standard TT versus the experimental intervention represented by TT endowed with augmented VR (AVR) applications. Here we show the preliminary results of the exploratory aim, i.e. the attempt to identify biomarkers of neuroplasticity detecting changes in Neurofilament Light Chain (NfL) concentration before and after training and prognostic biomarkers associated to blood-derived EVs.

Methods: Serum samples collected before and after the rehabilitation program were used for NfL measurement by Ella instrument, whereas EVs were isolated from serum combining size exclusion chromatography and ultracentrifugation methods. The biochemical characterization of EVs was obtained by Raman Spectroscopy and spectral differences in the EV fingerprint before and after rehabilitation were evaluated.

Results and conclusions: The preliminary data of the present project demonstrate modifications in soluble factors before and after rehabilitation. In particular, our data support the use of Raman spectroscopy to assess PD related modification in EV content to be used for the evaluation of the effect of rehabilitation and for the definition of a personalized treatment.

References:

[1] Gualerzi A, Picciolini S, Carlomagno C, Terenzi F, Ramat S, Sorbi S, Bedoni M. Raman profiling of circulating extracellular vesicles for the stratification of Parkinson's patients. Nanomedicine. 2019; 22:102097. doi: 10.1016/j.nano.2019.102097.
[2] ClinicalTrials.gov ID NCT05902065: Effect of a Progressive Treadmill Training Protocol for Parkinson's Disease.

P81

A wearable device (Q-Walk) for rehabilitation of gait impairment and for monitoring and fostering motor activity in Parkinson's disease

Daniele Volpe[1,2], L. Ghilardi[1], M. Norcini[1], F. Spolaor[3], F. Cibin[3], A. Guiotto[3], Z. Sawacha[3]

[1]Fresco Parkinson Institute, Fiesole, Florence, Italy
[2]Fresco Network of Excellence, Villa Margherita Parkinson Centre, Vicenza, Italy
[3]Department of Information Engineering of the University of Padua, Padua, Italy

Introduction: Gait disturbances in particular FOG occur frequently in mid-advanced Parkinson's disease (PD). In addition, people with PD seem to not practice sufficient physical activity during daily living at home. Many devices have been proposed for the rehabilitative treatment of gait impairment in particular for Freezing of Gait (FOG) showing that they are well-validated and are promising applications of objective measurements. The field of wearable sensors would benefit from more research efforts, increased collaboration among researchers, aligned data-collection protocols, and shared data sets. Furthermore, it could contribute to provide to clinicians with important information on the motor activity of PD patients during daily life.

Objectives: To test the feasibility, safety, and effectiveness of the use of a wearable device (QWalk) on gait impairment especially on FOG, and to test Q-Walk as a reliable device for monitoring motor performances during daily activities in a preliminary cohort of PD patients.

Methods: The pilot Q-Walk protocol was conducted in Villa Margherita and enrolled the first PD patients group. PD patients were randomized in two groups: G1 (Q-Walk active) and G2 (Q-Walk inactive device). All subjects were submitted to a gait training at the preferred speed for one hour per session. There were two testing moments: T0 at baseline and T1 after 4 weeks. All the PD subjects were submitted to clinical outcomes measures and to recording of 2D S/T parameters of gait from the device and 3D gait analysis.

Results: The preliminary results showed an improvement in both clinical and biomechanical outcomes measures (UPDRS III, 6mWT, kinematics in terms of joints angles and space-time parameters). The records from the device provided interesting information on motor activity at home confirming that PD subjects performed much less than reported in the literature (average 800min/month).

Conclusions: The preliminary study showed that the Q-Walk device seems to be a promising device for improving gait disturbances and also for monitoring and fostering motor activities in daily living in people with PD.

P82

Neuroinflammation and physical activity in Parkinson's disease: preliminary results from the "MOVE-ON" study

Carlo Fazio[1,2], R. De Icco[1,2], F. Bighiani[1,2], A. Calculli[1,2], D. Comolli[1,2], L. Martinis[3], R. Bottinelli[4], S. Porcelli[4], R. Greco[5], A.M. Zanaboni[1,5], S. Facchetti[1,5], M. Francavilla[1,5], C. De Martini[1,5], D. Di Martino[1,6], G. Ongari[6], S. Cerri[6], A. Pisani[1,2]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy
[4]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[5]Section of Translational Neurovascular Research, IRCCS Mondino Foundation, Pavia, Italy
[6]Section of Cellular and Molecular Neurobiology, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Clinical and experimental studies converge to suggest that exercise improves motor functions in Parkinson's disease (PD) [1]. We explored the effects of physical activity on neuroinflammation by measuring the levels of plasma cytokines in PD patients to investigate the mechanisms underlying these beneficial effects [2].

Objectives: To evaluate differences in cytokine levels and functional performances in a group of PD patients engaged in high-to-moderate intensity physical activity (PD-sport), compared to sedentary PD patients (PD-sedentary).

Methods: We included PD patients (age 40-75, H&Y 1-3), not affected by cognitive impairment, depression or conditions inducing a proinflammatory state (i.e. diabetes, tumors, infections, active smoking or alcohol consumption). In our case-control study, patients were divided into two groups (9 PD-sport vs. 4 PD-sedentary, 11 M, 2 F) according to the International-physical-activity-questionnaire (IPAQ). Each patient underwent clinical and instrumental evaluation (UPDRS score, neuropsychological evaluation, inertial gait analysis and ergometric test). IL-1 beta and TNF-alfa expression levels were measured in plasma through ELISA assay.

Results: IL-1 beta levels were significantly lower in PD-sport compared to PDsedentary group (mean values: 79.94 ±19.3, vs 107.1 ±11.4 pg/ml; p-value = 0.003, IC 95%). TNF-alfa also showed lower levels in PDsport vs PD-sedentary (mean values: 110.9 ±20.04 vs 128.6 ±30.8 pg/ml; p-value = 0.284, IC 95%), though not statistically significant. Functional tests showed better motor performances in PD-sport compared to the other group: 5 sit-to-stand test (p = 0.003), timedup- and-go test (p = 0.106) and hand-grip-strenght-test (p = 0.487).

Conclusions: Although preliminary, our data suggest that intensive exercise training reduces the proinflammatory state observed in patients, supporting its beneficial role in disease course. The current study is ongoing, will be integrated by a 8-week open-label pilot study, involving PD-sedentary patients in an intensive adaptive physical program, with the aim to evaluate the cytokine profile at the end of the training period.

References:

[1] Johansson H, Hagströmer M, Grooten WJA, Franzén E. Exercise-Induced Neuroplasticity in Parkinson's Disease: A Metasynthesis of the Literature. Neural Plast. 2020;2020:8961493.
[2] Hirsch EC, Hunot S. Neuroinflammation in Parkinson's disease: a target for neuroprotection? Lancet Neurol. aprile 2009;8(4):382–97.

P83

Disentangling the complex scenario of tremor progression in Parkinson's disease

Carolina Cutrona[1], M. Costanzo[1], G. Leodori[1,2], M.I. De Bartolo[1], A. Liguori[5], M. Mancuso[1], G. Vivacqua[3,4], A. Conte[1,2], G. Fabbrini[1,2], A. Berardelli[1,2], D. Belvisi[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli (IS), Italy
[3]Department of Experimental Morphology and Microscopy - Integrated Research Center (PRAAB) – Campus Biomedico University of Rome, Rome, Italy
[4]Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences,Sapienza University of Rome, Rome, Italy
[5]Department of Neurology, Ruggi D'Aragona and S. Giovanni di Dio Hospital, Salerno, Italy

Introduction: Patients with Parkinson's disease (PD) may show different types of tremor. Rest and re-emergent tremor are now considered as a clinical continuum that emerges in conditions of motor stability ("stability tremor") and is opposed to action tremor, including pure postural and kinetic tremor [1]. Cross-sectional clinical studies suggested that patients with stability tremor are milder than patients with action tremor [2,3]. Few longitudinal studies have investigated tremor trajectory during disease course but the progression of different types of tremor is unexplored [4,5].

Objective: i) To assess the progression of different PD tremors over disease course ii) to determine whether the clinical differences between patients with stability tremor and those with action tremor are consistent over time iii) to investigate if different PD tremors can predict specific trajectories of disease progression.

Methods: One-hundred PD patients participated in the study. Patients were clinically assessed off and on treatment at baseline and after a 4 years follow up. Motor and non-motor symptoms severity was assessed by standardized clinical scales. The clinical evaluation included an accurate assessment of stability and action tremor.

Results: The severity and the occurrence of tremor decreased during PD progression, with a more relevant reduction of action than stability tremor. Patients with stability tremor had milder motor symptoms at the baseline and milder motor and non-motor manifestations at the end of the follow up. Both stability and action predicted a lower non-motor symptoms progression with a stronger association between the presence of stability tremor and a slower non-motor progression.

Conclusions: Stability tremor exhibits greater consistency over time compared to action tremor in PD patients. The evidence that stability tremor is associated with milder severity of motor and non-motor symptoms over time and that is associated with a slower non-motor progression supports its significant role in defining the benignity of tremulous subtype in PD.

References:

[1] Dirkx, M.F.; Zach, H.; Bloem, B.R.; Hallett, M.; Helmich, R.C. The Nature of Postural Tremor in Parkinson Disease. *Neurology* **2018**, *90*, e1095–e1103, doi:10.1212/WNL.0000000000005215.
[2] Belvisi, D.; Conte, A.; Bologna, M.; Bloise, M.C.; Suppa, A.; Formica, A.; Costanzo, M.; Cardone, P.; Fabbrini, G.; Berardelli, A. Re-Emergent Tremor in Parkinson's Disease. *Parkinsonism Relat. Disord.* **2017**, *36*, 41–46, doi:10.1016/j.parkreldis.2016.12.012.
[3] Belvisi, D.; Conte, A.; Cutrona, C.; Costanzo, M.; Ferrazzano, G.; Fabbrini, G.; Berardelli, A. Re-Emergent Tremor in Parkinson's Disease: The Effect of Dopaminergic Treatment. *Eur. J. Neurol.* **2018**, *25*, 799–804, doi:10.1111/ene.13619.

[4] Pasquini, J.; Ceravolo, R.; Qamhawi, Z.; Lee, J.-Y.; Deuschl, G.; Brooks, D.J.; Bonuccelli, U.; Pavese, N. Progression of Tremor in Early Stages of Parkinson's Disease: A Clinical and Neuroimaging Study. *Brain* **2018**, *141*, 811–821, doi:10.1093/brain/awx376.
[5] Pasquini, J.; Deuschl, G.; Pecori, A.; Salvadori, S.; Ceravolo, R.; Pavese, N. The Clinical Profile of Tremor in Parkinson's Disease. *Mov. Disord. Clin. Pract.* **2023**, *10*, 1496–1506, doi:10.1002/mdc3.13845.

P84

Defining the minimal clinically important difference of average daily steps measured through a commercial smartwatch in people with Parkinson disease

Edoardo Bianchini[1,2], D. Rinaldi[1], M. Alborghetti[1], S. Galli[1], L. De Carolis[1], P. Pacilio[1], C. Hansen[3], F.E. Pontieri[1], N. Vuillerme[2,4,5]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Univ. Grenoble Alpes, AGEIS, Grenoble, France
[3]Department of Neurology, Kiel University, Kiel, Germany
[4]Institut Universitaire de France, Paris, France
[5]LabCom Telecom4Health, Orange Labs & Univ. Grenoble Alpes, CNRS, Inria, Grenoble INP-UGA, Grenoble, France

Introduction: Recent studies have reported the validity, reliability and accuracy of commercial smartwatch- measured daily steps in people with Parkinson's (PwPD) [1-3]. However, no study to date estimated the minimal clinically important difference (MCID) [4,5] for average daily steps (avDS), measured through a commercial smartwatch in PwPD.

Objectives: To calculate the MCID of avDS, measured through a commercial smartwatch, in PwPD.

Methods: Eighty-nine PwPD [females: 28 (32%); age: 68.7±8.4 years; disease duration: 6.4±3.6 years; LEDD: 571±311 mg; mHY: 2 (2-2.5; 1-3); MDS-UPDRS-III: 28 (22-32; 11-50)] wore a Garmin Vivosmart 4 smartwatch for 5 consecutive days on the wrist least affected by the disease. Daily steps were extracted and averaged. To define MCID, we used an anchor-based method [4] linked to clinical scales capturing changes in global mobility and motor functions (i.e., MDSUPDRS part III, mHY, SPPB). Linear regressions were used to estimate the incremental change in avDS per relevant variable change. To calculate the relevant changes, we used the already known MCID for each scale. In case of asymmetric MCID, we used the average value rounded to the higher next whole number. Global MCID was then calculated as the average of the variables included; range was also reported.

Results: The three regression models were statistically significant and correlation coefficients were >0.3. Each stage increase in mHY corresponded to a 1186 steps/day decrease. Similarly, each 4-point increase in MDS-UPDRS-III corresponded to 552 steps/day decrease and each 1-point decrease in SPPB score corresponded to 481 steps/day decrease. Overall, the mean MCID across the three scales was 740 steps/day (range = 481–1186 steps/day) corresponding to 13% of the mean avDS (5766±3014 steps/day) of our population.

Conclusions: We estimated a MCID for avDS of around 750 steps/day anchored to standardized measures of motor symptoms and mobility in PwPD. These findings could be relevant for designing future clinical trials involving avDS in PwPD as an outcome measure.

References:

[1] Bianchini, E.; Caliò, B.; Alborghetti, M.; Rinaldi, D.; Hansen, C.; Vuillerme, N.; Maetzler, W.; Pontieri, F.E. Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. Sensors (Basel) 2022, 23, 214, doi:10.3390/s23010214.

[2] Bianchini, E.; Galli, S.; Alborghetti, M.; De Carolis, L.; Zampogna, A.; Hansen, C.; Vuillerme, N.; Suppa, A.; Pontieri, F.E. Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch. Sensors (Basel) 2023, 23, 8971, doi:10.3390/s23218971.
[3] Ginis, P.; Goris, M.; De Groef, A.; Blondeel, A.; Gilat, M.; Demeyer, H.; Troosters, T.; Nieuwboer, A. Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. Sensors (Basel) 2023, 23, 4156, doi:10.3390/s23084156.
[4] Byrom, B.; Breedon, P.; Tulkki-Wilke, R.; Platko, J.V. Meaningful Change: Defining the Interpretability of Changes in Endpoints Derived from Interactive and mHealth Technologies in Healthcare and Clinical Research. J Rehabil Assist Technol Eng 2020, 7, 2055668319892778, doi:10.1177/2055668319892778.
[5] Mishra, B.; Sudheer, P.; Agarwal, A.; Srivastava, M.V.P.; Nilima, null; Vishnu, V.Y. Minimal Clinically Important Difference (MCID) in Patient-Reported Outcome Measures for Neurological Conditions: Review of Concept and Methods. Ann Indian Acad Neurol 2023, 26, 334–343, doi:10.4103/aian.aian_207_23.

P85

Clinically assessed walking capacity versus real-world walking performance in people with Parkinson's disease

Edoardo Bianchini[1,2], C. Hansen[3], D. Rinaldi[1], M. Alborghetti[1], S. Galli[1], L. De Carolis[1], P. Pacilio[1], F.E. Pontieri[1], N. Vuillerme[2,4,5]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Univ. Grenoble Alpes, AGEIS, Grenoble, France
[3]Department of Neurology, Kiel University, Kiel, Germany
[4]Institut Universitaire de France, Paris, France
[5]LabCom Telecom4Health, Orange Labs & Univ. Grenoble Alpes, CNRS, Inria, Grenoble INP-UGA, Grenoble, France

Introduction: Capacity is what an individual can do, performance is what the individual does do [1]. Gait parameters collected in supervised condition are widely used to estimate walking capacity in people with Parkinson's disease (PwPD) [2]. Meanwhile, the fastmoving market of commercial wearable sensors, such smartwatches, made assessment of walking performance under free-living, unsupervised conditions easy and accessible [3-4]. However, how much walking capacity contributes to walking performance in PwPD is still unclear [5-6].

Objective: To evaluate how much clinically assessed walking capacity contribute to real-world walking performance, measured through a commercial smartwatch, in PwPD.

Methods: In-clinic walking capacity was assessed though the instrumented 25-meter straight walking task and the Timed-Up-and- Go (iTUG) test in 71 PwPD in ON condition [females: 22 (31%); age: 68.8±8.6 years; disease duration: 5.7±3.89 years; LEDD: 526±265 mg; mHY: 2 (2-2.5; 1-3)]. A lower-back-mounted inertial sensor (BTS G-WALK) was used to compute spatio-temporal and kinematic gait parameters. Real-world walking performance was evaluated through average daily steps (avDS) measured over 5 consecutive days through a Garmin Vivosmart 4 smartwatch worn on the wrist least affected by the. Pearson's correlation coefficient was used to select the variables significantly associated with avDS that were included in a multivariate linear regression model. A backward elimination method was used to select the stronger predictors of avDS.

Results: Gait speed, normalized stride length, total TUG duration, mean and peak angular velocity of turning were significantly associated with avDS and were thus included in the regression model. After backward elimination, this model included gait speed and turn peak angular velocity ($p<0.001$) and explained 31% of variance of avDS. Only gait speed was a significant predictor of AvDS ($p=0.002$).

Conclusions: Clinically-assessed walking capacity significantly contributed to real-world walking performance in PwPD. However, only one-third of walking performance variance was explained by walking capacity. These results suggest that walking capacity may be a decent but not optimal surrogate of free-living walking performance.

References:

[1]. Mate, K.K.V.; Mayo, N.E. Clinically Assessed Walking Capacity Versus Real-World Walking Performance in People with MultipleSclerosis. Int J MS Care 2020, 22, 143–150, doi:10.7224/1537-2073.2019-047.

[2]. Hobert, M.A.; Nussbaum, S.; Heger, T.; Berg, D.; Maetzler, W.; Heinzel, S. Progressive Gait Deficits in Parkinson's Disease: AWearable-Based Biannual 5-Year Prospective Study. Front Aging Neurosci 2019, 11, 22, doi:10.3389/fnagi.2019.00022.
[3]. Porta, M.; Pilloni, G.; Pili, R.; Casula, C.; Murgia, M.; Cossu, G.; Pau, M. Association between Objectively Measured Physical Activity and Gait Patterns in People with Parkinson's Disease: Results from a 3-Month Monitoring. Parkinsons Dis 2018, 2018, 7806574, doi:10.1155/2018/7806574.
[4]. Bianchini, E.; Galli, S.; Alborghetti, M.; De Carolis, L.; Zampogna, A.;Hansen, C.; Vuillerme, N.; Suppa, A.; Pontieri, F.E. Four Days AreEnough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch. Sensors (Basel) 2023, 23, 8971, doi:10.3390/s23218971.
[5]. Galperin, I.; Hillel, I.; Del Din, S.; Bekkers, E.M.J.; Nieuwboer, A.; Abbruzzese, G.; Avanzino, L.; Nieuwhof, F.; Bloem, B.R.; Rochester, L.; et al. Associations between Daily-Living Physical Activity and Laboratory-Based Assessments of Motor Severity in Patients with Falls and Parkinson's Disease. Parkinsonism Relat Disord 2019, 62, 85–90, doi:10.1016/j.parkreldis.2019.01.022.
[6]. Zajac, J.A.; Cavanaugh, J.T.; Baker, T.; Duncan, R.P.; Fulford, D.; Girnis, J.; LaValley, M.; Nordahl, T.; Porciuncula, F.; Rawson, K.S.; et al. Does Clinically Measured Walking Capacity Contribute to Real-World Walking Performance in Parkinson's Disease? Parkinsonism Relat Disord 2022, 105, 123–127, doi:10.1016/j.parkreldis.2022.11.016.

P86

Correlation between cognitive function and swallowing functions in subjects with Parkinson's disease

Cinzia Baldanzi[1], F.L. Saibene[1], G. Fusari[1], P. Arcuri[1], M. Meloni[2], C. Scuderi[1], D. Cattaneo[1,3], C. Vitali[1]

[1]IRCSS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]UOC Neurologia; Azienda Ospedaliero-Universitaria, Cagliari, Italy
[3]Department of Physiopathology and Transplants, University of Milan, Milan, Italy

Introduction: People with Parkinson's Disease (PwPD) may experience a variety of motor and non-motor symptoms, including cognitive impairment and dysphagia [1]. Dysphagia involves oral, pharyngeal, or esophageal phases of swallowing [2], leading to malnutrition, dehydration, pneumonia, and even death [3]. Several studies suggest that the voluntary phase of swallowing (oral phase) can be influenced by cognitive functions [4].

Objectives: This study aimed to investigate the relationship between swallowing function and cognitive impairment in PwPD and determine which phase of swallowing is more linked to cognitive impairment.

Methods: 27 PwPD, according to the MDS Clinical Diagnostic Criteria, were recruited at IRCCS Don Gnocchi Foundation (Milan, Italy). The MDS-UPDRS Part III was used to evaluate motor disability; the Mini-Mental Parkinson Test (MMPT) [5], the Montreal Cognitive Assessment (MoCA) [6], and the Frontal Assessment Battery (FAB) [7] were used for cognitive assessment. The Dysphagia Outcome Severity Scale (DOSS) [8] and Videofluoroscopic Dysphagia Scales (VDS) [9] were used for swallowing evaluation during videofluoroscopy. Spearman correlation coefficient and logistic and linear models were used to analyze data.

Results: Swallowing problems during the oral phase correlated with cognitive functions (Spearman correlation coefficient, rho, between -0.69 and -0.89 across scales), even when controlling for UPDRS motor scores ($p<0.05$), with subjects having cognitive impairments concurrently demonstrating deficits in the oral phase of swallowing. Instead, no correlations were found between the pharyngeal phase and cognitive functions (rho between 0.03 and 0.06 across scales).

Conclusions: This study suggests that cognitive dysfunctions, especially frontal/executive and learning/memory, are mainly associated with the oral phase of swallowing in PwPD. Understanding the link between cognitive and swallowing functions will be useful for speech-language rehabilitation, especially regarding managing the oral phase of swallowing.

References:

[1] Potulska A, Friedman A, Królicki L, Spychala A. Swallowing disorders in Parkinson's disease. Parkinsonism Relat Disord. 2003 Aug;9(6):349-53. doi: 10.1016/s1353-8020(03)00045-2. PMID: 12853234.
[2] Kwon, Miseon, and Jae-Hong Lee. Oro-Pharyngeal Dysphagia in Parkinson's Disease and Related Movement Disorders."Journal of movement disorders vol. 12,3 (2019): 152-160.
[3] Cosentino, G., Avenali, M., Schindler, A. et al.A multinational consensus on dysphagia in Parkinson's disease: screening, diagnosis and prognostic value.J Neurol269, 1335–1352 (2022).
[4] Kim J., Jinyoung Youn, Mee Kyung Suh, Tae-Eun Kim, Juhee Chin, Suyeon Park, Jin Whan Cho: Cognitive and Motor Aspects of Parkinson's Disease Associated with Dysphagia (2015)
[5] Costa A, Bagoj E, Monaco M, Zabberoni S, De Rosa S, Mundi C, Caltagirone C, Carlesimo GA. Mini mental Parkinson test: standardization and normative data on an Italian sample. Neurol Sci. 2013 Oct;34(10):1797-803. doi: 10.1007/s10072-013-1342- 8. Epub 2013 Mar 12. PMID: 23479031.

[6] Santangelo G, Siciliano M, Pedone R, Vitale C, Falco F, Bisogno R, Siano P, Barone P, Grossi D, Santangelo F, Trojano L. Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurol Sci. 2015 Apr;36(4):585-91. doi: 10.1007/s10072-014-1995-y. Epub 2014 Nov 8. PMID: 25380622.
[7] Appollonio I, Leone M, Isella V, Piamarta F, Consoli T, Villa ML, Forapani E, Russo A, Nichelli P. The Frontal Assessment Battery (FAB): normative values in an Italian population sample. Neurol Sci. 2005 Jun;26(2):108-16. doi: 10.1007/s10072-005-0443- 4. PMID: 15995827.
[8] O'Neil KH, Purdy M, Falk J, Gallo L. The Dysphagia Outcome and Severity Scale. Dysphagia. 1999 Summer;14(3):139-45. doi: 10.1007/PL00009595. PMID: 10341109.
[9] Kim J, Oh BM, Kim JY, Lee GJ, Lee SA, Han TR. Validation of the videofluoroscopic dysphagia scale in various etiologies. Dysphagia. 2014 Aug;29(4):438-43. doi: 10.1007/s00455-014-9524-y. PMID: 24658847.

P87

Correlation between vocal intensity and executive functions in subjects with Parkinson's disease

Cinzia Baldanzi[1], F.L. Saibene[1], G. Fusari[1], P. Arcuri[1], M. Meloni[2], F. Stellari[1], D. Cattaneo[1,3], C. Vitali[1]

[1]IRCSS Fondazione Don Carlo Gnocchi, Milano, Italy
[2]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy
[3]Department of Physiopathology and Transplants, University of Milano, Milano Italy

Introduction: People with Parkinson's Disease (PwPD) may experience a variety of motor and non-motor symptoms, including decreased voice loudness (hypophonia) and cognitive impairments [1]. Hypophonia is due to anatomic alterations, such as difficulty in glottal closure [2] and several studies suggest that executive functions influence vocal performances. Moreover, executive functions are crucial in high-demanding tasks that require executive control, such as spontaneous speech [3].

Objectives: This study aimed to investigate the relationship between voice intensity and executive functions.

Methods: 38 PwPDs, according to the MDS Clinical Diagnostic Criteria, were recruited at IRCCS Don Gnocchi Foundation (Milan, Italy). The MDS-UPDRS Part III was used to evaluate motor disability; the Montreal Cognitive Assessment (MoCA) [4], the Frontal Assessment Battery (FAB) [5], and the Trial Making Test A e B (TMT-A e TMT-B) [6] were used to assess executive functions. Voice intensity (decibels, dB) was recorded and analyzed using the PRAAT software during a sustained /a/ and a one-minute monologue. Spearman correlation coefficients and logistic and linear models were used to analyze data.

Results: Voice intensity during spontaneous speech correlated with executive functions (Spearman correlation coefficient, rho, between 0.47 and 0.68 across scales, $p<0.05$), even when controlling for UPDRS motor scores ($p<0.05$), with subjects having reduced voice intensity during spontaneous speech concurrently demonstrating deficits in executive functions. Instead, no correlations were found between sustained /a/ and cognitive impairments (Spearman correlation coefficient, rho, between 0.19 and 0.21 across scales).

Conclusions: The present study found associations between voice intensity during spontaneous speech and executive functions. Subjects with deficits in executive functions have difficulty maintaining vocal intensity in complex tasks such as spontaneous speech, while they can maintain intensity in simple tasks such as sustained /a/. Thus, voice assessment in PD should combine simple and complex vocal tasks taking into consideration cognitive performance.

References:

[1] Potulska A, Friedman A, Królicki L, Spychala A. Swallowing disorders in Parkinson's disease. Parkinsonism Relat Disord. 2003 Aug;9(6):349-53. doi: 10.1016/s1353-8020(03)00045-2. PMID: 12853234.
[2] Ma A., Lau K., Thyagarajan D. (2019) Voice changes in Parkinson's disease: What are they telling us?, J Clin Neuroscience, 72: 1-7.
[3] Plummer-D'Amato P, Altmann LJ, Reilly K. Dual-task effects of spontaneous speech and executive function on gait in aging: exaggerated effects in slow walkers. Gait Posture. 2011 Feb;33(2):233-7. doi: 10.1016/j.gaitpost.2010.11.011. Epub 2010 Dec 28. PMID: 21193313.
[4] Santangelo G, Siciliano M, Pedone R, Vitale C, Falco F, Bisogno R, Siano P, Barone P, Grossi D, Santangelo F, Trojano L. Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurol Sci. 2015 Apr;36(4):585-91. doi: 10.1007/s10072-014-1995-y. Epub 2014 Nov 8. PMID: 25380622.

[5] Appollonio I, Leone M, Isella V, Piamarta F, Consoli T, Villa ML, Forapani E, Russo A, Nichelli P. The Frontal Assessment Battery (FAB): normative values in an Italian population sample. Neurol Sci. 2005 Jun;26(2):108-16. doi: 10.1007/s10072-005-0443-4. PMID: 15995827.
[6] Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M, Capitani E. Trail making test: normative values from 287 normal adult controls. Ital J Neurol Sci. 1996 Aug;17(4):305-9. doi: 10.1007/BF01997792. PMID: 8915764.

P88

Prokineticin-2 is highly expressed in colonic mucosa of early Parkinson's disease patients

Giovanni Palermo[1], G. Bellini[1], F. Rettura[2], J. Pasquini[1], L. Cori[1], E. Benevento[1], C. Ippolito[3], C. Pellegrini[3], D. Frosini[2], N. Bernardini[3], R. Ceravolo[1]

[1]Center for Neurodegenerative Diseases - Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Gastrointestinal Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
[3]Unit of Histology and Embryology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Introduction: Neuroinflammation is increasingly recognized as a pivotal factor in the pathophysiology of Parkinson's disease (PD) playing also a role in dopaminergic neurodegeneration [1]. Notably, recent investigations support the contention that gut alterations, such as dysbiosis, impairments of the intestinal barrier, colonic inflammation and enteric pathological α-synuclein accumulation, represent early events in PD that can contribute to the central pathology via the gut-brain axis [2]. In this context, prokineticin-2 (PK2), a chemokine-like protein, has been implicated both in gastrointestinal functions and gut inflammation. Specifically, it appears to modulate immune and inflammatory responses as well as neuronal damage in PD [3-6].

Methods: The study comprised 11 PD patients, with 5 individuals having a disease duration of less than 5 years (Early PD, SPD) and 6 patients with a longer disease duration (Long PD, LPD). A control group of 5 asymptomatic subjects, matched for age and sex, was also included. All participants underwent colonoscopy for colorectal cancer screening, and mucosal biopsies from the descending colon were collected. Subsequently, biopsy samples were processed for PK2 immunofluorescence.

Results: We found an increased PK2 expression in the colonic mucosa from EPD patients compared to controls (4.42 ± 1.06 vs 1.00 ± 0.07, $p = 0.0009$) and LPD (1.62 ± 0.56, $p = 0.028$). Importantly, this expression demonstrated an inverse correlation with disease duration.

Conclusions: PK2 is highly expressed within the colonic lamina propria of PD patients, suggesting PK2 as a potential marker of colonic immune activation in early disease.

References:

[1] Muñoz-Delgado L, Labrador-Espinosa MÁ, Macías-García D, Jesús S, Benítez Zamora B, Fernández-Rodríguez P, et al. Peripheral Inflammation Is Associated with Dopaminergic Degeneration in Parkinson's Disease. Mov Disord. 2023;38:755–63.
[6] Klann EM, Dissanayake U, Gurrala A, Farrer M, Shukla AW, Ramirez-Zamora A, et al. The Gut–Brain Axis and Its Relation to Parkinson's Disease: A Review. Front Aging Neurosci. 2022;13 January:1–17.
[2] Lattanzi R, Severini C, Maftei D, Saso L, Badiani A. The Role of Prokineticin 2 in Oxidative Stress and in Neuropathological Processes. Front Pharmacol. 2021;12 March:1–8.
[3] Lattanzi R, Maftei D, Petrella C, Pieri M, Sancesario G, Schirinzi T, et al. Involvement of the chemokine prokineticin-2 (PROK2) in alzheimer's disease: From animal models to the human pathology. Cells. 2019;8.
[4] Gordon R, Neal ML, Luo J, Langley MR, Harischandra DS, Panicker N, et al. Prokineticin-2 upregulation during neuronal injury mediates a compensatory protective response against dopaminergic neuronal degeneration. Nat Commun. 2016;7:1–18. doi:10.1038/ncomms12932.
[5] Schirinzi T, Maftei D, Passali FM, Grillo P, Zenuni H, Mascioli D, et al. OlfactoryNeuron Prokineticin-2 as a Potential Target in Parkinson's Disease. Ann Neurol. 2023;93:196–204.

P89

The placebo effect on behavioral and neuromuscular fatigability in Parkinson's disease: evidence from an isometric motor task

Miriam Braga[1], A. Marotta[1], E. Pizzolla[1,2], M. Emadi Andani[1], I.A. Di Vico[1], M. Tinazzi[1], M. Fiorio[1]

[1]Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of Psychological Sciences, Birkbeck University of London, London, UK

Introduction: Fatigue is a nonmotor symptom in Parkinson's disease (PD), with an overwhelming sense of tiredness and lack of energy that interferes with the daily life [1], while fatigability is an objective decrease in psychophysical performance. Non-pharmacological strategies are required to manage these symptoms. The placebo effect, the psychobiological response arising from the belief of receiving a beneficial intervention [2], may be a promising procedure.

Objectives: We investigated the placebo effect on fatigability in PD patients with and without the symptom of fatigue and in a sample of age-matched healthy controls (HS). The hypothesis was that the placebo procedure could differently impact objective and subjective fatigability in PD and HS, and that the effect could be mediated by the nonmotor symptom of fatigue.

Methods: In this cross-over, double-blind, mixed effect design all subjects underwent a placebo and control interventions on two separate days. Before and after the intervention, participants performed a fatiguing task (i.e., maximal isometric forearm contraction). As placebo intervention, we applied an inert stimulation (TENS), along with suggestions about its efficacy on resistance to fatigue (placebo) or its inert nature (control) [3]. We enrolled 15 PD patients without the symptom of fatigue (PD_NF), 12 presenting the symptom of fatigue (PD_F), and 12 HS. The Fatigability Index (FI) and Neuromuscular Fatigability (NMF) were collected as behavioral and neurophysiological markers of fatigability, as well as subjective scales of fatigue and effort.

Results: FI was increased in the control session, indicating an increase in fatigability after the control intervention in the three groups. NMF was decreased in PD_F group after the placebo. Subjective data revealed reduced perception of fatigue and effort in the placebo session and increased perception of fatigue in the control session.

Conclusions: PD patients and HS have the same positive response to a placebo intervention during a fatiguing task. A decrease in perception of fatigue and effort was found after the placebo procedure. The modulation of NMF in PD_F group suggests that the nonmotor symptom of fatigue might mediate the impact of the placebo intervention on neurophysiological correlates during a fatiguing task.

References:

[1] Di Vico et al., 2021. Parkinsonism Relat Disord; 86, 114–123.
[2] Benedetti et al., 2016. Lancet Neurol; 15(7), 736–747.
[3] Fiorio et al., 2014. J Neurosci, 34(11), 3993–4005.

P90

Are the criteria for PD-MCI diagnosis comprehensive? A Machine Learning study with modified criteria

Chiara Longo[1,2], D.L. Romano[2], M. Pennacchio[2,3], M.C. Malaguti[1], R. Di Giacopo[4], B. Giometto[1,3], C. Papagno[3]

[1]Department of Neurology, "Santa Chiara Hospital", Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[2]Department of Psychology, University of Milano-Bicocca, Milan, Italy
[3]Center for Mind/Brain Sciences (CIMeC), University of Trento, Rovereto, Italy
[4]Department of Neurology, "Santa Maria del Carmine Hospital", Azienda Provinciale per i Servizi Sanitari (APSS), Rovereto, Italy

Introduction: Mild cognitive impairment in Parkinson's disease (PD-MCI) can include deficits in attention, executive functions, episodic memory, language, visuospatial abilities, and social cognition [1]. The current criteria for PD-MCI diagnosis [2] do not consider social cognition and it is unclear which tests should be used for PD-MCI diagnosis. Machine Learning (ML) can be pivotal for optimizing cognitive assessment by evaluating the diagnostic accuracy of tests.

*Objective***:** Employ ML to compare "traditional" and "alternative" cognitive batteries identifying which tests best classify PD-MCI.

Methods: 275 patients were retrospectively selected and diagnosed in PD-CU or PDMCI. Four cognitive batteries were created to compare their diagnostic accuracy: two Standard ones (Levels I and II), applying Litvan's criteria and using "traditional" tests; two Alternative ones (Levels I and II), which included a test of social cognition using "modified" criteria. Such batteries were included in the Random Forest (RF) classifier, in which 75% of the patients were used for the training and 25% for the testing. To assess the RF performance, the AUC was considered. Furthermore, the Variable Importance Indexes were estimated to understand the contribution of each test in PD-MCI classification.

Results: Standard Level I and II showed an AUC of 0.852 and 0.892, respectively, while Alternative Level I and II showed an AUC of 0.898 of 0.906. Variable Importance Indexes revealed that TMT B-A, Ekman test, RAVLT-IR, MoCA, and Action Naming test contributed more to the PD-MCI classification.

Conclusion: This study reveals that the Level I assessment can have the same (or even higher) classification ability than the Level II assessment. This evidence can be attributed to the choice of the most accurate tests for this clinical population, including a test for social cognition, a domain not included in the current diagnostic criteria. Finally, our study suggests the need to review the criteria for the diagnosis of PD-MCI.

References:

[1] Papagno, C., & Trojano, L. (2018). Cognitive and behavioral disorders in Parkinson's disease: an update. I: cognitive impairments. Neurological Sciences, 39(2), 215–223.
[2] Litvan, I., Goldman, J. G., Tröster, A. I., Schmand, B. A., Weintraub, D., Petersen, R. C., et al. (2012). Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Movement Disorders, 27(3), 349–356.

P91

Cognitive reorganization in patients with PD-MCI: a neuropsychological network approach

Chiara Longo[1,2], D.L. Romano[2], M.C. Malaguti[1], R. Bacchin[1], C. Papagno[3]

[1]Department of Neurology, "Santa Chiara Hospital", Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[2]Department of Psychology, University of Milano-Bicocca, Milan, Italy
[3]Center for Mind/Brain Sciences (CIMeC), University of Trento, Rovereto, Italy

Introduction: Parkinson's Disease (PD) can be characterized by heterogeneous cognitive deficits that can configure cognitive phenotypes [1]. Cluster Analysis studies have described them in a "macro" manner, but only one study has applied Network Analysis (NA) in PD [2]. NA represents an abstract model for studying the possible relationships between cognitive abilities to better understand cognitive phenotypes.

Objectives: Employ NA to compare the cognitive system of PD patients cognitively unimpaired (PD-CU) or with mild cognitive impairment (PD-MCI).

Methods: A Level II cognitive assessment was performed on 275 PD patients. On the grounds of such assessment, PD patients were divided into two diagnostic classes: 171 PD-CU and 104 PD-MCI. NA was performed on the said diagnostic classes to quantify the relationship between cognitive abilities in two different Gaussian Graphical Models. In such diagnostic classes-neuropsychological networks, nodes represent cognitive tests and demographical data, and their connection (i.e., partial correlations) is represented by edges .

Results: NA revealed noticeable differences between PD-CU and PD-MCI. Specifically, the two diagnostic classes-neuropsychological networks differed in three main aspects: 1) the role of demographic data in the network, where in PD-MCI these variables lose most of the relationship with the other nodes; 2) the relationship between Copy and Delay-Recall of the ROCF, that in PD-CU was mediated by Semantic Verbal Fluency, while in PD-MCI the two tests are directly related; 3) the role of WM in the network, i.e., it is central in PD-CU, while in PD-MCI it disconnects from the network.

Conclusions: The networks of PD-CU and PD-MCI are different. Specifically, NA revealed that cognitive decline masks the influence of demographic variables on cognitive functioning. Furthermore, differences are noted in the association between cognitive abilities with new connections and loss of others, suggesting a reorganization of the cognitive system for probable functional compensation mechanisms in case of cognitive decline.

References:

[1] Barvas, E., Mattavelli, G., Zappini, F., Giardina, F., Ottaviani, D., & Papagno, C. (2021). Cognitive phenotypes in Parkinson's disease: A latent profile analysis. Neuropsychology , 35(4), 451–459
[2] Ferguson, C. E., & Foley, J. A. (2023). The influence of working memory and processing speed on other aspects of cognitive functioning in de novo Parkinson's disease: Initial findings from network modeling and graph theory. Journal of Neuropsychology.

P92

Integrated management of persons with parkinsonism: a new model of patient-centered healthcare at home coordinated by a Case Manager via Telenursing

Roberto Cilia[1], C. Leuzzi[2], M. Catotti[2], J. Cordasco[1,2], G.C. Moreschi[2], R. Eleopra[1]

[1]Parkinson and Movement Disorders Unit, Department of Clinical Neurosciences, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]D.A.P.S. Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Introduction: Persons with Parkinson's disease, atypical or secondary parkinsonism (PwP) experience a wide range of symptoms and complications that are associated with increasing disability and complexity of care delivery. An integrated approach, involving a PwP nurse specialist (Case Manager), could offer benefits to PwP and caregivers [1,2].

Objectives: To explore a new model of integrated patient-centered care based on telemedicine ('Telenursing') for home management through a Case Manager aiming to improve PwP/caregivers quality of life by:
(a) optimizing management of motor/non-motor symptoms;
(b) supervising medication compliance to minimize side effects;
(c) minimizing complications and unscheduled hospital admissions/visits (reducing direct/indirect costs for the NHS).

Methods: From the COVID-19 pandemic, fragile PwP with motor and/or nonmotor disability are followed remotely by a 'digital' case manager by telephone (3 hours/day, 5 days/week) or email [3]. Interventions are both 'Reactive' (on-demand) and 'Proactive' (regular active follow-up, ranging from 1-week to 3-month).
The Case Manager managed and resolved medical issues (a) independently; (b) interacting with the neurologist; (c) interacting with a multidisciplinary team (physiatrist, psychologist, gastroenterologist, GP, etc.).

Results: Awaiting the results of two ongoing multicentre clinical trials (NCT05273957, NCT05792332), we report the experience gained at our Institute over the last 3 years.
From 25/11/2020 to 31/10/2023, 898 PwP have been included and followed-up.
The Case Manager managed a total of 1739 interventions ('Reactive' or 'Proactive') based on PwP and/or caregiver requests, of which:
- 52% resolved independently
- 20% resolved after discussing with the treating neurologist
- 17% managed involving the multidisciplinary team
- 11% required the neurologist intervention (email, telephone, televisit, in-person visit).

Conclusions: The Case Manager managed almost 90% of PwP medical issues, substantially reducing the neurologist's intervention to a few well-selected cases.
This model is highly innovative and has the potential to change the management of patients with parkinsonism in routine clinical practice.

References:

[1] Lennaerts H, et al. A Guideline for Parkinson's Disease Nurse Specialists, with Recommendations for Clinical Practice. J Parkinsons Dis. 2017;7(4):749-754.
[2] van der Marck MA, et al. Effectiveness of multidisciplinary care for Parkinson's disease: a randomized, controlled trial. Mov Disord 2013;28:605–11.

[3] Cilia R, Mancini F, Bloem BR, Eleopra R. Telemedicine for parkinsonism: A two-step model based on the COVID-19 experience in Milan, Italy. Parkinsonism Relat Disord. 2020;75:130-132.

P93

Can α-synuclein oligomers in skin biopsies predict the worsening of cognitive functions in Parkinson's disease? Preliminary evidence from a single-center longitudinal cohort study

Elena Contaldi[1], S. Mazzetti[2,3], M. Basellini[2], A. Colombo[1,3], V. Cereda[1,3], V. Ferri[1,3], I.U. Isaias[1,4], D. Calandrella[1,3], G. Cappelletti[2,5], G. Pezzoli[1,3]

[1]Parkinson Institute Milan, ASST G. Pini-CTO, Milano, Italy
[2]Department of Biosciences, Università degli Studi di Milano, Milano, Italy
[3]Fondazione Grigioni per il Morbo di Parkinson, Milano, Italy
[4]Department of Neurology, University Hospital of Würzburg and Julius Maximilian University of Würzburg, Würzburg, Germany
[5]Center of Excellence on Neurodegenerative Diseases, Università degli Studi di Milano, Milano, Italy

Introduction: Proximity ligation assay (PLA) has been used [1] to detect α-synuclein oligomers within synaptic terminals of autonomic fibers in skin biopsies from Parkinson's disease (PD) patients. It is still unknown whether this biomarker can inform about the progression of PD.

Objective: Evaluate whether the PLA score can predict future worsening of cognitive function in PD.

Methods: Twenty-six patients with PD (61.5% males, age 59.2±8 years, disease duration 5.3±3 years, 34% with RBD) were consecutively recruited and underwent a skin biopsy at baseline. They were followed up yearly for an average of 4.8±1 years. A neuropsychological assessment was performed at each visit. The patients had idiopathic PD and were classified [2,3] with normal cognition (PD-NC), mild cognitive impairment (PD-MCI), or dementia (PDD). At the last follow-up, patients were either cognitively stable (CS) or deteriorated (CD). Skin biopsy quantitative analysis was conducted on the samples containing the sweat gland and α-synuclein oligomers were quantified as PLA score [1]. Differences between groups and the correlation between skin biopsy measures and cognition were explored. The discrimination power of the PLA score was assessed by ROC curve analysis.

Results: At baseline, three and 23 patients were respectively classified as PD-MCI and PD-NC. At the last available follow-up, 27% were CD (two PD-MCI, five PDD) and 73% CS. PLA score was higher in CD than CS (432.1±188.3 vs 186.2±151.1; p=0.004, after controlling for age and disease duration). No significant correlations were found between PLA and cognitive scores, but a trend (r=-0.479, p=0.07) was observed for changes in MMSE score at the last follow-up. ROC curve analysis of PLA score to detect CD showed AUC=0.857, p=0.006, sensitivity=71.4%, specificity=89.5%.

Conclusions: Higher PLA scores can identify parkinsonian patients susceptible to cognitive decline, in line with the hypothesis of faster nonmotor progression in the body-first subtype of α-synuclein pathology.

References:

[1] Mazzetti S, Basellini MJ, Ferri V, et al (2020) α-Synuclein oligomers in skin biopsy of idiopathic and monozygotic twin patients with Parkinson's disease. Brain 143:920–931. https://doi.org/10.1093/brain/awaa008.
[2] Litvan I, Goldman JG, Tröster AI, et al (2012) Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Dis order Society Task Force guidelines: PD-MCI Diagnostic Criteria. Mov Disord 27:349–356. https://doi.org/10.1002/mds.24893.
[3] Emre M, Aarsland D, Brown R, et al (2007) Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord 22:1689–1707. https://doi.org/10.1002/mds.21507.

P94

Vestibular and saccadic abnormalities in Parkinson's disease patients with heterozygous GBA mutation and idiopathic PD: comparison between groups and correlations with motor features

Francesco Cavallieri[1], A. Castellucci[2], S. Grisanti[3], V. Fioravanti[1], G. Di Rauso[1,3], E. Monfrini[4], G. Toschi[1], J. Rossi[1,3], G. Portaro[1], M. Menichetti[2], A. Tozzi[5], G. Ferrulli[5], V. Ferrari[1], A. Melpignano[6], M. Scarano[7], A. Groppi[1], R. Sabadini[1], A. Scaglioni[8], A.B. Di Fonzo[3], A. Ghidini[2], F. Valzania[1]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Otolaryngology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[4]Neurology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[5]Otorhinolaryngology-Head and Neck Surgery Department, University Hospital of Modena, Modena, Italy
[6]Presidio Ospedaliero Fidenza AUSL Parma, Fidenza, Italy
[7]Dipartimento di Cure Primarie, Azienda Unità Sanitaria Locale (AUSL) Modena, Modena, Italy
[8]Centro S. Maria ai Servi, Fondazione Don Gnocchi, Parma, Italy

Introduction: Vestibular dysfunction has been recently suggested as a possible non-motor feature of Parkinson's Disease (PD), hovewer to date literature data are still lacking. In addition, saccadic eye movements have been previously studied in patients with PD showing conflicint results. Very few studies have reported vestibular and saccadic abnormalities in Gaucher disease.

Objectives: To assess vestibulo-ocular reflex (VOR) gain and voluntary saccade eye movements in a cohort of consecutive cohort of GBA-PD patients compared with a matched cohort of consecutive idiopathic (I) PD patients (I-PD).

Methods: A consecutive cohort of GBA-PD patients has been paired for age, sex, disease duration, Hoehn & Yahr stage, and comorbidities (Charlson Comorbidity Index) with a cohort of consecutive I-PD patients. Clinical assessment included the MDS-UPDRS total scores and subscores, the Montreal Cognitive Assessment (MoCA), the video head impulse test (vHIT) and saccadic instrumental assessment. Continous variables between groups were compared through the Mann-Whitney test while nominal/ordinal variables through the chi-squared test. Correlation analyses between clinical and vestibular/saccadic variables in the whole cohort were performed by calculating the respective Spearman's ρ values and their significance level.

Results: Twenty GBA-PD (male:13; age:63.47 years; MDS-UPDRS III:29.47; MoCA: 22.84) and 20 I-PD (age:63.72 years; MDS-UPDRS III:28.72; MoCA:23.00) patients were included. No differences were found in vestibular and saccadic variables between GBA-PD and I-PD. In the whole cohort, bilateral saccadic latency directly correlated with age ($p<.05$), disease duration ($p<.001$) and PIGD subscore ($p<.001$) while it negatively correlated with MoCA score ($p<.05$). The bilateral vHIT gain of the lateral semicircular canal directly correlated with disease duration ($p<.05$) while the gain of the posterior semicircular canal negatively correlated with rigidity subscore ($p<.05$).

Conclusions: This study confirmed that vestibular and saccadic abnormalities may be associated with clinical characateristcs in PD patients. In particular saccadic latency may represent a markers of axial involvement.

P95

Toward the detection of pathogenic α-synuclein seeds from Parkinson's disease patients in tears using α-syn RT-QuICR

Beatrice Pinna[1], C.D Orrù[1], S. Vascellari[3], G. Pisano[3], G. Serra[3], G. Fenu[3], D. Murgia[3], S. Pusceddu[2], F. Angius[2] A. Manzin[2], G. Cossu[3], B. Caughey[1]

[1]Laboratory of Neurological Infectious and Immunity (NII), Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Health (NIH), Hamilton, MT, USA
[2]Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy
[3]S.C. Neurology and Stroke Unit, AO Brotzu, Cagliari, Italy

Introduction: aSyn-RT-QuICR is a seed amplification assay that detects disease associated α-Synuclein (aSynD) in tissues such as CSF, intestinalmucosa, and skin from Parkinson's disease (PD) patients, sparking interest in its use for early diagnosis. Given that human tears can be collected non-invasively, we initiated a project to test if RT-QuICR can detect α-SynD in tears from PD patients. Here, we describe progress in collecting specimens and testing the recovery of α-SynD seeds from tears applied to Schirmer's strips.

Methods: This study was approved by the Ethics Committee (Prot. PG/2017/17817) of the ARNAS-Brotzu-Cagliari, Italy. Tears were collected using Schirmer's strips from both eyes from PD patients (n=76) and healthy subjects (n= 40). To initially assess RT-QuICR with tear fluid on Schirmer's strips, we spiked tear fluid with PD or healthy brain homogenates, applied it to strips, eluted using SDS with or without a capture on iron-oxide-beads, and seeded the eluates into the assay.

Results: Study participants had a mean age of 71 years for PD and 60 years for healthy controls with similar numbers of male and female participants in each cohort. The mean disease duration was 7.32 years, with Hoehn and Yahr stages ranging from 1-5. Although these patients' specimens await testing, our spiking experiments have revealed that by using SDS to elute α-SynD from the Schirmer's strips and iron oxide beads to capture the seeds we can detect brainderived α-SynD diluted ~105-fold in tear fluid within ~15 hours.

Conclusions: Here we describe the panel of human tear specimens that we have collected, and show preliminary data that SDS in combination with iron oxide beads allows a more efficient α-SynD recovery from Schirmer's-strips. This protocol will now be used to blindly test the utility of RT-QuICR in discriminating PD cases from heathy controls using tear fluid as an accessible diagnostic biospecimen.

P96

Psychometric properties of the SCale for Outcomes in Parkinson's disease Psychiatric Complications (SCOPA-PC) in Parkinson disease

Maria Autuori, S. Cuoco, A. Cappiello, I. Carotenuto, R. Bisogno, A.R. Avallone, R. Erro, M. Amboni, M.T. Pellecchia, P. Barone, M. Picillo

Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Italy

Introduction: The SCale for Outcomes in Parkinson's disease - Psychiatric Complications (SCOPA-PC) [1] is a quick and easy tool to evaluate psychiatric disturbances in Parkinson's disease (PD) [2]. An Italian version of the scale is lacking.

Objectives: We studied the psychometric properties of the Italian version of SCOPA-PC in PD.

Methods: The SCOPA-PC was translated into Italian and administered to 130 consecutive PD outpatients from October 2022 to December 2023, at the Center for Neurodegenerative Diseases (CEMAND) at the University of Salerno, along with a clinical interview and motor, cognitive and behaviour evaluations.

Results: First of all we describe the distribution of psychiatric disorders in our PD sample. The Cronbach's alpha of the SCOPA-PC was equal to 0.6. The SCOPA-PC total score was significantly correlated with all items. The SCOPA-PC total score did not correlate with demographic nor motor variables nor with the Montreal Cognitive Assessement (MoCA) test ($p>0.05$) but correlated with the QUIP ($p<0.001$) and the NPI ($p<0.001$). The hallucinations (item_1) and illusions/misidentification of persons (item_2) correlated with NPI_hallucination ($p< 0.005$), paranoid ideation (item_3) correlated with NPI_delusions ($p<0.001$), altered dream phenomena (item_4) correlated with NPI_sleep disorders ($p=0.055$), confusion (item_5) correlated with MOCA ($p<0.001$), sexual preoccupation (item_6) correlated with QUIP_ sex ($p<0.001$) and compulsive behavior (item_7) correlated with the sum of QUIP_gambling and QUIP_shopping ($p<0.001$). Compulsive behavior correlated with H&Y ($p=0.004$). A principal component analysis, with Varimax rotation, showed that in men the Factor 1 (items:1, 4, 5,7), Factor 2 (items: 3, 6) and Factor 3 (item: 2) explain a cumulative variance equal to 64.43%. In women, the Factor 1 (items: 1, 3, 4, 5), Factor 2 (items: 2, 7) and Factor 3 (item: 6) explain a cumulative variance equal to 64.73%.

Conclusions: In conclusion, the SCOPA-PC Italian version is a reliable, valid, and easy toll to screen psychiatric disturbances in PD.

References:

[1] Visser M., Verbaan D., van Rooden S.M., Stiggelbout A.M., Marinus J., van Hilten J.J. Assessment of psychiatric complications in Parkinson's disease: The SCOPA-PC. Mov Disord. 2007 Nov 15;22(15):2221-8. doi: 10.1002/mds.21696. PMID: 17712843.

[2] Barone P, Antonini A, Colosimo C. et al. The PRIAMO study: A multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. Mov Disord. 2009 Aug 15;24(11):1641-9. doi: 10.1002/mds.22643. PMID: 19514014.

P97

Peripheral neuropathy in Parkinson's disease and role of levodopa: the experience from Rome "Tor Vergata"

Elena Garasto[1], R. Cerroni[1,2], K. Meksi[1], A. Stefani[1,2], M. Pierantozzi[1,2], N.B. Mercuri[1], C. Rocchi[1]

[1]Unit of Neurology, Department of Systems Medicine, Tor Vergata University of Rome, Italy
[2]Parkinson's Center, Department of Systems Medicine, Tor Vergata University of Rome, Italy

Introduction: Polyneuropathy (PN) has been described in Parkinson's disease (PD), mainly after levodopa-carbidopa intestinal gel infusion (LCIG) [1]. Still, literature suggests the possibility of large-fiber neuropathy being intrinsic of PD [2]. On the other hand, LCIG is believed to cause or worsen PN because of its peculiar infusional site [3].

Objectives: We aimed to assess the prevalence of PN in PD patients and possible determinants, and exploring its progression after LCIG, in a subgroup of patients, through nerve conduction study.

Methods: Nerve conduction studies, clinical evaluation and blood test (with vitamine B12, B9, homocysteine, other than screening for PN risk factors) were performed at baseline on 74 patients. A subgroup of 17 patients, who strarted LCIG, were re-evaluated after a mean follow-up of 40 months, with clinical and neurophysiological assessment.

Results: Among 66 patients included, 15 had diagnosis of idiopathic PN (22,7%), mainly sensory-motor assonal PN. PD patients with PN (PDwPN) differed from patients without PN (PDwoPN) in having higher cumulative Levodopa daily dose (Lev) and homocysteine (Hcy), lower B9 and B12. No differences were found for age, gender, disease severity/duration and therapy with ICOMT. Stratifing our population on the base of Lev, we observed that the prevalence of PN significantly differed between groups (10% in noLev, 13,3% in Lev<900mg/day and 38,4% in Lev>900mg/day). Also, Lev directly correlated with Hcy and inversely with B12 and with amplitude of sural sensory (sAMP), motor peroneal (pAMP) and tibial (tAMP) action potentials. On follow-up, the incidence of PN was 35,7%. Furthermore, from baseline to follow up, we noted a significant linear regression between the reduction of sAMP and pAMP and the variation of Lev (ΔLev), adjusted with age and LCIG duration.

Conclusions: This study supports the hypothesis of iatrogenic origin of PN in PD and suggests moderating the increase of Levodopa cumulative dose, when LCIG starts.

References:

[1] Merola A, Romagnolo A, Zibetti M, Bernardini A, Cocito D, Lopiano L. Peripheral neuropathy associated with levodopa-carbidopa intestinal infusion: A long-term prospective assessment. Eur J Neurol. 2016;23(3):501–9.
[2] Nolano M, Provitera V, Manganelli F, Iodice R, Stancanelli A, Caporaso G, et al. Loss of cutaneous large and small fibers in naive and l -dopa-treated PD patients. Neurology. 2017;89(8):776–84.
[3] Jugel C, Ehlen F, Taskin B, Marzinzik F, Müller T, Klostermann F. Neuropathy in Parkinson's Disease Patients with Intestinal Levodopa Infusion versus Oral Drugs. PLoS One. 2013;8(6):1–6.

P98

Blood D-serine levels correlate with aging and dopaminergic treatment in Parkinson's disease

Alberto Imarisio[1,2], I. Yahyavi[3,4], M. Avenali[5,6], A. Di Maio[3,4], G. Buongarzone[5,6], M. Picascia[6], A. Filosa[7], C. Gasparri[7], M.C. Monti[7], M. Rondanelli[7], C. Pacchetti[6], F. Errico[4,8], E.M. Valente[1,2], A. Usiello[3,4]

[1]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[2]Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Environmental, Biological and Pharmaceutical Sciences and Technologies, Università degli Studi della Campania "Luigi Vanvitelli", Caserta, Italy
[4]CEINGE Biotecnologie Avanzate Franco Salvatore, Naples, Italy
[5]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[6]Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[7]Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy
[8]Department of Agricultural Sciences, University of Naples "Federico II", Portici, Italy

Introduction: We recently described increased D- and L-serine concentrations in the striatum of MPTP-treated monkeys and human Parkinson's disease (PD) brains and in the CSF of de novo living PD patients compared to controls [1,2]. However, data regarding peripheral D-serine levels in PD are scarce.

Objective: We assessed whether the serum levels of serine enantiomers and the other NMDA receptor-related aminoacids (i) differ between PD patients and HC and (ii) correlate with demographic, clinical features and dopaminergic treatment in PD.

Methods: We recruited 83 consecutive PD patients and 41 age-matched healthy controls (HC). PD cohort underwent an extensive motor, cognitive, quality of life and antiparkinsonian treatment characterization. The serum levels of D- and L-serine, L-glutamate, L-glutamine, L-aspartate, L-asparagine and glycine were determined using High Performance Liquid Chromatography.

Results: In age- and sex-adjusted analyses, no differences emerged in the serum levels of D-serine, L-serine or the other NMDA receptor-stimulating aminoacids between PD and HC. D-serine and D-/Total serine ratio positively correlated with age in PD ($r=0.313$, $p=0.004$ and $r=0.311$, $p=0.004$, respectively), but not in HC. Moreover, we found that (i) D-serine and D-/Total serine, but not the other neuroactive aminoacids, increase with older age at PD onset ($r=0.379$, $p<0.001$ and $r=0.325$, $p=0.003$, respectively); (ii) higher LEDD correlate with lower levels of D-serine ($r=-0.248$, $p=0.027$) and the other excitatory aminoacids; (iii) MDS-UPDRS-III positively correlate with glycine ($r=0.241$, $p=0.033$). Finally, the addition of LEDD as covariate disclosed higher serum D-serine in PD compared to HC ($\Delta=38.7\%$; $p=0.038$).

Conclusions: Increased serum D-serine levels represent a putative biochemical signature of PD. The positive correlation between D-serine and age at PD onset supports the hypothesis that D-serine may play a neuroprotective role in PD by delaying the onset of the disease [3].

References:

[1] A. Di Maio, T. Nuzzo, L. Gilio, M. Serra, F. Buttari, F. Errico, A. De Rosa, M.S. Bassi, M. Morelli, J. Sasabe, D. Sulzer, M. Carta, D. Centonze, A. Usiello, Homeostasis of serine enantiomers is disrupted in the post-mortem caudate

putamen and cerebrospinal fluid of living Parkinson's disease patients, Neurobiol. Dis. 184 (2023) 106203. https://doi.org/10.1016/j.nbd.2023.106203.
[2] M. Serra, A. Di Maio, V. Bassareo, T. Nuzzo, F. Errico, F. Servillo, M. Capasso, P. Parekh, Q. Li, M.-L. Thiolat, E. Bezard, P. Calabresi, D. Sulzer, M. Carta, M. Morelli, A. Usiello, Perturbation of serine enantiomers homeostasis in the striatum of MPTP-lesioned monkeys and mice reflects the extent of dopaminergic midbrain degeneration, Neurobiol. Dis. 184 (2023) 106226. https://doi.org/10.1016/j.nbd.2023.106226.
[3] E. Gelfin, Y. Kaufman, I. Korn-Lubetzki, B. Bloch, I. Kremer, D.C. Javitt, U. Heresco-Levy, D-serine adjuvant treatment alleviates behavioural and motor symptoms in Parkinson's disease, Int. J. Neuropsychopharmacol. 15 (2012) 543–549. https://doi.org/10.1017/S1461145711001015.

P99

Efficacy of multidisciplinary intensive rehabilitation treatment in Parkinson's disease

Giulia Donzuso, A. Russo, F. Zagari, A. Luca, G. Mostile, C.E. Cicero, A. Nicoletti, M. Zappia

Department of Medical, Surgical Sciences and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy

Objectives: To evaluate the efficacy of an 8-week multidisciplinary intensive rehabilitation treatment (MIRT) [1] and virtual reality training (VRT) in patients with Parkinson's disease (PD) assessed with clinical and magnetic resonance imaging (MRI) markers [2].

Methods: This is a prospective, parallel-group, randomized study (Ethical committee register 149/2020/PO). PD patients attending the Movement Disorders Center of the University of Catania were enrolled and randomly assigned to MIRT treatment without (group A) or with (group B) a VRT with BTs-Nirvana (BTsN). Each patients underwent a comprehensive clinical assessment at baseline (T0), after the rehabilitation treatment (week 8, T1) and after one month without (T2).

Results: Seventeen PD patients were enrolled according to Brain Bank Criteria (10 male, 7 female, age 64.3 ± 8.7 years, UPDRS-ME 56.4 ± 21.2 score). Ten patients were randomized into group A, and 7 into group B. There were no differences between the two-treatment group in demographics and clinical features at baseline. Considering the whole PD sample, patients showed an improvement in the FOG-Q score between T0 and T2 (4.3 ± 4.1 vs 3.0 ± 3.7 score, p-value 0.02), and T1 and T2 (3.6 ± 3.9 vs 3.0 ± 3.7 score, p-value 0.05). Between group analysis showed significant differences between group A and group B at T1 in TUG (11.3 ± 2.2 vs 6.1 ± 2.7 seconds, p-value <0.001), and 10-meters performances (8.5 ± 1.2 vs 5.3 ± 2.4 score, p-value 0.002).

Conclusions: This study showed that physical rehabilitation improves motor symptoms of PD patients [3]. The use of VRT could further improve motor performance of PD patients.

Project "IR3MA Parkinson Cyclone in Life" Code 088690110504 CUP G69J18001070007, D.D.G. nr 3607/5S del 21/11/2019 – Funded by PO FESR SICILIA 2014/2020 Obiettivo Tematico 1 – Avviso Pubblico Azione 1.1.5 - D.D.G. nr 1349/5 del 14/6/2017

References:

[1] Frazzitta G, Maestri R, Bertotti G, Riboldazzi G, Boveri N, Perini M, Uccellini D, Turla M, Comi C, Pezzoli G, Ghilardi MF. Intensive rehabilitation treatment in early Parkinson's disease: a randomized pilot study with a 2-year follow-up. Neurorehabil Neural Repair. 2015 Feb;29(2):123-31.
[2] Yang Y, Wang G, Zhang S, Wang H, Zhou W, Ren F, Liang H, Wu D, Ji X, Hashimoto M, Wei J. Efficacy and evaluation of therapeutic exercises on adults with Parkinson's disease: a systematic review and network meta-analysis. BMC Geriatr. 2022 Oct 21;22(1):813.
[3] Ferrazzoli D, Ortelli P, Zivi I, Cian V, Urso E, Ghilardi MF, Maestri R, Frazzitta G. Efficacy of intensive multidisciplinary rehabilitation in Parkinson's disease: a randomised controlled study. J Neurol Neurosurg Psychiatry. 2018 Aug;89(8):828-835.

P100

Diabetes impact on nigrostriatal vulnerability in Parkinson's Disease

Alice Galli[1], A. Pilotto[1], C. Zatti[1], C. Tirloni[1], A. Lupini[1], B. Paghera[2], A. Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Nuclear Medicine Unit, University of Brescia, Brescia, Italy

Introduction: Several studies suggested a possible association between diabetes mellitus (DM) and Parkinson's disease (PD) [1,2]. Aim of the study was to investigate in vivo whether diabetes mellitus influences motor function via its impact on nigrostriatal dopaminergic vulnerability in two independent cohorts of drug-naïve patients with early-stage Parkinson's Disease (PD).

Methods: The study included two independent prospective cohorts of drug naïve PD patients who underwent a standardized neurological examination, and 123I-FP-CIT brain SPECT imaging. Each cohort comprised two subgroups of PD patients with diabetes mellitus (PDDM) or without diabetes mellitus (PD), which were matched 1:1 for age, sex, motor and cognitive impairment at baseline. We tested differences in striatal binding using an ANCOVA test adjusted for age, sex, and handedness. Longitudinal analysis on a subset of PD patients was conducted to evaluate annual difference in striatal binding driven by diabetes mellitus.

Results: One-hundred sixty-six drug-naïve PD patients entered the study, namely 54 patients from the single-center DMA-PD cohort, and 112 patients from the PPMI dataset. Compared to PD, PD-DM showed a higher dopamine uptake in left putamen in both the considered cohorts. The longitudinal evaluation revealed that PD-DM had a faster annual decline of left putamen binding than PD (-20% vs. -9%).

Conclusions: Findings showed that diabetes mellitus may impact on compensatory mechanisms of nigrostriatal systems resulting in less dopamine deficits even with comparable degree of motor and nonmotor impairment at baseline. This result was further confirmed by the follow-up evaluation showing a greater annual difference in left putamen binding. Results were confirmed in both an Italian monocentric cohort and in the multicentric PPMI cohort.

References:

[1] Gennaro Pagano, Sotirios Polychronis, Heather Wilson, Beniamino Giordano, Nicola Ferrara, Flavia Niccolini, Marios Politis Neurology May 2018, 90 (19) e1654-e1662; DOI:10.1212/WNL.0000000000005475
[2] Craft S, Watson GS. Insulin and neurodegenerative disease: shared and specific mechanisms. Lancet Neurol 2004;3:169–178.

P101

Motor reserve impact on nigrostriatal vulnerability and motor severity in Parkinson's disease

Alice Galli[1,2], A. Pilotto[1,3], A. Rizzardi[1,3], C. Zatti[1,3], M. Ogliani[1], A. Lupini[1], C. Hansen[4], R. Romijnders[4], S.P. Caminiti[5], E. Premi[6], S. Lucchini[7], F. Bertagna[7], B. Paghera[7], W. Maetzler[4], M. Nucci[8], S. Mondini[8], A. Padovani[1-3,9]

[1]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Laboratory of Digital Neurology and Biosensors, University of Brescia , Brescia, Italy
[3]Department of Continuity of Care and Frailty, Neurology Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[4]Department of Neurology, University Hospital Schleswig-Holstein and Kiel University, Kiel, Germany
[5]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[6]Stroke Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[7]Nuclear Medicine Unit, University of Brescia, Brescia, Italy
[8]Department of General Psychology, University of Padua, Padua, Italy
[9]Brain Health Center, University of Brescia, Brescia, Italy

Introduction: Increasing evidence supports the beneficial effects of lifelong physical activities on cognition or mobility [1]. Recently, it has been hypothesized that motor reserve (MR) may be associated with a greater ability to cope with normal or pathological motor skill decline [2].

Objectives: Aim of the study was analyzing the possible impact of MR on dopamine binding and motor severity in early-diagnosed patients with Parkinson's disease (PD).

Methods: The study included drug-naïve PD patients, who underwent cognitive and motor assessment- and 123I-FP-CIT-SPECT imaging. Gait parameters were evaluated in normal, fast and dual-task conditions using Mobile Health Technologies (MHT) in supervised setting. Motor Reserve Index questionnaire (MRIq) was administered [3] and individuals were categorized into high-MR or low-MR. The relationship between MR and dopamine binding was assessed using a voxel-wise regression model. Clinical differences between patients with high and low MR were assessed using two-sample t-test or chi-squared test, whereas differences in and motor parameters was explored using a MDS-UPDRS-III, sex and height-adjusted ANCOVA model.

Results: Forty drug-naïve PD patients entered the study (age 68.35±7.5). MR was negatively correlated with dopamine binding in left putamen and pallidum in the voxel-wise model. High vs. low-MR PD were comparable for demographics, motor and cognitive severity, whereas High-MR PD showed lower dopamine binding in left putamen ($p=0.029$) as compared to low-MR. No differences in gait parameters emerged in normal conditions, whereas in motor dual task condition, high-MR vs. low-MR PD showed lower step-time ($p=0.002$), motor cost ($p<0.001$), step-time variability ($p=0.045$), and higher step-length ($p=0.045$).

Conclusions: Motor reserve emerged as important modulator of dopamine basal ganglia circuitries at onset of PD, with important impact on motor impairment and performances assessed by mobile health technology. These mechanisms might explain the wide heterogeneity of progression and response to treatments in early disease phases and need to be verified in ongoing longitudinal studies.

References:

[1] Pettigrew, C., & Soldan, A. (2019). Defining cognitive reserve and implications for cognitive aging. Current neurology and neuroscience reports, 19, 1-12.
[2] Chung, S. J., Lee, J. J., Lee, P. H., & Sohn, Y. H. (2020). Emerging concepts of motor reserve in Parkinson's disease. Journal of Movement Disorders, 13(3), 171.
[3] Pucci, V., Guerra, C., Barsi, A., Nucci, M., & Mondini, S. (2023). How long have you exercised in your life? The effect of motor reserve and current physical activity on cognitive performance. Journal of the International Neuropsychological Society, 1-7.

P102

Action Observation and Motor Imagery as a treatment in patients with Parkinson's Disease

Gaia Bonassi[1], S. Mezzarobba[1,2], L. Avanzino[2,3]*, E. Pelosin[1,2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, and RAISE Ecosystem, Genova, Italy.
[2]IRCCS Ospedale Policlinico San Martino, Genoa, Italy.
[3]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy.

Action Observation (AO) and Motor Imagery (MI) has emerged as promising tool for physiotherapy intervention in Parkinson Disease (PD). This narrative review summarizes why, how, and when applying AO and MI training in individual with PD. We report the neural underpinning of AO and MI and their effects on motor learning. We examine the characteristics and the current evidence regarding the effectiveness of physiotherapy interventions, and we provide suggestions about their implementation with technologies.
Neurophysiological data suggest a substantial correct activation of brain networks underlying AO and MI in people with PD, although the occurrence of compensatory mechanisms has been documented.
Regarding the efficacy of training, in general evidence indicates that both these techniques improve mobility and functional activities in PD. However, these findings should be interpreted with caution due to variety of the study designs, training characteristics, and the modalities in which AO and MI were applied. Finally, results on longterm effects are still uncertain.
Several elements should be considered to optimize the use of AO and MI in clinical setting, such as the selection of the task, the imagery or the video perspectives, the modalities of training. However, a comprehensive individual assessment, including motor and cognitive abilities, is essential to select which between AO and MI suite the best to each PD patients. Much unrealized potential exists for the use AO and MI training to provide personalized intervention aimed at fostering motor learning in both the clinic and home setting.

Acknowledgments including sources of support: This work was carried out within the framework of the project "RAISE - Robotics and AI for Socio-economic Empowerment" and has been supported by European Union - NextGenerationEU.

P103

Cortical fingerprints of reach-to-grasp movements in Parkinson's disease

Silvia Manfroni[1,2], C. Palmisano[4], M. Lassi[3], A. Mazzoni[3], A. Pedrocchi[1], I.U. Isaias[2,4]

[1]Department of Electronics, Information and Bioengineering, NearLab, Politecnico di Milano, Milan, Italy
[2]Centro Parkinson ASST G. Pini-CTO, Milan, Italy
[3]The BioRobotics Institute and Department of Excellence in Robotics and AI, Sant'Anna School of Advanced Studies, Pisa, Italy
[4]Department of Neurology, University Hospital and Julius Maximilian University, Würzburg, Germany

Introduction: Reliable biomarkers of disease severity and motor performance in Parkinson's disease (PD) could be a significant resource to support clinical decisions and guide the clinical management of patients [1]. In this scenario, electroencephalography (EEG) microstate analysis can be employed for assessing disease specific features of cortical activity, characterized in terms of transient topographies (microstates) whose spatiotemporal characteristics can be considered quantifiable biomarkers [2-3].

Objectives: To test the ability of EEG microstate parameters during resting and reach-to-grasp movements to identify the level of disease severity and motor performance in parkinsonian patients.

Methods: Eight parkinsonian patients with idiopathic PD (age: 57.1 ± 5.9, disease duration: 11.3 ± 4.3, UPDRS-III: 42.4 ± 12.8) were recorded with a 128-channels EEG device during resting (60 seconds) and reach-to-grasp movements (ten repetitions for three times) after overnight pausing all dopaminergic medications [4]. We extracted four microstates (A, B, C, D) for both conditions and characterized the temporal dynamics of the microstate sequences. For the reach-to-grasp task, we recorded the kinematic of the upper limb (right/dominant hand) with a motion capture system and task duration and wrist velocity were extracted.

Results: During resting, the microstate B coverage was significantly higher in advance patients and microstate A average duration negatively correlated with the UPDRS-III score. Coherently, the temporal features of microstate B and A correlated positively and negatively with the task duration, respectively. The microstate A coverage was significantly higher during the reach-to-grasp task than at rest. The Lempel-Ziv complexity, representative of either the repetitiveness or the diversity of the microstate sequence, positively correlated with the movement velocity.

Conclusions: We showed the capability of EEG microstate parameters to capture the severity of parkinsonian symptoms and motor performances. These parameters can be considered potential EEG biomarkers in the definition of different clinical conditions and in the evaluation of PD-related alterations of motor control strategies.

References:

[1] E. Tolosa, A. Garrido, S. W. Scholz, and W. Poewe, "Challenges in the diagnosis of Parkinson's disease.," Lancet Neurol , vol. 20, no. 5, pp. 385–397, May 2021, doi: 10.1016/S1474-4422(21)00030-2.
[2] C. M. Michel and T. Koenig, "EEG microstates as a tool for studying the temporal dynamics of whole-brain neuronal networks: A review.," Neuroimage, vol. 180, no. Pt B, pp. 577–593, Oct. 2018, doi: 10.1016/j.neuroimage.2017.11.062.

[3] A. Khanna, A. Pascual-Leone, C. M. Michel, and F. Farzan, “Microstates in resting-state EEG: current status and future directions.,” Neurosci Biobehav Rev, vol. 49, pp. 105–13, Feb. 2015, doi: 10.1016/j.neubiorev.2014.12.010.
[4] M. Vissani et al., “Impaired reach-to-grasp kinematics in parkinsonian patients relates to dopamine-dependent, subthalamic beta bursts,” NPJ Parkinsons Dis, vol. 7, no. 1, Dec. 2021, doi: 10.1038/s41531-021-00187-6.

P104

Analysing the bradykinesia features combination in people with Parkinson's disease and elderly healthy individuals

Giulia Paparella[1,2], M. De Riggi[1], A. Cannavacciuolo[1,2], D. Costa[1], D. Birreci[1], M. Passaretti[1], L. Angelini[1], A. Berardelli[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: Bradykinesia is defined as movement slowness and a progressive decrease in amplitude and velocity during movement repetition (i.e., sequence effect) and it is the main diagnostic feature of Parkinson's disease (PD) [1]. Recently, we proposed redefining bradykinesia, based on a dual-axis approach, i.e., describing the major phenomenological features of bradykinesia in a given patient (Axis I), and elucidating the underlying etiology (Axis II) [2].

Objectives: To evaluate, through kinematic analysis, the major phenomenological features of bradykinesia, with a specific focus on their combination, in a relatively large sample of individuals with PD and elderly healthy controls (HC).

Methods: We examined a sample of 172 PD patients (OFF medication) and 145 HC. Kinematic techniques were used for finger-tapping analysis. ROC curve analysis was used to determine cut-off values for movement velocity, amplitude, rhythm, and sequence effect. We then quantified the percentage of movement abnormalities in the two groups, whether occurring in isolation or variable combinations.

Results: Among PD patients, 171 (99.9%) exhibited at least one movement abnormality. Movement slowness or sequence effect, occurred in 77.2% and 80.9% of cases, respectively. Concerning current clinical criteria, the combination of movement slowness and sequence effect was observed in only 59.6% of cases. Movement abnormalities were also present in a significant proportion of HC; however, in these cases, they predominantly occurred as isolated abnormalities. The combination of 3-4 abnormalities was observed in 66.7% of PD patients and 15.9% of HC ($p<0.05$ by X^2 test).

Conclusions: The study objectively outlines the phenomenological features of bradykinesia in a large group of people with PD and healthy elderly individuals. Further information on bradykinesia features combination will be obtained from the analysis of their clinical correlates and the effects of pharmacological therapies.

References:

[1] Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015 Oct;30(12):1591- 601. doi: 10.1002/mds.26424.
[2] Bologna M, Espay AJ, Fasano A, Paparella G, Hallett M, Berardelli A. Redefining Bradykinesia. Mov Disord. 2023 Apr;38(4):551-557. doi: 10.1002/mds.29362.

P105

Clinical and neuroimaging correlates of arterial hypertension in Parkinson's disease

Francescopaolo Cucinotta[1,2], A. Zarkali[1], I. Cociasu[1], F. Morgante[1], L. Ricciardi[1]

[1]Neurosciences and Cell Biology Institute, St George's, University of London, London, UK
[2]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Background and Objective: High blood pressure is rarely reported in Parkinson's disease (PD). It is unclear how high blood pressure relates to dopaminergic state in PD and its clinical and neuroimaging correlates. This study aimed to explore the relationship between blood pressure values and dopaminergic medication state (OFF and ON) in people with advanced PD. Moreover, we aim to explore the clinical and neuroimaging correlates of blood pressure values in patients with PD.

Materials and Methods: A total of 61 PD patients were included in the study. Clinical characteristics, including age, gender, disease duration, and levodopa equivalent daily dose, were recorded. Motor and non-motor symptoms were evaluated using standardized rating scales. Blood pressure measurements were taken in the practically defined OFF-MED (after 12 hours without medication) and ON-MED (at 1 hour after administering 150% of morning Levodopa dose) in sitting and standing up (at 3 minutes) position. The diagnosis of hypertension was based on the 2018 ESC/ESH Clinical Practice Guidelines for the Management of Arterial Hypertension. Accordingly, we categorized subjects in hypertensive-PD and normotensive-PD. Presence and burden of small vessel disease was analyzed on structural brain MRI. The total small vessel disease (SVD) score from brain MRI was calculated and used for correlation with clinical variables.

Results: Thirty-five patients exhibited hypertension in the OFF-MED condition; 26 (74.3%) of them had normal value of BP in the ON-MED condition. Only 6 of these hypertensive subjects had a documented history of hypertension and were receiving anti-hypertensive medication. Frequency of orthostatic hypotension in both ON and OFF-MED did not differ between the group with and without hypertension. The Wearing Off Questionnaire 19 Total Score (p=.047) and the Gait and Falls Questionnaire Total Score (p=0.006) scored significantly higher in the PD group with hypertension compared to the one without hypertension. MRI scan analysis disclosed significantly higher SVD in the PD with hypertension group (p<0.05). After controlling for age, gender and disease duration, a significant correlation was observed between the SVD score and the PDQ39 index (p=0.007, r=.36).

Discussion and Conclusion: Our findings indicate that hypertension is common in PD patients OFF medication, potentially contributing to the severity of both motor and non-motor symptoms.

P106

Sex differences in body composition and resting metabolic rate in patients with Parkinson's disease

Maria Claudia Russillo[1], M. Picillo[1], V. Fetoni[2], G. Volpi[3], P. Barone[1], M.T. Pellecchia[1]

[1]Center for Neurodegenerative diseases (CEMAND), Department of Medicine, Surgery and Odontology "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]SS Neurology Fatebenefratelli - ASST Fatebenefratelli Sacco, Milan, Italy
[3]SSD Endocrine Diseases and Diabetology - ASST Fatebenefratelli Sacco, Milan, Italy

Introduction: Parkinson's disease (PD) is known to cause alterations in body composition and resting metabolic rate (RMR) [1-3].

Objective: To describe sex-related differences in body composition and RMR in PD patients.

Methods: This substudy is part of a longitudinal study conducted on PD patients requiring levodopa treatment. Patients were observed over 24 months since introduction of levodopa and underwent followup visits at 1 and 2 years after baseline. A subgroup of patients underwent evaluation of RMR (measured using the Cosmed FitMate MED® indirect calorimetry system during OFF state after 12-hour fasting) and body composition (assessed using the BiaAkern101® bioelectrical impedance analysis in supine position).

Results: 32 patients, including 24 (75%) males and 8 (25%) females, underwent body composition analysis at baseline; 30 of these patients, including 23 (76.66%) males and 7 (23.34%) females, completed follow-up 1 visit and 31, including 24 (77.42%) males and 7 (22.58%) females, also completed follow-up 2 visit. 30 patients, including 23 (76.66%) males and 7 (23.34%) females, underwent RMR measurement at baseline; 18 of these patients, including 13 (72.22%) males and 5 (27.78%) females, completed follow-up 1 visit and 29, including 22 (75.86%) males and 7 (24.14%) females completed follow-up 2 visit. At baseline, fat free mass was significantly higher in males than females ($p=0.0136$), while no statistically significant differences were found in the other parameters. At follow-up visits, except for RMR at follow-up visit 1 that resulted significantly higher in males than females ($p=0.0271$), there were no statistically significant sex-related differences.

Conclusions: The changes in body composition and metabolism that occur in PD patients are still not well understood, especially if we consider sex as a variable. The data obtained from our study provide new insights regarding the metabolism of PD patients and will need to be integrated with other clinical data for a more complete interpretation.

References:

[1] Capecci M, Petrelli M, Emanuelli B, Millevolte M, Nicolai A, Provinciali L, Ceravolo MG. Rest energy expenditure in Parkinson's disease: role of disease progression and dopaminergic therapy. Parkinsonism Relat Disord. 2013 Feb;19(2):238-41. doi: 10.1016/j.parkreldis.2012.10.016. Epub 2012 Nov 20. PMID: 23182312.
[2] Barichella M, Cereda E, Faierman SA, Piuri G, Bolliri C, Ferri V, Cassani E, Vaccarella E, Donnarumma OV, Pinelli G, Caronni S, Pusani C, Pezzoli G. Resting energy expenditure in Parkinson's disease patients under dopaminergic treatment. Nutr Neurosci. 2022 Feb;25(2):246-255. doi: 10.1080/1028415X.2020.1745427. Epub 2020 Apr 7. PMID: 32264793.
[3] Wilczyński J, Półrola P. Body composition assessment by bioelectrical impedance analysis among patients treated with L-dopa for Parkinson's disease. Medical Studies/Studia Medyczne. 2018;34(2):120-126. doi:10.5114/ms.2018.76872.

P107

GCase enzymatic activity, neuronal and glial markers in PD and DLB patients with and without GBA mutations: a multicenter deepphenotyping biological study

Alessandro Magliozzi[1,2], A. Lupini[3,4,5], C. Zizzo[6], V. Quaresima[3,4,5], C. Tolassi[3,4,5], M. Catania[3,4,5], C. Zatti[3,4,5], A. Galli[3,4,5], C. Tirloni[3,4,5], G. Anzini[1,2], S. Toro[1,2], G. Duro[6], A.B. Di Fonzo[7,8], A. Padovani[3,4,5], V. Di Lazzaro[1,2], M. Marano[1,2], A. Pilotto[3,4,5]

[1]Department of Neurology, Università Campus Bio-Medico di Roma, Rome, Italy
[2]Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy
[3]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[4]Laboratory of Digital Neurology and Biosensors, University of Brescia, Brescia, Italy
[5]Department of Continuity of Care and Frailty, Neurology Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[6]Institute for Biomedical Research and Innovation (IRIB-CNR), National Research Council of Italy, Palermo, Italy
[7]Neuroscience Section, Department of Pathophysiology and Transplantation, Dino Ferrari Center, University of Milan, Milan, Italy
[8]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy

Introduction: Glucocerebrosidase (GCase) is a lysosomal enzyme, encoded by GBA1 gene, that represent the most relevant genetic risk factor for Parkinson disease (PD) and Lewy Body Dementia (DLB)[1]. In presence of GBA1 mutations, glucocerebrosidase defective activity plays a pivotal role in the accumulation of alpha-synuclein. Molecular evidence suggests a broader role for GCase in sporadic alpha-synucleinopathies [2], yet its contribution to neurodegeneration based on in vivo data requires further investigation.

Objectives: We aimed to explore the relationship between alterations in GCase enzymatic activity, plasma biomarkers, motor and nonmotor features in a substantial cohort of PD and DLB patients, encompassing both GBA-carriers and GBA-noncarriers.

Methods: We enrolled 89 patients from two Italian movement disorders centers (Campus Biomedico of Rome and ASST of Spedali Civili di Brescia), with 49 carrying GBA mutations and 40 GBA-wild type. All the subjects underwent a comprehensive neurological examination. Motor symptoms' severity was assessed using Part III of the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS III). Non-motor symptoms' burden was evaluated using the Italian version of Non-Motor Symptoms Scale (NMSS), Montreal Cognitive Assessment (MOCA). GCase enzymatic activity was determined via dried blood spot assay in both GBA-mutated (30/49) and GBA-nonmutated cohorts (34/40), and plasma biomarkers, Glial fibrillary acid protein (GFAP) and neurofilament light chain (NfL), were measured using SIMOA technique in a subset of patients (69/89).

Results: The GBA-carriers cohort exhibited a more pronounced nonmotor symptom burden, with higher prevalence of visual hallucinations (61.2%, p=0.014) and cognitive impairment (75.5%, p=0.042) in spite of similar motor severity compared to the GBA-wildtype cohort. GCase enzymatic activity was lower in GBA-carriers (p=0.001) and similar between DLB and PD subjects. In unadjusted analysis, GCase enzymatic activity showed a significant negative correlation with GFAP and NfL (p=0.026, ρ=-0.399*; p=0.048, ρ=-0.358*) only in GBA-wildtype patients. Moreover, GCase enzymatic activity displayed a significant negative correlation with nonmotor variables, such

as NMSS total score and MOCA (p=0.001, ρ=-0.568**; p=0.001, ρ=-0.615**) only in the GBA-negative subjects.

Conclusions: Clinical profiles differed between GBA-carriers and GBA-noncarriers, particularly in nonmotor symptoms. GCase defective activity correlated significantly with clinical and biomarker variables only in the GBA-noncarriers cohort, possibly due to lower variability expected in GBA-carriers. These findings, partially corroborated by existing in vitro evidence [2], warrant further investigation for their possible new therapeutic implications.

References:

[1] Smith, Laura, and Anthony H V Schapira. “GBA Variants and Parkinson Disease: Mechanisms and Treatments.” Cells vol. 11,8 1261. 8 Apr. 2022, doi:10.3390/cells11081261.

[2] Murphy KE, Gysbers AM, Abbott SK, Tayebi N, Kim WS, Sidransky E, Cooper A, Garner B, Halliday GM. Reduced glucocerebrosidase is associated with increased α-synuclein in sporadic Parkinson's disease. Brain. 2014 Mar;137(Pt 3):834-48. doi: 10.1093/brain/awt367. Epub 2014 Jan 28. PMID: 24477431; PMCID: PMC3927701.

P108

A multifaceted approach to parkinson's disease: clinical, neurophysiological, and biological insights into levodopa-induced dyskinesias

Benedetta Angeloni[1], A.T. Cimmino[1], G. Di Lazzaro[2], R. Di Iorio[1,2], F. Bove[2], D. Di Giuda[3,4], A. Picca[5], A.R. Bentivoglio[1,2], P. Calabresi[1,2]

[1]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3]Department of Radiological Sciences and Hematology, Section of Nuclear Medicine, Università Cattolica del Sacro Cuore, Rome, Italy
[4]Nuclear Medicine Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[5]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Backgorund and objectives: The most effective treatment for PD is L-Dopa, however, as PD progresses, involuntary movements named L-Dopa-induced dyskinesia (LIDs), appear [1]. The aim of this study was to determine the clinical, neurophysiological and biological features of PD patients with LIDs.

Materials: We collected clinical data of 104 patients. All patients underwent venipuncture for serum collection; 54 patients also underwent lumbar puncture for CSF collection. Total-alpha-synuclein (t-a-syn) levels were measured in both serum and CSF, with commercially available ELISA kits. Uptake values of 123I-FP-CIT-SPECT were available for 50 patients. A subgroup of 30 patients, 15 without LIDs and 15 with LIDs, underwent neurophysiological examination with TMS.

Results and Discussion: Overall, patients had a mild parkinsonism (MDS-UPDRS III score 22 ± 13) with a mean disease duration of 8 ± 5 years and oral LEDD intake of 577 ± 422mg. LIDs were observed in 42 patients (Dysk), while 62 patients were defined as non-dyskinetic (Non Dysk). Patients with LIDs had a longer disease duration, higher LEDD intake and worse MDS-UPDRS III scores.
In our cohort, patients with LIDs showed a higher degree of putaminal dopaminergic denervation at diagnosis, measured with semiquantitative analysis of 123I-FP-CIT-SPECT uptake values. This association was significant also when corrected with age, LEDD and disease duration ($p = 0.032$) in a logistic regression model. In our study, no differences were found in t-α-syn levels in patients with and without LIDs in both serum and CSF. At the neurophysiological examination with TMS, a significant depotentiation in the group of Non Dysk patients and a not significant depotentiation in the group of Dysk patients was found. Furthermore, we found a significant negative correlation between the amplitude of depotentiation and the score of UDysRS part III in Dysk patients ($r = -0.67$, $p = 0.006$), i.e., the less depotentiation the more severe the LIDs.

Conclusion: From our data emerges that nigrostriatal DA denervation remains the major determinant in the pathogenesis of LIDs [2], while duration and dosage of L-Dopa treatment represent secondary factors, independently from other modifiable and non-modifiable risk factors. Conversely, t-a-syn levels in serum and CSF did not show any relationship with the presence of LIDs. Finally, the lack of homeostatic plasticity at both striatal and cortical regions is a constant pathophysiological feature of LIDs [3].

References:

[1] Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015;30(12):1591- 1601. doi:10.1002/mds.26424.

[2] Eusebi P, Romoli M, Paoletti FP, Tambasco N, Calabresi P, Parnetti L. Risk factors of levodopa-induced dyskinesia in Parkinson's disease: results from the PPMI cohort. NPJ Parkinsons Dis. 2018; 4:33. Published 2018 Nov 16. doi:10.1038/s41531-018-0069-x.
[3] Vucic, S., K. H. Stanley Chen, M. C. Kiernan, M. Hallett, D. H. Benninger, V. Di Lazzaro, P. M. Rossini, A. Benussi, A. Berardelli, A. Currà, S. M. Krieg, J. P. Lefaucheur, Y. Long Lo, R. A. Macdonell, M. Massimini, M. Rosanova, T. Picht, C. M. Stinear, W. Paulus, Y. Ugawa, U. Ziemann and R. Chen (2023). "Clinical diagnostic utility of transcranial magnetic stimulation in neurological disorders. Updated report of an IFCN committee." Clin Neurophysiol 150: 131-175.

P109

Effect of aging on biomarkers and clinical profile in Parkinson's disease

Giulia Di Lazzaro[1], M. Petracca[1], T. Schirinzi[2], G. Bellomo[3], F. Paolini Paoletti[3], A. Picca[1,4], L. Parnetti[3], N.B. Mercuri[2], A.R. Bentivoglio[1,5], P. Calabresi[1,5]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]Università degli Studi di Roma Tor Vergata, Rome, Italy
[3]Università degli Studi di Perugia, Perugia, Italy
[4]LUM, Casamassima, Italy
[5]Università Cattolica del Sacro Cuore, Rome, Italy

Introduction: Parkinson's disease (PD) is a common neurodegenerative disease of the elderly [1]. However, PD is increasingly diagnosed in younger patients. Clinical evidence indicates that PD patients have different progression rates and disease characteristics [2, 3] the younger being less cognitively affected and experiencing more motor fluctuations.

Objective: To explore the different pathophysiology underlying PD in patients of different age, in an early-middle phase of the disease, independently from disease duration through CSF biomarkers.

Methods: Patients with clinically established diagnosis of PD were enrolled at Policlinico Gemelli, University of Perugia and Policlinico Tor Vergata and underwent clinical evaluation through MDS-UPDRS, NMSS, MoCA. CSF inflammatory (YKL-409, TREM-2) and neurodegeneration (Abeta42 and 40, tau, p-tau, sAPP-a and -b, NfL, Ng) biomarkers were analysed.

Results: 95 patients were recruited, 27 younger than 60years-old, and 68 older. Age and age at onset strongly correlate with neurofilament CSF levels, both light and heavy chain, with YKL-40 and Alzheimer's related pathology biomarkers, in a stronger manner with tau species. Younger and older patients showed different biomarkers profile. In particular, younger patients showed significantly lower levels of inflammatory molecules (YKL-40 and sTREM2), of degeneration biomarkers (neurogranin, tau species, neurofilament light and heavy chains) and sAPP-beta, independently from disease duration. From the clinical point of view, younger patients had better scores at UPDRS parts I, II and III and MoCA.

Conclusions: Our data support the hypothesis that PD has different features in younger and older patients, with a different pathology underlying the observed clinical differences. This could reflect a more preponderant loss of integrity of neuronal circuits independently from the nigrostriatal degeneration, as the higher prevalence of amyloid pathology and higher burden of neurodegeneration could be related to worse cognitive performances in older patients and lower dyskinesia, for which an aberrant plasticity is the major recognized pathophysiological mechanism.

References:

[1] A. Ascherio and M. A. Schwarzschild, "The epidemiology of Parkinson ' s disease: risk factors and prevention," Lancet Neurol., vol. 15, no. 12, pp. 1257–1272, 2016, doi: 10.1016/S1474-4422(16)30230-7.
[2] L. W. Ferguson, A. H. Rajput, and A. Rajput, "Early-onset vs. Late-onset Parkinson ' s disease: A Clinical-pathological Study," no. May, pp. 113–119, 2019, doi: 10.1017/cjn.2015.244.
[3] A. W. Willis, M. Schootman, N. Kung, and B. A. Racette, "Epidemiology and neuropsychiatric manifestations of Young Onset Parkinson's Disease in the United States," Park. Relat. Disord. , vol. 19, no. 2, pp. 202–206, 2013, doi: 10.1016/j.parkreldis.2012.09.014.

P110

Advanced perspectives for the diagnosis of Parkinson's and Alzheimer's disease through machine learning techniques

Antonio Malvaso[1,2,4], S. Panarese[2,4,5], M. Catalano[2,4,6], M. Migliore[5,7], D. Caligiore[2,3,4]

[1]IRCCS Mondino Foundation, Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]Computational and Translational Neuroscience Laboratory, Institute of Cognitive Sciences and Technologies, National Research Council (CTNLab-ISTC-CNR), Rome, Italy
[3]AI2Life s.r.l., Innovative Start-Up, ISTC-CNR Spin-Off, Rome, Italy
[4]Advanced School in Artificial Intelligence (AS-AI), Rome, Italy
[5]Dipartimento di Biologia e Biotecnologie, Sapienza Università di Roma, Rome, Italy
[6]Dipartimento di Biologia, Università degli Studi di Roma Tor Vergata Rome, Italy
[7]Institute of Biophysics, National Research Council, Palermo, Italy

Introduction and Objective: A new paradigm called Neurodegenerative Elderly Syndrome proposed by Caligiore et al.[1], conceives Parkinson's disease (PD) and Alzheimer's disease (AD) as different manifestations of a single disease at very early stages. Accordingly, in this study we aim to observe and compare PDs and ADs features importance at baseline, 12-months and 24-months of follow-up, to predict disease conversion and differentiate or classify both pathologies.

Methods: We analyzed 1378 Prodromal-PDs, 1219 PDs, 714 MCIs, 458 ADs and 1202 Healthy Controls from ADNI and PPMI databases. Machine Learning (ML) approaches like Random-Forest Classifier, Features Importance Analysis and K-means Clustering Analysis were used. A combination of six groups of features was selected: demographic, cognitive/neuropsychological, clinical, genetic, neuroimaging and neuropathological.

Results: Classification accuracy of 96%/86% and precision of 92%/87% were obtained for PDs/ADs respectively. At baseline and 24-months, age and gender showed higher importance in predicting PDs classification ($p<0.05$). At baseline, MMSE, MOCA, Clock Drawing Test, Digit Span Backward, and Boston Naming Test are more predictive in PDs classification than in ADs ($p<0.05$). Notably, F-Fluency test has a higher importance in predicting PDs classification than in ADs ($p<0.05$). Clinically, postural instability and right/left hand tremor are important only in predicting PDs categorization at baseline. Interestingly, at 12-months of follow-up, $APOE^{\varepsilon 3\text{-}\varepsilon 4/\varepsilon 4}$ demonstrated higher importance in PDs classification than in ADs.

Conclusions: To our knowledge, this is the first attempt to analyze and compare different AD and PD variables at baseline and during disease progression, based on non-invasively ML approaches. A possible practical implication for clinicians could be having predictive ML models of neurodegeneration curves to consult when PD and AD pathologies are clinically indistinguishable or very similar. Further studies are needed to validate our findings by testing and refining our predictive models on different multi and monocentric cohorts of patients.

References:

[1] Caligiore D, Giocondo F, Silvetti M. The Neurodegenerative Elderly Syndrome (NES) hypothesis: Alzheimer and Parkinson are two faces of the same disease. IBRO Neurosci Rep. 2022 Sep 26;13:330-343. doi: 10.1016/j.ibneur.2022.09.007. PMID: 36247524; PMCID: PMC9554826.

P111

Freezing of gait detection and prediction: the effect of sensor type, position, activities, datasets, and machine learning model

Ruggero Bacchin[1,2], L. Borzì[3], F. Demrozi[4], G. Fazzina[5,6], G. Balestro[2], D. Rinaldi[7], C. Turetta[8], L. Sigcha[9], A. Picelli[2], G. Pravadelli[8], G. Olmo[3], S. Tamburin[2], L. Lopiano[5,6], C.A. Artusi[5,6]

[1]Neurology Unit, S. Chiara Hospital, Pisa, Italy
[2]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona,Italy
[3]Department of Control and Computer Engineering, Politecnico di Torino, Turin, Italy
[4]Department of Electrical Engineering and Computer Science, University of Stavanger, Stavanger, Norway
[5]Neurology 2 Unit, A.O.U. Città Della Salute e della Scienza di Torino, Turin, Italy
[6]Department of Neuroscience, University of Turin, Turin, Italy
[7]Department of Neuroscience, Mental Health and Sense Organs, Sapienza Università di Roma, Roma, Italy
[8]Department of Engineering for Innovation Medicine, University of Verona, Verona, Italy
[9]Department of Physical Education and Sports Science (PESS), Health Research Institute (HRI), & Data-Driven Computer Engineering (D2iCE) Group, University of Limerick, Limerick, Ireland

Introduction: Freezing of gait (FoG) is a complex, frequent, and disabling motor symptom of Parkinson's disease (PD). Wearable technology has the potential to improve FoG assessment by providing objective, quantitative, and continuous monitoring.

Objectives: The study aims to develop a robust FoG detection algorithm that can be embedded in a simple and unobtrusive wearable sensor system and can lead to a reliable home assessment.

Methods: Twenty-two subjects with PD and FoG were enrolled, equipped with four inertial modules on the ankles, back, and wrist, and asked to perform different tasks. Feature-driven and data-driven machine learning approaches were implemented, optimized, and evaluated. Further testing was conducted on two external datasets including a total of 545 FoG episodes.

Results: A single sensor on the ankle, with an adequate algorithm of data analysis based on machine learning, can provide a non-invasive approach for accurate FoG monitoring. The model proved robust on the independent datasets, with 88–95% FoG episodes correctly detected. Moreover, 25–36% episodes were predicted 1–2s before FoG occurrence, 9–25% were timely detected, and 26–56% were detected with a delay of 1–2s. Interestingly, while FoG can be easily discriminated from walking, static positions, and postural transitions, turning represents a major challenge. The collected dataset also includes data from different sensors at different body positions.

Conclusions: The rigorous methodology in labelling process and the high-level of details on FOG episodes and patient's activities which have been collected with the present study provide a significant contribution to research on automatic FoG detection and characterization. Althought the high number of false alarms still represents the main limitation, data from a single sensor at the ankle is accurate for generation of FoG recognition/prediction algorithms.

P112

Emotional atypical arousal rating for unpleasant stimuli in patients with Parkinson disease

Stefano Toro[1], F. Proietti[1], A. Magliozzi[1], G. Anzini[1], S. Migliore[2], G. Curcio[2], M. Marano[1]

[1]Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine, Fondazione Policlinico Campus Bio-Medico, Rome, Italy
[2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, Italy

Introduction: Parkinson's disease involves progressive and chronic degeneration of the nigrostriatal and mesocorticolimbic dopamine systems. In addition to motor symptoms, mild deficits in emotional processing have also been described [1,2,5].

Objectives: To observe differences between PD patients and Healthy Control (HC), on the emotional behavior rating by affective visual stimuli.

Methods: We enrolled 22 patients with diagnosis of idiopathic PD and 22 HC matched by age, gender and education. After clinical assessment, they were asked to evaluate arousal and valence of affective visual stimuli by the International Affective Picture System (IAPS) [3] and response time was detected.

Results: One-way ANOVA revealed a significant Group effect ($F1.42 = 4.116$; $p = 0.049$) indicating a higher valence rating (RESP_VAL) in PD (6.37 ± 0.87) respect to HC (5.8 ± 0.98). Also, a significant Group type of images effect on "RESP_VAL" variable ($F2.44 = 5.840$; $p<0.006$) was emerged evidencing, in the post hoc comparisons, higher valence rating for PD patients respect to HC in unpleasant images (7.32 ± 0.88 vs 5.43 ± 2.06. $p<0.001$). Finally PD patients showed higher arousal response for negative/unpleasant pictures, compared to control. No other significant behavioral effect was shown between groups.

Conclusions: Our data finds conflicting results in literature, even if only few studies investigated the emotional processing of visual information, and made it through the adoption of neurophysiological biomarkers [4,5]. Given the importance of emotional processing for the development and maintenance of close interpersonal relationships, and for coping specific medical situations it is crucial to direct patients towards therapeutic intervention focused on the recognition and processing of emotions [6,7,8].
Differences between groups in valence rating on type of image. PD patients in blue, HC in orange; RESP_VAL, valence; RESP_AR, arousal; *p<0.05, **p<0.01.

References:

[1] Argaud S, Vérin M, Sauleau P, Grandjean D (2018) Facial emotion recognition in Parkinson's disease: A review and new hypotheses. Mov Disord 33:554–567.
[2] Péron J, Dondaine T, Le Jeune F, Grandjean D, Vérin M (2012) Emotional processing in Parkinson's disease: a systematic review. Mov Disord 27:186–199.
[3] Lang, P.J., Bradley, M.M., Cuthbert, B.N., 1997. International Affective Picture System (IAPS): Technical manual and Affective Ratings. NIMH Center for the Study of Emotion and Attention, 39–58.
[4] Bowers D, Miller K, Mikos A, Kirsch-Darrow L, Springer U, Fernandez H, Foote K, Okun M (2006) Startling facts about emotion in Parkinson's disease: blunted reactivity to aversive stimuli. Brain 129:3356–3365.
[5] Miller KM, Okun MS, Marsiske M, Fennell EB, Bowers D (2009) Startle reflex hyporeactivity in Parkinson's disease: an emotionspecific or arousal-modulated deficit? Neuropsychologia 47:1917– 1927.

[6] Nielen MM, Heslenfeld DJ, Heinen K, Van Strien JW, Witter MP, Jonker C, Veltman DJ. Distinct brain systems underlie the processing of valence and arousal of affective pictures. Brain Cogn. 2009 Dec;71(3):387-96. doi: 10.1016/j.bandc.2009.05.007. Epub 2009 Aug 8. PMID: 19665830.
[7] Li R, Zou T, Wang X, Wang H, Hu X, Xie F, Meng L, Chen H. Basal ganglia atrophy-associated causal structural network degeneration in Parkinson's disease. Hum Brain Mapp. 2022 Feb 15;43(3):1145-1156. doi: 10.1002/hbm.25715. Epub 2021 Nov 18. PMID: 34792836; PMCID: PMC8764481.
[8] Bodden ME, Dodel R, Kalbe E. Theory of mind in Parkinson's disease and related basal ganglia disorders: a systematic review. Mov Disord. 2010 Jan 15;25(1):13-27. doi: 10.1002/mds.22818. PMID: 19908307.

P113

The use of opicapone for the treatment of motor fluctuations in Parkinson's disease: real-life experience of two Italian Movement Disorders Centers

Marco Liccari[1], R. Bacchin[2], M. Catalan[1], M.C. Malaguti[2], L. Antonutti[1], B. Giometto[2], P. Manganotti[1]

[1]Clinical Unit of Neurology, Department of Medicine, Surgery and Health Sciences, University Hospital of Trieste ASUGI, University of Trieste, Trieste, Italy
[2]Clinical Unit of Neurology, Department of Emergency, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy

Introduction: Opicapone (OPC) is commonly used as add-on to LDopa (LD) therapy for management of motor fluctuations (MFs) in idiopathic Parkinson's Disease (iPD). Its benefit on PD population has been established by different clinical trials, and a recent post-hoc analysis has demonstrated its better tolerability when used early in iPD.

Objectives: Data are missing about the use of OPC on Italian population of iPD patients, so the aim of this paper is to report the real-life experience of the two Centers of Trieste and Trento.

Methods: Retrospective data have been gathered of Italian iPD patients followed for at least two years after OPC introduction for MFs.

Results: 152 patients have been enrolled, 35% reported adverse events (AEs) on the two-year follow-up. 27% discontinued OPC because of a severe AE, which in 76% of cases was a dopaminerelated AE. Incidences of any AE were lower in "earlier" subgroup of patients accordingly to disease course and LD treatment pathway in the majority of comparisons. Univariate analysis recognized as clinical predictors of treatment discontinuation because of any AE were age, disease duration, MFs duration, Hoehn-Yahr stage, past history of hallucinations or addictive behaviour, mild cognitive complaint, falls, and for treatment discontinuation due to dopamine-related AE were age, MFs duration, Hoehn & Yahr stage, past history of addictive behaviour, MCI, falls, and use of therapy combinations different from LD plus DA and iMAO. Predictors of OPC withdrawn accordingly to multivariate were MFs duration and Hoehn-Yahr.

Conclusions: Real life data on Italian population of iPD patients confirm good tolerability and safety profiles of OPC for the treatment of MFs, moreover when introduced early according to disease course and LD treatment pathway. MFs duration and Hoehn-Yahr stage have been shown to be important predictors of OPC therapy maintenance over a follow-up of at least 2 years.

P114

Deep brain stimulation does not worsen cognitive decline in GBA-Parkinson disease patients. A longitudinal study of the Italian PARKNET cohort

Micol Avenali[1,2], C.A. Artusi[3], R. Cilia[4], G. Giannini[5,6], G. Cuconato[7], C. Pasquini[2], A. Albanese[8], N. Golfrè Andreasi[4], A. Antonini[9,10], A.R. Bentivoglio[11,12], F. Bove[12], M. Bozzali[3], G. Calandra Buonaura[5,6], V. Carelli[5,6], F. Cavallieri[13], A. Cocco[8], F. Cogiamanian[14], F. Colucci[4], P. Cortelli[5,6], A.B. Di Fonzo[14], V. D'Onofrio[9,10], R. Eleopra[5,6], A.E. Elia[5,6], V. Fioravanti[13], A. Guerra[9,10], C. Ledda[3], M. Liccari[15], C. Longo[16], L. Lopiano[3], M.C. Malaguti[16], F. Mameli[14], R. Minardi[6], E. Monfrini[14], C. Pacchetti[2], C. Piano[11,12], M.G. Rizzone[3], L.M. Romito[5,6], L. Sambati[6], F. Spagnolo[17], C. Tassorelli[1,2], F. Valentino[2], F. Valzania[13], R. Zangaglia[2], M. Zibetti[3], the PARKNET Study Group, E.M. Valente[7,2]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Torino, Italy
[4]SC Neurologia 1, Fondazione IRCCS Istituto Neurologico C. Besta, Milano, Italy
[5]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[6]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[7]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[8]Department of Neurology, IRCCS Humanitas Research Hospital, Milan, Italy
[9]Parkinson and Movement Disorder Unit, Department of Neuroscience, University of Padua, Padua, Italy
[10]Padova Neuroscience Center, University of Padua, Padua, Italy
[11]Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy
[12]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[13]Azienda USL IRCCS Reggio Emilia, Reggio Emilia, Italy
[14]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[15]Department of Medical, Surgical and Health Sciences, Cattinara University Hospital, ASUGI, University of Trieste, Trieste, Italy
[16]Department of Neurology, Santa Chiara Hospital, Trento, Italy
[17]Department of Neurology, A. Perrino Hospital, Brindisi, Italy

Introduction: GBA mutations are known to increase risk of Parkinson disease (PD) and to influence mainly its non-motor outcome. Deep brain stimulation (DBS) is a good therapeutic option for advanced PD, with major improvement of motor symptoms also in GBA-PD patients [1]. However, a recent study suggested that DBS could accelerate cognitive decline in GBA carriers [2,3], raising concerns on its indication.

Objectives: To elucidate long-term impact of DBS on motor and nonmotor features in GBA-PD.

Methods: From the multicentric Italian PD PARKNET cohort, we selected 563 patients: i) 405 DBS-nonGBA-PD; ii) 94 DBS-GBA-PD; iii) 64 nonDBS-GBA-PD (patients who fulfilled CAPSIT-PD criteria for DBS but eventually were not operated). Detailed clinical info were retrospectively collected at baseline (pre-DBS / time of CAPSIT-PD assessment) and, whenever possible, after 1, 3 and 5 years.

Results: At baseline, DBS-GBA-PD patients were younger and had earlier age at onset than other groups. Besides this, the three cohorts were fully comparable in terms of motor, cognitive and other nonmotor symptoms, with only LEDD being higher in the two groups who then underwent DBS. At

longitudinal assessment, both DBS groups showed sustained motor improvement with fluctuation control and significant LEDD decrease, a benefit which was absent in the nonDBSGBA-PD cohort. Noteworthy, a more marked deterioration of cognitive scores was evident in both GBA groups compared to nonGBA-PD, and regardless of DBS. Cognitive worsening in GBA carriers was already significant at 1-year and became more evident at longer follow-ups, with no difference between DBS and non-DBS groups. After 5 years, 28% DBS-GBA-PD and 43% nonDBS-GBA-PD had dementia, compared to 11% DBS-nonGBA-PD.

Conclusions: In the PARKNET GBA-PD cohort, DBS does not seem to impact on the rate of cognitive decline, while significantly improving the motor phenotype. If confirmed, this finding will have major implications to address therapeutic choices in GBA-PD.

References:

[1] Avenali M, Zangaglia R, Cuconato G, Palmieri I, Albanese A, Artusi CA, Bozzali M, Calandra-Buonaura G, Cavallieri F, Cilia R, Cocco A, Cogiamanian F, Colucci F, Cortelli P, Di Fonzo A, Eleopra R, Giannini G, Imarisio A, Imbalzano G, Ledda C, Lopiano L, Malaguti MC, Mameli F, Minardi R, Mitrotti P, Monfrini E, Spagnolo F, Tassorelli C, Valentino F, Valzania F, Pacchetti C, Valente EM; PARKNET Study Group. Are patients with GBA-Parkinson disease good candidates for deep brain stimulation? A longitudinal multicentric study on a large Italian cohort. J Neurol Neurosurg Psychiatry. 2023 Oct 25:jnnp-2023- 332387. doi: 10.1136/jnnp-2023-332387.

[2] Pal GD, Corcos DM, Metman LV, Israel Z, Bergman H, Arkadir D. Cognitive Effects of Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease with GBA1 Pathogenic Variants. Mov Disord. 2023 Dec;38(12):2155-2162. doi: 10.1002/mds.29647.

[3] Pal G, Mangone G, Hill EJ, Ouyang B, Liu Y, Lythe V, Ehrlich D, Saunders-Pullman R, Shanker V, Bressman S, Alcalay RN, Garcia P, Marder KS, Aasly J, Mouradian MM, Link S, Rosenbaum M, Anderson S, Bernard B, Wilson R, Stebbins G, Nichols WC, Welter ML, Sani S, Afshari M, Verhagen L, de Bie RMA, Foltynie T, Hall D, Corvol JC, Goetz CG. Parkinson Disease and Subthalamic Nucleus Deep Brain Stimulation: Cognitive Effects in GBA Mutation Carriers. Ann Neurol. 2022 Mar;91(3):424-435. doi: 10.1002/ana.26302.

P115

High Intensity Focused Ultrasound (HIFU) treatment: evaluation of long-term cognitive outcomes

Gennaro Saporito[1], P. Sucapane[2], F. Bruno[1,4], A. Catalucci[4], T. Russo[2], C. Marini[2,3], D. Cerone[2], E. Di Cesare[1,4], A. Splendiani[1,4], R. Totaro[2], F. Pistoia[1,2]

[1]Department of Biotechnology and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[2]Department of Neurology, S. Salvatore Hospital, L'Aquila, Italy
[3]Department of Life, Health and Environmental Science, University of L'Aquila, L'Aquila, Italy
[4]Department of Neuroradiology San Salvatore Hospital, L'Aquila, Italy

Introduction: Magnetic resonance imaging-guided focused ultrasound (MRgFUS) is a recent thermal ablation treatment for Essential Tremor (ET) and Parkinson Disease (PD) related tremor. Data about cognitive changes are controversial.

Objectives: Aim of this study was to confirm the long-term cognitive safety following the MRgFUS treatment.

Methods: In this prospective study, patients consecutively undergoing MRgFUS were assessed through a comprehensive neuropsychological and behavioral battery before, six months and 1 year following the treatment. Data were analyzed with paired T-Test or Wilcoxon signedrank tests and verified with Bonferroni's correction. A p value <0.003 was considered statistically significant.

Results: Fifty patients (male 76%; mean age ± SD 69.0 ± 8.56; mean disease duration ± SD 12.13 ± 12.59) with ET (n=28) and PD (n=22) were included. A significant improvement was detected at six months after the treatment in anxiety feeling (HAM-A 5.66 ± 5.02 Vs 2.70 ± 4.09, p < 0.001), memory (RAVLT: Immediately re-enactment 31.76 ± 7.60 Vs 35.51 ± 8.38; p = < 0.001; RAVLT: Deferred re-enactment 5.57 ± 2.75 Vs 7.03 ± 3.85; p = < 0.001) frontal functions (14.24±3.04 Vs 15.24±2.38; p= 0.003), and in the quality of life [QUEST (35.00±12.08 Vs 8, 93±9.86, p= < 0.001), PDQ-8 (7.86±3.10 vs.3.10±1.52, p=<0.001). A similar improvement in behavioral assessment (HAM-A 5.66±5.02 Vs 2.69±3.76, p=<0.001; BDI-II 3.74±3.80 Vs 1.80±2.78, p= 0.001), memory domains (RAVLT:Immediately re-enactment 31.76±7.60 Vs 35.38±7.72, p= 0.001; RAVLT: Deferred re-enactment 5.57±2 .75 Vs 6.41±2.48), frontal functions (14.24±3.04 Vs 15.16±2.74) and in the quality of life [QUEST 35.00±12.08 Vs 9.03±10 .64, p=<0.001; PDQ-8 7.86±3.10 vs. 3.09±2.29, p= <0.001). was also detected 1 year following the procedure.

Conclusions: Our study takes a step toward in endorsing the long-term neuropsychological safety of unilateral MRgFUS and encourage the implementation of staged bilateral treatments.

P116

Impact of subthalamic nucleus-deep brain stimulation on cognitive and behavioural profile of patients with Parkinson's disease: a case - control study

Valentina D'Onofrio[1], R. Biundo[2,3,4], L. Weis[2,5], M. Garon[1], E. Fiorenzato[2], D. Ciprietti[2], M.L. Nasi[2], A. Landi[6], A. Antonini[1,2,4], A. Guerra[4]

[1]Padova Neuroscience Center (PNC), University of Padova, Padova, Italy
[2]Parkinson's Disease and Movement Disorders Unit, Department of Neuroscience, Centre for Rare Neurological Diseases (ERN-RND), University of Padova, Padova, Italy
[3]Department of General Psychology, University of Padua, Padua, Italy
[4]Department of Neuroscience, Center for Neurodegenerative Disease Research (CESNE), University of Padova, Padova, Italy
[5]IRCCS, San Camillo Hospital, Venice, Italy
[6]Academic Neurosurgery, Department of Neurosciences, University of Padova, Padova, Italy

Introduction: Subthalamic Nucleus-Deep Brain Stimulation (STN-DBS) is an established therapy for patients with advanced Parkinson's Disease (APD). Despite the positive outcomes in improving motor symptoms, the effects on cognitive and behavioural functions are still debated [1,2].

Objective: In this single-centre study, we used a case-control design to verify the impact of STN-DBS on multiple disease axes.

Methods: Sixty-eight APD patients who satisfied the clinical criteria and had no major contraindication for undergoing DBS were enrolled. Patients were evaluated with extensive neuropsychological testing, including standardized scales for functional impairment and quality of life (QoL axis), attention, executive, memory, language and visuospatial abilities (cognitive axis), and depression, impulsivity, apathy and anxiety (behavioural axis). Motor symptoms were evaluated using the MDS-UPDRS-III and H&Y scales (motor axis). After initial screening, 35 patients underwent DBS (APD-DBS, case group), while 33 did not (APD-BMT, control group). Clinical neuropsychological evaluations were performed before (T0) and 1-2 years after surgery (T1) (or at comparable timepoints in APD-BMT patients). Possible differences between groups in clinical demographic characteristics at T0 and in the different axes over time (T1-T0 changes) were tested using non-parametric statistics.

Results: Clinical-demographic characteristics were similar between groups at T0. When analysing changes in clinical scales over time, APD-DBS patients showed a significant amelioration in the motor and QoL axes compared to APD-BMT patients. Importantly, there was no major difference in changes in the scales reflecting cognitive (all domains) and behavioural axes between groups, except for a slight improvement in the state anxiety (STAI-Y1 scale) in APD-DBS than APD-BMT patients.

Conclusions: Our results confirmed the efficacy of STN-DBS in improving motor symptoms in APD. In line with a few previous observations, we provide novel data demonstrating that STN-DBS does not induce detrimental effects on cognitive and behavioural patients' profiles compared to those occurring in APD per se [3].

References:

[1] Rački V, Hero M, Rožmarić G, Papić E, Raguž M, Chudy D, Vuletić V (2022) Cognitive Impact of Deep Brain Stimulation in Parkinson's Disease Patients: A Systematic Review. Front Hum Neurosci 16:867055.

[2] Williams AE, Arzola GM, Strutt AM, Simpson R, Jankovic J, York MK (2011) Cognitive outcome and reliable change indices two years following bilateral subthalamic nucleus deep brain stimulation. Parkinsonism & Related Disorders 17:321–327.
[3] Cernera S, Okun MS, Gunduz A (2019) A Review of Cognitive Outcomes Across Movement Disorder Patients Undergoing Deep Brain Stimulation. Front Neurol 10:419.

P117

Potential usefulness of fast beta-band survey for deep brain stimulation programming in Parkinson's disease: a pilot study

Valentina D'Onofrio[1], D. Ciprietti[2], C. Fogliano[2], C. Porcaro[1,2,3,4], A. Landi[5], A. Antonini[1,6,7], A. Guerra[7]

[1]Padova Neuroscience Center (PNC), University of Padova, Padova, Italy
[2]Department of Neuroscience, University of Padova, Padova, Italy
[3]Institute of Cognitive Sciences and Technologies-National Research Council, Rome, Italy
[4]Centre for Human Brain Health and School of Psychology, University of Birmingham, Birmingham, UK
[5]Academic Neurosurgery, Department of Neuroscience, University of Padova, Padova, Italy
[6]Parkinson's Disease and Movement Disorders Unit, Department of Neuroscience, Centre for Rare Neurological Diseases (ERN-RND), University of Padova, Padova, Italy
[7]Center for Neurodegenerative Disease Research (CESNE), Department of Neuroscience, University of Padova, Padova, Italy

Introduction: With the improvement of Deep Brain Stimulation (DBS) technology and new possibilities for stimulation programming, the need for biomarkers reflecting the optimal stimulation site is emerging [1]. Sensing-enabled DBS systems allow the recording of local field potentials (LFPs), offering the opportunity to assess pathological activities such as enhanced beta oscillations (13-30 Hz) in advanced Parkinson's disease (APD) [2]. We aimed to evaluate ifshort LFP recordings can reliably identify the best stimulating contact clinically assessed with monopolar review (MR).

Methods: Thirteen APD patients treated with the sensing-enabled DBS device and quadripolar segmented leads targeting the subthalamic nucleus (STN – seven patients) or globus pallidus internus (GPi – six patients) were enrolled. Bipolar LFP recordings from each hemisphere (26 nuclei) were obtained from rings and segments using the Brainsense Survey at 3-4 weeks (T0) and 6-12 months (T1) after surgery [2]. LFP power spectra were computed, and beta peaks were identified and ordered based on their power. For ring recordings, the optimal contact was selected by comparing peaks in 0-2 and 1-3 levels, while for segments, intra-level 1 and 2 recordings were considered.

Results: Beta peaks were identified in 21/26 (80,7%) of ring recordings and 23/26 (88,4%) segment recordings. The frequency of peaks with the highest power was stable between T0 and T1 in 24/26 (94,4%) cases. In 21/26 (80,7%) recordings, segments showing the highest beta peak corresponded to the levels chosen for chronic stimulation according to MR (blindly performed with respect to LFP results at T0). There were no differences between STN-DBS and GPi- DBS patients.

Conclusions: We here report a single-centre experience with the new sensing-enabled DBS system for APD. Our results show that contacts with the highest beta peak frequently correspond to those selected clinically with MR. Our observations support the hypothesis that the Brainsense Survey could facilitate selecting the optimal stimulation site and reduce programming times.

References:

[1] Swinnen MJ Stam AWG, Buijink MGJ, De Neeling PR, Schuurman RMA, De Bie M, Beudel M. Employing LFP recording to optimize stimulation location and amplitude in chronic DBS for Parkinson's disease: A proof-of-concept pilot study; Deep Brain Stimulation. 2 (2023) 1–5.
[2] Jimenez-Shahed J. Device profile of the percept PC deep brain stimulation system for the treatment of Parkinson's disease and related disorders; Expert Review of Medical Devices. 18 (2021) 319–332.

P118

Technical and clinical aspects of closed-loop deep brain stimulation: results of a Delphi consensus on current feasibility and future challenges

Matteo Guidetti[1], T. Bocci[1,2], M. De Pedro Del Álamo[3], G. Deuschl[4], A. Fasano[5,6,7,8], R.M. Fernandez[3,9], C. Gasca-Salas[3,9], C. Hamani[10,11,12], J.K. Krauss[13], A. Kühn[14,15,16,17,18], P. Limousin[19], S. Little[20], A.M. Lozano[5,6,21], N.V. Maiorana[1], M. Okun[22,23], S. Oliveri[1,2], J. Ostrem[20], E. Scelzo[2], A. Schnitzler[24,25], P. Starr[26,27,28], Y. Temel[29], L. Timmermann[30], G. Tinkhauser[31], V. Visser-Vandewalle[32], J. Volkmann[33], A. Priori[1,2]

[1]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Clinical Neurology Unit, "Azienda Socio-Sanitaria Territoriale Santi Paolo e Carlo", Department of Health Sciences, University of Milan, Milan, Italy
[3]Centro Integral de Neurociencias Abarca Campal, Hospital Universitario HM Puerta del Sur, HM Hospitales, Madrid, Spain
[4]Department of Neurology, University Hospital Schleswig-Holstein, Campus Kiel and Christian Albrechts-University of Kiel, Kiel, Germany
[5]Krembil Research Institute, University Health Network, Toronto, ON, Canada
[6]CRANIA Center for Advancing Neurotechnological Innovation to Application, University of Toronto, ON, Canada
[7]KITE, University Health Network, Toronto, ON, Canada
[8]Division of Neurology, Edmond J. Safra Program in Parkinson's Disease Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada
[9]Instituto Carlos III, CIBERNED, Madrid, Spain
[10]Sunnybrook Health Sciences Centre, Toronto, Canada
[11]Harquail Centre for Neuromodulation, Toronto, Canada
[12]Department of Surgery, University of Toronto, Toronto, Canada
[13]Department of Neurosurgery, Medizinische Hochschule Hannover, Hannover, Germany
[14]Department of Neurology, Charité-Universitätsmedizin Berlin, Berlin, Germany
[15]Bernstein Center for Computational Neuroscience, Humboldt-Universität, Berlin, Germany
[16]NeuroCure, Exzellenzcluster, Charité-Universitätsmedizin Berlin, Berlin, Germany
[17]DZNE, German Center for Neurodegenerative Diseases, Berlin, Germany
[18]Berlin School of Mind and Brain, Humboldt-Universität zu Berlin, Berlin, Germany
[19]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology and the National Hospital for Neurology and Neurosurgery, London, UK
[20]Movement Disorders and Neuromodulation Centre, University of California San Francisco, San Francisco, CA, USA
[21]Division of Neurosurgery, Department of Surgery, University of Toronto, Toronto, ON, Canada
[22]Department of Neurology, Norman Fixel Institute for Neurological Diseases, University of Florida, Gainesville, USA
[23]Department of Neurosurgery, Norman Fixel Institute for Neurological Diseases, University of Florida, Gainesville, USA
[24]Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
[25]Department of Neurology, Center for Movement Disorders and Neuromodulation, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
[26]UCSF Department of Neurological Surgery, University of California San Francisco, San Francisco, CA, USA

[27]UCSF Weill Institute for Neurosciences, University of California San Francisco, San Francisco, CA, USA
[28]UCSF Department of Physiology, University of California San Francisco, San Francisco, CA, USA
[29]Department of Neurosurgery, Maastricht University Medical Center, Maastricht, Netherlands
[30]Department of Neurology, University Hospital of Marburg, Marburg, Germany
[31]Department of Neurology, Bern University Hospital and University of Bern, Bern, Switzerland
[32]Department of Stereotactic and Functional Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany
[33]Department of Neurology, University Hospital Würzburg, Würzburg, Germany

Introduction: Conventional DBS (cDBS) delivers continuous electrical stimulation to targeted brain structures regardless the actual functional state of the patient. Thus, cDBS may cause stimulation-induced adverse effects, such as speech impairments and increased risk of falls [1]. Closed-loop DBS (CL-DBS) is a novel technology where the stimulation is contingency-based, i.e., decided according to feedback signals (e.g., brain signals) that correlate to the actual patient's clinical state [2]. Despite the encouraging results, CL-DBS for movement disorders is still not of clinical use.

Objectives: (I) Gather the opinion of clinical and academic DBS experts on CL-DBS.

Methods: We identified clinical and academic DBS experts (n=21), defined as positional leaders in the field [3], to discuss the challenges related to CL-DBS research and clinical applications, and to reply a 5-points Likert scale questionnaire according to Delphi method process [4].

Results: Panellists strongly agreed that CL-DBS is a safe technology (85% agree, median ± IQR: 4 ± 0) that will be of clinical routine in 10 years (85% agree, median ± IQR: 4 ± 0), with positive long-term impact for patients (80% agree, median ± IQR: 4 ± 0) such as a faster stable treatment response after setting definition (80% agree, median ± IQR: 4 ± 0). However, they agreed it requires high level of expertise (80% strongly agree, median ± IQR: 5 ± 0) and technological advancements (80% agree, median ± IQR: 4 ± 0), although current pacemaker technology might be suitable enough to implement it (90% Agree, median ± IQR: 4 ± 0).

Conclusions: CL-DBS is a safe and promising technology, ready now to become soon a clinical reality for movement disorders patients.

References:

[1] Xie, T. et al. Translational Neurodegeneration 6, 13 (2017).
[2] Krauss, J.K. et al. Nature reviews. Neurology 17, 75 (2021).
[3] Ludwig, B.G. (The Ohio State University: 1994).
[4] Hsu, C.-C. & Sandford, B.A. Practical assessment, research, and evaluation 12, 10 (2007).

P119

The effect of Magnetic Resonance Imaging-guided Focused Ultrasound on voice emission in essential tremor: machine-learning study

Francesco Asci[1], G. Costantini[2], G. Saggio[2], F. Pistoia[3,4], P. Sucapane[4], A. Suppa[1,5]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy
[3]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[4]Neurology Unit, San Salvatore Hospital, L'Aquila, Italy
[5]IRCCS Neuromed Institute, Pozzilli, Italy

Introduction: The Magnetic Resonance Imaging-guided Focused Ultrasound (MRgFUS) is an innovative therapeutic strategy in essential tremor (ET) [1]. Although the MRgFUS has demonstrated to improve the upper limb tremor, its effect on voice emission of ET patients is still largely unknown.

Objectives: In this longitudinal study, we objectively and automatically assess short-term changes in voice emission of ET patients undergoing MRgFUS through machine-learning analysis [2,3]. We analysed and compared voice recordings collected in ET patients before and after procedures and in healthy subjects (HS).

Methods: Fifty patients affected by ET (mean age±SD 69.9±7.4 years) and 74 age- and gender-matched HS (mean age±SD 71.0±12.4 years) were enrolled in the study. ET patients were clinically assessed before and 24 hours after MRgFUS targeting the ventralis intermediate nucleus (Vim). Sustained emissions of the vowel /e/ were recorded in HS and in ET patients before and after MRgFUS, through a commercially available smartphone. Voice samples were then processed through specific machine-learning procedures, for examining the diagnostic accuracies of comparisons by means of receiver operating characteristic (ROC) curves.

Results: We reported high diagnostic accuracy when comparing HS and ET patients before MRgFUS (AUC ROC: 0.991). Also, similar high statistic results were achieved when comparing voice recordings collected in HS and ET patients after MRgFUS (AUC ROC 0.954). Lastly, an intermediate accuracy was calculated when comparing voice samples recorded in ET patients before and after MRgFUS (AUC ROC 0.867).

Conclusions: In this study based on machine-learning procedures, we first confirmed our previous findings of abnormal voice emission in ET patients when compared to controls. Interestingly, for the first time, we objectively and automatically demonstrated that the MRgFUS targeting the Vim changes voice performances in patients with ET.

References:

[1] Elias, W. J. et al. A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor. N Engl J Med 375, 730–739 (2016).
[2] Suppa, A. et al. Voice Analysis with Machine Learning: One Step Closer to an Objective Diagnosis of Essential Tremor. Mov Disord (2021) doi:10.1002/mds.28508.
[3] Asci, F., Costantini, G., Saggio, G. & Suppa, A. Fostering Voice Objective Analysis in Patients with Movement Disorders. Mov Disord 36, 1041 (2021).

P120

Prospective evaluation of staged bilateral MRgFUS thalamotomy for the treatment of Essential and Dystonic Tremor

Nico Golfrè Andreasi[1], A. Braccia[1], V. Levi[2], N. Castelli[2], M. Stanziano[3], V. Caldiera[4], F. Colucci[1], R. Telese[1], S. Rinaldo[1], L.M. Romito[1], R. Cilia[1], A.E. Elia[1], G. Devigili[1], V. Leta[1], E. Ciceri[4], M. Grisoli[3], S.H.M.J. Piacentini[5], R. Eleopra[1]

[1]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Functional Neurosurgery Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[3]Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Interventional Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[5]Clinical Neuropsychology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Introduction: MRgFUS is an incisionless surgical technique that allows to precisely ablate target tissue through high intensity focused ultrasound with MRI guidance. Since its introduction in clinical practice, it has been largely applied for unilateral treatment, but EMA recently approved the staged bilateral thalamotomy for Essential Tremor (ET) [1-3].

Objective: To report our preliminary data on safety and efficacy of staged bilateral thalamotomy in a cohort of patients with drug resistant ET and Dystonic Tremor (DT) and to compare benefits and Adverse Events (AE) between first and second thalamotomy.

Methods: Patients with ET or DT consecutively undergoing second side thalamotomy in our Institute were enrolled in this study. Patients were evaluated by TETRAS Scale, which comprises both Activities of Daily Living (ADL) and tremor severity (Performance) assessments.

Results: 14 patients (12 ET, 2 DT; 2 women) were enrolled. Median time from first to second side thalamotomy was 14 months (min 6, max 52 months). At 6-months follow-up after the first thalamotomy, we observed a significant average improvement in ADL and Performance (63±25% and 57±32% compared to baseline, respectively); these improvements did not significantly change before the second treatment. After the second thalamotomy, both ADL (mean improvement 74±19% compared to baseline) and Performance improved; in particular, after the second treatment ADL associated with two-hands coordination and social impact of tremor significantly improved. AE (in particular dysarthria) were more frequent after the second thalamotomy; however, all AE were mild with no negative impact on patients' daily life, improved over time and the majority completely resolved six months after thalamotomy.

Conclusion: Second side thalamotomy appears to be effective, even though in our cohort a higher risk of dysarthria compared with the first thalamotomy was observed [3]. However, as reported by other groups [1,3] AE were mild and improved over time. Larger longitudinal studies are needed to evaluate long-term safety and efficacy.

References:

[1] Scantlebury N, et al. Safety of Bilateral Staged Magnetic Resonance-Guided Focused Ultrasound Thalamotomy for Essential Tremor. Mov Disord Clin Pract 2023; 10(10): 1559–1561. doi: 10.1002/mdc3.13882.
[2] Bruno F, et al. Bilateral MRgFUS thalamotomy for tremor: A safe solution? Case report and review of current insights. Clin Neurol Neurosurg 2020; 197:106164; doi: 10.1016/j.clineuro.2020.106164.
[3] Fukutome K, et al. Bilateral Magnetic Resonance Imaging-Guided Focused Ultrasound Thalamotomy for Essential Tremor. Stereotact Funct Neurosurg 2022; 100:44–52. doi: 10.1159/000518662.

P121

Effects of levodopa/carbidopa intestinal gel infusion on autonomic symptoms in advanced Parkinson's disease: a systematic review

Lanfranco De Carolis[1], S. Galli[1], E. Bianchini[1], M. Alborghetti[1], B. Caliò[2], P. Pacilio[1], A. Fanciulli[2], F.E. Pontieri[1], D. Rinaldi[1]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria

Introduction: Autonomic failure severely affects the quality of life and autonomy of Parkinson's disease (PD) patients, especially in advanced stages. Levodopa/carbidopa intestinal gel (LCIG) infusion is a well-established treatment for advanced PD with severe motor complications and provides substantial benefit in managing some non-motor symptoms (NMS) such as sleep, fatigue and neuropsychiatric issues. Nevertheless, the effect of LCIG on autonomic symptoms is not well known.

Objectives: To perform a systematic review of the literature on the influence of LCIG therapy on autonomic dysfunction in PD patients.

Methods: Following the PRISMA guidelines, we systematically searched for studies including autonomic outcome measures in LCIGtreated PD patients. Relevant articles were identified through a PubMed database search. Original articles published between January 2005 and June 2023 in English language were selected. We evaluated improvement, stability, or worsening of gastrointestinal, urinary, and cardiovascular symptoms at six different timepoints: <6 months (T1), 6 months (T2), 12 months (T3), 12-24 months (T4), 24-36 months (T5) and >36 months (T6), according to clinimetric scale change compared to baseline (T0, defined as the last visit prior to beginning LCIG treatment). Autonomic adverse events (AEs) possibly related to LCIG treatment were collected.

Results: Of 2312 studies identified, 16 met inclusion criteria and underwent quality assessment and data extraction for a total of 1361 PD patients. Thirteen studies reported improvement or stability of gastrointestinal, urinary, and cardiovascular symptoms over the interventional period. One study found a worsening of cardiovascular symptoms and two urological symptoms. Concerning safety, seven studies reported gastrointestinal (8.4%), urinary (0.5%), and cardiovascular (1.1%) autonomic LCIG-related AEs.

Conclusions: LCIG infusion is relatively safe and may help reduce the autonomic symptoms burden in advanced PD. Prospective studies specifically addressing the effect of LCIG on autonomic symptoms in advanced PD are warranted.

P122

A sustained benefit of GPI-DBS for genetic dystonia is maintained in the long-term

Fabiana Colucci[1,2], R. Telese[1], N. Golfrè Andreasi[1], A.E. Elia[1], A. Braccia[1], V. Leta[1], B. Garavaglia[3], C. Panteghini[3], G. Devigili[1], R. Cilia[1], R. Eleopra[1], L.M. Romito[1]

[1]Parkinson and Movement Disorders Unit, Department of Clinical Neurosciences and 3 Medical Genetics and Neurogenetics Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy

Introduction: Deep Brain stimulation (DBS) of bilateral Globus internal pallidum nuclei (GPi) has been reported to be effective in patients affected by dystonia [1]. However, the role of the genetic profile as a determinant of outcome is still under scrutiny [2].

Objectives: To determine the GPi-DBS outcome in patients affected by diverse genetic dystonia.

Methods: We assessed and compared the BFMDRS-Motor scores (BFMDRS-M) in 34 (female/F=13; male/M=21) inherited dystonia patients who underwent GPi-DBS at baseline, 1 (1Y) and 5 years (5Y) following surgery.

Results: The mean age at disease onset (OA) and surgery (SA) were 13,5±10,3 y and 31,3±14,9 y, respectively. Pre-implant BFMDRS-M was 41,5±22,7. At 1Y patients had BFMDRS-M=23,8±22,1 (improvement 42,6%;p<0,01). In 29 patients, a greater baseline improvement was detected at 5Y (52,7%;p<0,01;BFMDRSM=19,6±17,84). DYT-TOR1A patients (10=2F+8M;AO 11,1±13,5;AS 36,6±15,2) had BFMDRS-M=34,9±10,4 at baseline, with an improvement of 61% at 1Y (p<0,01). It improved at 5Y with a 73,3% reduction in BFMDRS-M score (p<0,01). DYT-SGCE patients (5=2F+3M;AO 4,4±3,3;AS 23,2±7,6) had BFMDRS-M=26,4±19,1 at baseline and BFMDRS-M-1Y=9,7±5,9 (improvement 63,2%;p<0,05). BFMDRS-M score was gradually worse at 5 years compared to the first years, but patients still showed a trend of benefit from surgery (p=0,07; BFMDRS-M-5Y=11,2±3,8). DYT-THAP1 patients (4=2F+2M;AO 16,7±15,9;AS 27,7±15,6) showed BFMDRS-M=38,8±18,4 at baseline, with about 50% of stable improvement at 1Y and 5Y (p<0,05;BFMDRS-M-1Y=19±10,6;BFMDRSM-5Y=17,5±7,3;54%). DYT-VPS16 patients (5=2F+3M;AO 13,5±1,5;AS 35±13,1) presented a BFMDRS-M=44,1±27,1 at baseline and BFMDRS-M-1Y=19,7±5,7 with 55,3% of improvement (p<0,05), remaining stable at 5-year (BFMDRS-M =20,8±8,5;p=0,05). NBIA/DYT-PANK2 patients (3=2F+1M;AO 6,7±8,1;AS 13,7±10) showed a progressive improvement in BFMDRS-M score over the years, although less high than the other genetic patients (p=0,05; BFMDRS-M=88±8,8 at baseline,BFMDRS-M-1Y=78,2±3,1,6 -11%- ;BFMDRS-M=73,3±3,8 -16%-). The two female DYT-GNAL patients (AO 39,5±3,5;AS 52,5±14,8) had a gradual improvement over the years up to 48% (p<0,01;BFMDRSM= 25±1,4;1Y=18±5,6;5Y=13). Similarity occurred in the two male DYT-KMT2B patients (AO 18±14,1;AS 30,5±20,5) who showed improvement up to 57% (p<0,01;BFMDRSM= 27,5±0,7;1Y=12±2,8;5Y=11,8±4,5). The only DYT-AOPEP male patient showed at 5Y an improvement of 36% (BFMDRS-M= 63,1Y=65, and 5Y=40). At 1Y following DBS-GPi surgery, the DYT-GALC male patient had 47% of improvement (BFMDRS-M=57,1Y=30), contrarily the NBIA/DYT/PARK-PLA2G6 female patient showed only a 9% of improvement from baseline (BFMDRS-M=66,5;1Y=60,5).

Conclusions: Globally, genetic dystonia patients benefited from DBSGPi surgery for up to 5 years. Patients affected by DYT-TOR1A benefit the most from DBS implant.

References:

[1] Jinnah HA, Alterman R, Klein C, Krauss JK, Moro E, Vidailhet M, Raike R. Deep brain stimulation for dystonia: a novel perspective on the value of genetic testing. J Neural Transm (Vienna). 2017 Apr;124(4):417-430. doi: 10.1007/s00702-016-1656-9.
[2] Tisch S. Deep brain stimulation in dystonia: factors contributing to variability in outcome in short and long term follow-up. Curr Opin Neurol. 2022 Aug 1;35(4):510-517. doi: 10.1097/WCO.0000000000001072.

P123

Magnetic resonance-guided focused ultrasound thalamotomy for medically refractory essential tremor: a single-center 3-year follow-up study

Stefano Tamburin[1,7], F. Paio[1,7], T. Bovi[1], G. Bulgarelli[2], M. Longhi[2], R. Foroni[2,4], E. Mantovani[1,7], P.M. Polloniato[4], M. Tagliamonte[5], E. Zivelonghi[4], C. Zucchella[1], C. Cavedon[4], A. Nicolato[2], B. Petralia[5], F. Sala[3,8], B. Bonetti[1], M. Tinazzi[1,7], S. Montemezzi[6], G.K. Ricciardi[5]

[1]Neurology Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[2]Stereotactic Neurosurgery and Radiosurgery Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[3]Neurosurgery Unit, Department of Neurosciences, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[4]Medical Physics, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[5]Neuroradiology, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[6]Radiology Units, Department of Pathology and Diagnostics, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[7]Neurology Secton, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
8Neurosurgery Section, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Magnetic resonance–guided focused ultrasound (MRgFUS) thalamotomy of the ventralis intermediate (Vim) nucleus is a non-invasive treatment for medically refractory essential tremor (ET). We present our clinical experience with 49 consecutive cases of MRgFUS Vim thalamotomy followed-up for three years and report the clinical outcomes and side effects.

Methods: A retrospective chart review of patients who underwent MRgFUS thalamotomy between January 2018 and December 2020 at our institution was performed. CRST tremor scores were obtained pre-operatively and at each follow-up visit along with an assessment of side effects (SE). All patients had post-operative MRIs within 24 h and at 1 month to determine the location, size, and extent of the MRgFUS lesion.

Results: The CRST total score and subscores and the QUEST score showed a significant improvement that was stable during the three-year follow-up period. Some patients reported reoccurrence of tremor during follow-up and two of them were satisfactorily retreated. Side effects were mild and transient in most cases.

Conclusions: Our data confirmed the effectiveness and safety of MRgFUS Vim thalamotomy in medically refactory ET. We also documented a long-lasting beneficial effect at three-year follow-up in most patients.

P124

Frequency, timeline, and predictors of axial symptoms after Deep Brain Stimulation of subthalamic nucleus in patients affected by Parkinson's disease

Giulia Saccardin[1,2], S. Coniglio[1,2,3], G. Argenziano[1,2], F. Cavallieri[4], A. Gessani[2], V. Fioravanti[4], G. Di Rauso[4,5], E. Bardi[2], M.G. Corni[2], M.A. Molinari[2], S. Contardi[6], E. Menozzi[7], C. Budriesi[2], F. Antonelli[2], A. Puzzolante[8], R. Stanzani[8], A. Feletti[9], G. Pavesi[8], F. Valzania[4], S. Meletti[1,2], V. Rispoli[2]

[1]Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Center for Neurosciences and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy
[4]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[6]IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Neurologia e Rete Stroke Metropolitana, Ospedale Maggiore, Bologna, Italy
[7]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK
[8]Neurosurgery, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[9]Institute of Neurosurgery, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Deep brain stimulation (DBS) of subthalamic nucleus (STN) is an effective therapy for advanced Parkinson's disease. Although motor symptoms are broadly controlled by DBS, axial symptoms, such as dysarthria and gait disorders, may occur or worse over time. In literature, few data about axial symptoms development after DBS are reported.

Objectives: To evaluate frequency and onset latency of dysarthria, freezing of gait (FoG), and falls after STN-DBS. To explore predictive factors of axial symptoms occurrancy after STN-DBS.

Methods: An observational retrospective single-center study was conducted, recruiting patients with at least 24 months of post-surgery clinical data. Demographic, pre-operative, and post-operative data were analyzed.

Results: 49 patients were enrolled. At time of surgery, mean age was 58,08 ± 6,26 years, mean disease duration 11,57 ± 5,57 years. The 46,94% of cohort developed dysarthria, while 57,14% FoG and 56,06% falls. Mean post-surgery latency of dysarthria, FoG and falls onset was 40, 48, and 56 months, respectively. Statistical analysis highlighted that patients with more severe gait impairment were more susceptible to development of dysarthria ($p=0,043$); moreover, patients with previous hypophonia were prone to develop FoG ($p=0,022$) and falls ($p=0,003$); previous dysarthria was associated with earlier FoG and falls onset (both $p<0,001$), with an higher risk of developing FoG ($p=0,030$). Patients with visuo-spatial impairment were more susceptible to experiencing axial symptoms earlier ($p<0,001$), while attention and executive functions were impaired in patients with earlier dysarthria and FOG onset (both $p<0,001$). Finally, older age at surgery was associated to an earlier FoG onset

(p=0,008).

Conclusions: This study shows frequency, timeline occurrence and several predictive factors of axial symptoms after STN-DBS. Overall, a more advanced disease with cortical symptoms and dysphonia prior to surgery pointed toward a higher and earlier risk of developing axial symptoms.

P125

Atypical progression of motor symptoms in Facio-Scapulo-Humeral Dystrophy: clinical worsening or overlap?

Dario Calisi, M.A. De Rosa, M. Russo, S.L. Sensi

Department of Neuroscience, Imaging and Clinical Science, "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

Introduction: In his early 60s, a man came to our Movement Disorder outpatient service due to progressive slowness and fatigue for the last 5 years. His medical history included FSHD confirmed by muscle biopsy and genetic workup in his early 40s.

Objectives: Our paper provides critical points for clinical reasoning when the neurologist is challenged with the coexisting clinical manifestations of a disease associated with muscle hypotonia and another pathological condition exhibiting rigidity.

Methods: The neurological examination revealed hyposthenia of the mimic and antigravity muscles, with severe involvement of the deltoids, compatible with the FSHD diagnosis. However, the patients also showed amimia, the "procerus sign", severe bradykinesia, hypophonia, vertical gaze limitation, fragmentation and hypometria of saccadic movements, lateral gaze-evoked nystagmus, and retrocollis. Rigidity was severe in the axial district, whereas the limbs were only mildly affected. Hypokinesia was also observed at finger tapping. Postural control was severely affected, and balance tests could not be performed. During the visit, the patient exhibited frequent freezing episodes. Moreover, he reported dysphagia for liquids. Executive dysfunction was observed, whereas cognition was preserved regarding orientation, autobiographical memory, and language. The patient spent several hours daily playing online card games and performed it even during the visit.

Results: A scintigraphy exam indicated reduced tracer uptake in the putamina and in the caudate nuclei. The brain MRI scan showed diffuse signs of atrophy and involvement of the tegmental mesencephalon. The radiological signs combined with the clinical presentation were compatible with a diagnosis of probable Progressive Supranuclear Paralysis-Richardson's Syndrome, according to current criteria [1].

Conclusions: Although rare, parkinsonian syndromes can overlap with neuromuscular disorders [2,3]. The differential diagnosis between the worsening of a neuromuscular condition and the onset of a movement disorder can be challenging but can be supported by neuroimaging exams [1].

References:

[1] Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, et al. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017;32:853–64.
[2] Pareés I, Kojovic M, Prasad Korlipara L V, Bhatia KP. Cervical dystonia associated with facioscapulohumeral dystrophy: expanding the clinical spectrum? Vol. 26, Movement disorders: official journal of the Movement Disorder Society. United States; 2011. p. 765–6.
[3] Paucar M, Beniaminov S, Solders G, Svenningsson P. Concomitant Facioscapulohumeral Muscular Dystrophy and Parkinsonism Mimicking Multiple System Atrophy. Mov Disord Clin Pract. 2016;3:194–6.

P126

Abnormal sensory attenuation as a potential biomarker of fatigue in functional movement disorder

*Angela Marotta**, E. Pizzolla*, M. Emadi Andani, I. Lozzi, M. Tinazzi*, M. Fiorio*
**Authors contributed equally to this work.*

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Functional movement disorder (FMD) is characterized by motor symptoms that resemble voluntary movements (e.g., are altered by distraction) but are perceived by patients as involuntary [1]. Fatigue is commonly associated with FMD, consistently interfering with patients' quality of life [2]. The mechanisms underlying fatigue in FMD remain unclear, thus limiting the development of treatment strategies for managing this disabling non-motor symptom. A recent model has conceptualized fatigue as a disorder of sensory attenuation (SA), i.e., a perceptual phenomenon by which self-generated stimuli are perceived as less salient than external ones [3]. Yet, experimental evidence for this model is still lacking.

Objectives: The present study will investigate whether reduced SA is related to fatigue in FMD patients with fatigue (FMDFatigue) compared with patients without it (FMDNo fatigue) and healthy controls (HC).

Methods: The force matching task will be used to estimate SA. Participants will be asked to match different target forces exerted on the left index finger by pressing directly on the finger (direct condition) or by operating an external device (indirect condition). Usually, participants overestimate the target force in the direct condition due to SA [4].

Results: We expect an overestimation of target force in the direct compared to indirect condition in HC and FMDNoFatigue, while no difference between the two conditions in the FMDFatigue group, due to a selective impairment of SA in patients with fatigue.

Conclusions: The present study will provide novel insights into the mechanisms underlying pathological fatigue in FMD by unveiling the link between this disabling non-motor symptom and sensory attenuation.

References:

[1] Nahab FB, Kundu P, Maurer C, Shen Q, Hallett M (2017) Impaired sense of agency in functional movement disorders: An fMRI study. PLOS ONE 12(4): e0172502. https://doi.org/10.1371/journal.pone.0172502
[2] Di Vico IA, Cirillo G, Tessitore A, Siciliano M, Venturelli M, Falup-Pecurariu C, Tedeschi G, Morgante F, Tinazzi M. Fatigue in hypokinetic, hyperkinetic, and functional movement disorders. Parkinsonism Relat Disord. 2021 May;86:114-123. doi: 10.1016/j.parkreldis.2021.03.018. Epub 2021 Mar 29. PMID: 33839028.
[3] Kuppuswamy A. The fatigue conundrum. Brain. 2017 Aug 1;140(8):2240-2245. doi: 10.1093/brain/awx153. PMID: 28899013; PMCID: PMC5806506.
[4] 4. hergill SS, Bays PM, Frith CD, Wolpert DM. (2003). Two eyes for an eye: the neuroscience of force escalation. Science, 301(5630), 187.

P127

Investigating the impact of SARS-CoV-2 infection on essential tremor: a survey-based study and retrospective analysis of clinical and kinematic data

Anna Sofia Grandolfo[1], D. Costa[1], D. Birreci[1], L. Angelini[1], M. Passaretti[1], A. Cannavacciuolo[1,2], A. Martini[1], M. De Riggi[1], G. Paparella[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: In the last three years, the SARS-CoV-2 infection has significantly affected public health, giving rise to numerous well documented health issues. In addition to the commonly recognized respiratory symptoms, a subset of individuals has reported new neurological manifestations or a deterioration of pre-existing neurological conditions. In our recent reports, we documented two cases of essential tremor (ET), who experienced a notable deterioration in tremor following SARS-CoV-2 infection [1,2]. Nevertheless, the effects of SARS-CoV-2 on ET remain largely unexplored.

Objective: This study aimed to assess the impact of SARS-CoV-2 infection more thoroughly on a cohort of patients diagnosed with ET. We employed a retrospective approach to compare clinical and kinematic data collected both before and after SARS-CoV-2 infection.

Methods: A survey was conducted to evaluate the impact of SARSCoV- 2 infection on tremor features in ET. Subsequently, we retrospectively analyzed clinical data, e.g., the Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS), and kinematic data, encompassing accelerometric recordings of postural and kinetic tremor.

Results: Our study enrolled 45 patients diagnosed with ET, including 21 females, with a mean age of 69 ± 12.2 years. Among the 25 patients who reported SARS-CoV-2 infection, 11 (44%) noted a subjective worsening of tremor. Notably, all patients (100%) reporting a subjective worsening of tremor also exhibited long COVID symptoms, whereas the prevalence of these symptoms was significantly lower (50%) in those without subjective exacerbation. The retrospective clinical data analysis revealed a deterioration of tremor in infected patients, although kinematic analysis did not disclose significant changes of tremor features.

Conclusion: The occurrence of long COVID frequently contributes to a subjective worsening of motor symptoms in ET patients. Conversely, the deterioration of ET, possibly due to central nervous system involvement during SARS-CoV-2 infection, as previously reported, appears to be a less common phenomenon.

References:

[1] Passaretti M, De Biase A, Paparella G, Angelini L, Cannavacciuolo A, Colella D, Berardelli A, Bologna M. Worsening of Essential Tremor After SARS-CoV-2 Infection. Cerebellum. 2023 Feb;22(1):155-158. doi: 10.1007/s12311-022-01366-8.

[2] Costa D, Birreci D, Passaretti M, Angelini L, Colella D, Cannavacciuolo A, Paparella G, Berardelli A, Bologna M. One-Year Follow-Up on Essential Tremor Worsening After SARS-CoV-2 Infection: a Series of Two Cases. Cerebellum. 2023 Aug 26. doi: 10.1007/s12311-023-01598-2.

P128

Anti-IgLON5 disease: two case reports and discussion about pathogenesis

Giovanni Ermanis[1,2], M. Fabris[2,3], L. Verriello[4], M. Rana[5], M. Valente[1,2], A. Vogrig[1,2]

[1]Clinical Neurology Unit, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy
[2]Department of Medicine, University of Udine, Udine, Italy
[3]Institute of Clinical Pathology, Department of Laboratory Medicine, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy
[4]Neurology Unit, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Santa Maria della Misericordia University Hospital, Udine, Italy
[5]Neurology Unit, Hospital of Gorizia, Gorizia, Italy

Introduction: Anti-IgLON5 disease is a recently discovered syndrome characterised by sleep disorders, bulbar symptoms and movement disorders, but clinical presentation can be protean and resemble other parkinsonian syndromes [1]. Presence of both autoimmune and neurodegenerative mechanisms are thought to play a role in pathogenesis: autoantibodies against neuronal cell-adhesion proteins and tauopathy involving brainstem and hypothalamus have been both described, but we still lack a comprehensive mechanistic theory.

Objectives: Here we report two patients affected by anti-IgLON5 disease followed in our Centers. Based on current knowledge of other neurodegenerative disorders, we tried to speculate about the role of immune system and protein misfolding in triggering such disease, with the aim of shedding light on its pathogenesis.

Methods: Both patients showed an atypical parkinsonian syndrome with prominent impairment of bulbar function and sleep. We confirmed their diagnosis by detecting high titer of anti-IgLON5 antibodies in CSF and blood samples. We then proceeded to analyse a panel of neurodegeneration markers and, in one patient, inflammatory cytokines on cerebrospinal fluid.

Results: Our data showed an Alzheimer's disease-like pattern in CSF samples involving Beta-amyloid deposition. Tau and phospho-tau titers were coherent to such pattern in one patient, whereas in the other one this was not confirmed, thus possibly reflecting a shorter disease duration. Inflammatory cytokines revealed a chronic inflammatory process, similar to other neurodegenerative diseases [2]. Interestingly, a previous autopsy case showed AD-related pathology [3].

Conclusions: On the basis of our data and of current knowledge about neurodegenerative disorders, we speculate that the link between the autoimmune process and neurodegeneration is driven by Beta-amyloid deposition. It is already known a role of anti-IgLON5 antibodies in inducing a direct damage on neurons [4], but Beta-amyloid could work itself as a trigger for inducing immunoreactive processes leading to auto-IgLON5 antibodies, which in turn can lead to further protein misfolding and neuronal loss.

References:

[1] Sabater L, Gaig C, Gelpi E, Bataller L, Lewerenz J, Torres-Vega E, Contreras A, Giometto B, Compta Y, Embid C, Vilaseca I, Iranzo A, Santamaría J, Dalmau J, Graus F. A novel non-rapid-eye movement and rapid-eye-movement parasomnia with sleep breathing disorder associated with antibodies to IgLON5: a case series,characterisation of the antigen, and post-mortem study. Lancet Neurol. 2014 Jun;13(6):575-86. doi: 10.1016/S1474-4422(14)70051-1. Epub 2014 Apr 3. Erratum in: Lancet Neurol. 2015 Jan;14(1):28. PMID: 24703753; PMCID: PMC4104022.

[2] McLarnon JG (2016) Chemokine Interleukin-8 (IL-8) in Alzheimer's and Other Neurodegenerative Diseases. J Alzheimers Dis Parkinsonism 6: 273. doi: 10.4172/2161-0460.1000273
[3] Erro ME, Sabater L, Martínez L, Herrera M, Ostolaza A, García de Gurtubay I, Tuñón T, Graus F, Gelpi E. Anti-IGLON5 disease: A new case without neuropathologic evidence of brainstem tauopathy. Neurol Neuroimmunol Neuroinflamm. 2019 Dec 11;7(2):e651. doi: 10.1212/NXI.0000000000000651. PMID: 31826985; PMCID: PMC7007636.
[4] Landa J, Gaig C, Plagumà J, Saiz A, Antonell A, Sanchez-Valle R, Dalmau J, Graus F, Sabater L. Effects of IgLON5 Antibodies on Neuronal Cytoskeleton: A Link between Autoimmunity and Neurodegeneration. Ann Neurol. 2020 Nov;88(5):1023-1027. doi: 10.1002/ana.25857. Epub 2020 Aug 27. PMID: 32740999.

P129

The cerebellar cognitive affective syndrome in ET subtypes

Rossella Bisogno, M. Russo, C. Giordano, C. Sorrentino, S. Cuoco, P. Barone, R. Erro

Dipartimento di Medicina, Chirurgia ed Odontoiatria "Scuola Medica Salernitana", Università di Salerno, Salerno, Italy

Introduction: Essential tremor (ET) is defined by upper limb action tremor possibly sustained by cerebellar dysfunction. The cerebellum, crucial for movement coordination, also influences cognition, with cerebellar lesions leading to the Cerebellar Cognitive Affective Syndrome (CCAS).

Objectives: To explore CCAS presence and its correlation with cerebellar motor signs in a sample of ET+ and perform a comparison with a published sample of 20 pure ET patients.

Methods: The CCAS scale (CCAS-S) and a structured motor examination was performed in 33 consecutive ET+ patients. Thirty-three healthy controls (HC), matched for age, sex and education were also recruited.

Results: A higher percentage of ET+ patients failed the switching category (p=0.041), digit span forward (p=0.006) and backward (p=0.024) CCAS items. Almost 70% of ET+ (vs. 33.3% of HC, x2=8.735, p=0.003) met the criteria for definite CCAS. Severity of CCAS did not correlate with age-at-onset, disease duration, tremor severity, number of missteps or SARA score. Definite CCAS was found in a similar proportion of pure ET (65%) and with a similar severity (t=1.028; p=0.309). Thedigit span forward was the only task that revealed a more pronounced deficit in ET+.

Conclusions: Despite a high prevalence of CCAS in ET+ (70%), its severity did not correlate with cerebellar motor signs or tremor severity. This suggests a potential dissociation of cerebellar circuits (motor vs. cognitive) or the involvement of additional brain circuits in ET+ compared to pure ET. The latter hypothesis is further supported by the more significant deficit of the digit span forward which is less sensitive to cerebellar damage.

P130

"My ear is clicking": a case of secondary palatal tremor

Giulia Saccardin[1,2], S. Coniglio[1,2,3], G. Argenziano[1,2], D. Fontanesi[1,2], G. Federici[4], F. Antonelli[2], V. Rispoli[2]

[1]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Center for Neurosciences and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy
[4]Department of Otolaryngology-Head and Neck Surgery, University Hospital of Modena - University of Modena and Reggio Emilia, Modena, Italy

Introduction: Palatal tremor (PT) is a rare disorder involving soft palate [1]. Differential diagnosis can be wide and challenging: in this regard, choosing the best work-up is essential.

Case presentation: A 54-years-old man was referred because of a four-year history of nonprogressive unsteadiness with near falls. Yet, he complained mild dysphagia and rhythmic, low-frequency palate movement with audible clicks in the last three months. Clinical assessment disclosed bilateral 1,5Hz palatal tremor with preserved palatal motility, rotatory gaze-evoked bilateral nystagmus, delayed vertical saccades and unsteady walk with positive Romberg sign. Brain MRI showed diffuse hemosiderin deposits from the pons to the bulbo-pontine junction, left cerebral peduncles, cerebellar tonsils spreading to both cerebellar hemispheres and dentate nuclei with chronic blood dripping from cavernomas and DVA. Olivary nuclei hypertrophy and cortical cerebellar atrophy were present too.

Discussion: PT can be essential (EPT) when not attributable to structural causes and symptomatic (SPT) when secondary to dentato-rubro-olivary pathway lesions [1,2]. Hypertrophic olivary degeneration (HOD) is a common and specific feature of SPT, representing nucleus vacuolation and cell body enlargement due to olivary deafferentation [1,2]. Usually, in SPT other symptoms than PT are present, whereas in EPT it is generally isolated [3]. Conversely, common features in EPT are audible click and disappearance during sleep [2]. In our case, despite the presence of a click, the association of PT with cerebellar syndrome led us to perform MRI, that showed micro-haemorragic lesions involving dentato-rubro-olivary pathway: it was of extreme relevance the choice of non-conventional MRI sequence, such as SWAN, as the iron deposits were not detectable by T1, T2 and FLAIR, while bilateral HOD was not an obvious feature from T2/FLAIR sequence.

Conclusions: PT can be secondary to several lesions involving dentato-rubro-olivary pathway: it is mandatory for patients with PT to undergo MRI to exclude consistent lesions.

References:

[1] Fadil Khoyratty, Thomas Wilson - The Dentato-Rubro-Olivary Tract: Clinical Dimension of This Anatomical Pathway – Case Reports in Otolaryngology - 2013 - 2013 - 1-3.
[2] Shakya Bhattacharjee - Palatal Tremor â€“ Pathophysiology, Clinical Features, Investigations, Management and Future Challenges - Tremor and Other Hyperkinetic Movements - 2020 - 10-1-12.
[3] Bharath Kumar Surisetti, Shweta Prasad, Vikram V. Holla, Koti Neeraja, Nitish Kamble, Manjunath Netravathi, Ravi Yadav, Pramod Kumar Pal - Clinical and Imaging Profile of Patients with Palatal Tremor - Movement Disorders Clinical Practice – 2021 - 8 - 435-444.

P131

Characterizing the role of alexithymia in functional movement disorders

Giovanni Ostuzzi[1], C. Geroin[2], F. Tedeschi[1], C. Barbui[1], M. Tinazzi[2]

[1]WHO Collaborating Centre for Research and Training in Mental Health and Service Evaluation, Department of Neuroscience, Biomedicine and Movement Sciences, Section of Psychiatry, University of Verona, Verona, Italy
[2]Neurology Unit, Parkinson Disease and Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences University of Verona, Verona, Italy

Introduction: Alexithymia is characterized by difficulties in recognizing, processing, and expressing emotions. Higher prevalence of alexithymia has been reported in individuals with Functional Movement Disorders (FMDs) compared to the general population [1]; however, whether this psychological construct might be associated with specific clinical features of FMDs, such as its phenotype or co-occurring nonmotor symptoms, is still unclear.

Objectives: This cross-sectional study aims to assess the possible association of several clinical characteristics of FMD with alexithymia in a large sample of individuals.

Methods: We will extract data from the Italian Registry of Functional Motor Disorders [3], using the Toronto Alexithymia Scale 20-items [2] score as a predictor for a set of clinical outcomes, while controlling for socio-demographic variables. Clinical outcomes will include predisposing and precipitating factors; type, severity, and duration of the functional movement disorder; medical and psychiatric comorbidities; nonmotor symptoms. We will conduct logistic models using penalized maximum likelihood regression. We will use a jack-knife estimator and adjust p-values according to Bonferroni-Hochberg.

Results: We included 500 participants, 74.6% of which were females, with a mean age of 45.3 years (standard deviation (SD) 16.5). The most frequent motor symptoms were weakness (56%), tremor (40%), and dystonia (24%). 61.4% showed two or more motor symptoms combined. The mean score on the Simplified Functional Movement Disorders Rating Scale was 13.9 (SD 9.1). 90% had at least one nonmotor symptom, most frequently fatigue (58.4%) and pain (56.6%). 38% had a psychiatric comorbidity, most frequently anxiety (21.4%). 483 participants provided data on the TAS-20, with a mean total score of 53.2 (SD 14.5); high and borderline levels of alexithymia emerged for 31.5% and 20.7%, respectively.

Conclusions: In our presentation, we will describe the clinical variables for which an association with alexithymia emerged, discussing methodological limitations, possible theoretical explanations, and implications for clinical practice.

References:

[1] Cole RH, Elmalem MS, Petrochilos P. Prevalence of autistic traits in functional neurological disorder and relationship to alexithymia and psychiatric comorbidity. J Neurol Sci. 2023;446:120585.
[2] Leising D, Grande T, Faber R. The Toronto Alexithymia Scale (TAS-20): A measure of general psychological distress. J Res Personality. 2009; 43(4), 707–710.
[3] Tinazzi M, Geroin C, Marcuzzo E, Cuoco S, Ceravolo R, Mazzucchi S, Pilotto A, Padovani A, Romito LM, Eleopra R, Zappia M, Nicoletti A, Dallocchio C, Arbasino C, Bono F, Magro G, Demartini B, Gambini O, Modugno N, Olivola E, Bonanni L, Zanolin E, Albanese A, Ferrazzano G, De Micco R, Lopiano L, Calandra-Buonaura G, Petracca M, Esposito M, Pisani A, Manganotti P, Tesolin L, Teatini F, Ercoli T, Morgante F, Erro R. Functional motor phenotypes: to lump or to split? J Neurol. 2021;268(12):4737-4743.

P132

A case report of atypical parkinsonism with unusual presentation: when dysarthria is the only primary complaint

Adriano Iacono[1,2], G. Grigioni[1,2], A. Govoni[1], L. Caremani[1], F. Piattellini[1,2], S. Valente[1,2], D. Greco[1,2], S. Ramat[1]

[1]Parkinson Unit, Department of NeuroMuscular–Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[2]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy

Introduction: Atypical parkinsonian disorders, despite some similarities with Parkinson disease, present additional features that allow them to be classified into dementia with Lewy bodies (DLB), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), and corticobasal degeneration (CBD)

Objectives: To introduce the case of a 68-year-old woman with unusual presentation of atypical parkinsonism.

Methods: The patient underwent a series of neurological evaluations, EEG, MRI and PET imaging studies, along with cerebrospinal fluid (CSF)-biomarkers, neuronal surface, anti-IgLON5 and onconeuronal antibodies.

Results: The patient's primary complaint was an overly compromised speech function, without other main symptoms or signs. She underwent previous nephrectomy due to kidney neoplasm; family history was mute. Brain MRI showed severe cortical atrophy and reduction in corpus callosum thickness; numerous non-contrastenhancing lesions in the cortico-subcortical supratentorial regions, and at C7 level, were displayed and firstly regarded as possible signs of demyelinating disease. CSF analysis showed normal levels of tau and beta-amyloid; neuronal surface, anti-IgLON5 and onconeuronal antibodies were negative. EEG showed sporadic, nonspecific isolated sharp waves in the posterior bilateral regions; motor evoked potentials were normal. Cerebral FDG-PET evidenced moderate prefrontal medial and lateral cortical glucose hypometabolism, as well as left parietal, left temporal medial and lateral regions, with concern of precuneus: findings prompted a CBD-like pattern, despite poor clinical correlation with the manifestation. Within 4 years, speech became progressively dysarthric, poor, punctuated. She showed plastic rigidity and bradykinesia on upper limbs. Upward gaze was impaired; also, visual apraxia was demonstrated. Gait disturbances were noticeable while no alien-limb related signs were present. Hoffmann and Myerson signs were positive.

Conclusions: Clinical cases of atypical parkinsonism configure a diagnostic and therapeutic challenge for everyday clinical practice, although insights on the more typical forms may be inferred. Further studies are needed to elucidate the pathogenetic basis and help the diagnostic process.

P133

"Belly dancer": a clinical case of propriospinal myoclonus

Davide Fontanesi[1,2], G. Argenziano[1,2], G. Saccardin[1,2], S. Coniglio[1,2,3], F. Antonelli[2], S. Meletti[1,2], V. Rispoli[2]

[1]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology Unit, Neuroscience Head Neck Department, Ospedale Civile Baggiovara (OCB), Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Center for Neurosciences and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy

Introduction: Propriospinal myoclonus (PSM) is a rare hyperkinetic movement disorder described in 1991 [1]. It is characterized by myoclonic jerks of the trunk that may spread to the limbs, neck, and face, often exacerbated by supine position. A complete neurophysiological study, including EEG-poliEMG and evoked potentials, is essential for diagnosis [2,3]. Spinal MRI is strongly recommended to detect structural causes of PSM.

Case presentation: A 76-year-old man presented with involuntary abdominal jerking that had started 19 years earlier, shortly after a local back infiltration procedure for a herniated disc at L4-L5. These symptoms first occurred when lying down and then had gradually deteriorated, with sleep disturbance, dyspnea and occasional jerking movements while sitting. Neurological examination revealed abdominal jerks in supine position and occasionally in sitting position, wide-based gait with small steps. Spinal MRI showed disc protrusions at C4-C5, D8-D9 and L1-L2 and spinal cord central canal enlargement from C4 to D11. Chest and abdominal CT scan disclosed no lesion. Somatosensory evoked potentials were within normal range (including amplitude). EEG-poliEMG was performed with standard EEG, and EMG derivation on the right orbicularis oculi, ipsilateral trapezius, cervical, dorsal, and lumbar paraspinalis, rectus femoris and rectus abdominis muscles.
Isolated bursts or short run of 3-4 bursts of variable length (186-314 ms) were found at the rectus abdominis, followed by analogous bursts in other muscles. The velocity of propagation was slow (6.2 m/s) with a consistent generator within the dorsal spinal. EEG showed no evidence of cortical activation preceding muscular activity, which was not influenced neither by dual task nor by motor activation.

Conclusions: A comprehensive neurophysiological study is mandatory to assess myoclonus to locate its anatomical generator. EEG-poliEMG parameters provide precious cues for differential diagnosis, particularly to distinguish functional, symptomatic, and idiopathic PSM. In this case, clinical, neurophysiological and neuroimaging data suggest a functional origin.

References:

[1] Brown, P., Thompson, P. D., Rothwell, J. C., Day, B. L. & Marsden, C. D. Axial myoclonus of propriospinal origin. Brain 114A, 197–214 (1991).
[2] Erro, R., Bhatia, K. P., Edwards, M. J., Farmer, S. F. & Cordivari, C. Clinical diagnosis of propriospinal myoclonus is unreliable: An electrophysiologic study. Movement Disorders 28, 1868–1873 (2013).
[3] Van Der Salm, S. M. A. et al. Propriospinal myoclonus: Clinical reappraisal and review of literature. Neurology 83, 1862 (2014).

P134

Central and peripheral correlates of negative expectations: toward a new model to explain functional neurological disorders

Irene Lozzi, M. Emadi Andani, A. Marotta, M. Tinazzi, M. Fiorio

Dipartimento di Neuroscienze, Biomedicina e Movimento, Università degli Studi di Verona, Verona, Italy

Introduction: Functional neurological disorders (FND) are characterized by one or more symptoms usually of a motor or sensory nature, such as limb weakness, tremor, numbness and dissociative crises, which are incompatible with organic damage or the diseases that typically cause them. Anxiety and stress are considered important factors in the etiopathogenesis of FND. Several studies, in fact, show how the physiological correlates of anxiety and stress are altered in these patients. Through learning phenomena, patients would come to form negative expectations about the nature of sensory and bodily stimuli. Negative expectations, in turn, could fuel physiological anxiety and stress responses in an anticipatory manner. This study aims at developing a deeper understanding of the neurocognitive mechanisms underlying negative expectations in functional neurological disorders.

Methods: To this end, electroencephalogram and electrodermal activity (skin conductance responses, SCR) were preliminarily recorded in a group of 10 healthy adults who completed a Pavlovian threat-conditioning task that included an acquisition and an extinction phase. Two Landolt rings with different orientation were presented, one was reinforced with an extremely annoying but not painful short electrical stimulation (CS+) during the acquisition phase, while the other was never reinforced (CS-). We also collected subjective ratings of CSs valence and CS-shock contingency awareness to confirm the successfulness of the conditioning procedure. To get a complete picture of any individual differences in conditioned physiological response, we also assessed the role of personality traits through standardized questionnaires.

Results: Here we present preliminary results for subjective ratings and SCR. CSs valence and contingency were coherently recognized by the participants, validating the acquisition and extinction of the threat-conditioning. SCR data provided an additional confirmation of successful conditioning, with greater responses for the CS+ than the CS- during the acquisition phase; the difference between responses to the two stimuli quickly ran out during the extinction phase.

Conclusions: These preliminary results confirmed that it is possible to successfully induce threat-learning and negative expectations throughout this specific paradigm, associated with its psychophysiological correlates. The results of this first preliminary phase conducted on healthy adults will be compared with a group of FND undergoing the same paradigm to tackle the question of the role of negative expectations in the pathophysiology of the disorder.

P135

Neurological symptoms in adults with Gaucher disease: a systematic review

Gabriele Imbalzano[1], C. Ledda[1], A. Romagnolo[1,2], A. Covolo[1], L. Lopiano[1,2], C.A. Artusi[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Torino, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Torino, Italy

Introduction: Gaucher disease (GD) is classically divided into three types, based on the presence or absence of neurological signs [1,2], with GD type II and III being typically associated with neurological involvement [1,3,4]. However, the neurological signs and symptoms associated with GD in adult patients can be highly variable and to date they have not been systematically addressed in the literature so far [1–4].

*Objective***:** We aimed to systematically review literature to analyze the entire spectrum of neurological manifestations in adult patients previously classified as GD type I, II or III, analyzing the role of variants on the different neurological manifestations.

Methods: We searched databases for studies reporting clinical data of adult GD patients (age ≥ 18). Data extraction included GD types, *GBA1* gene variants, age at disease onset and at diagnosis of GD, duration of GD and age at onset, type, and severity of neurological symptoms.

Results: 85 studies met the full inclusion criteria (28 case reports, 26 case series, 31 cohort studies). Among a total of 4190 GD patients, 555 of them exhibited neurological symptoms in adult age. The median age at evaluation was 46.8 years (IQR 26.5), age at neurological symptoms onset was 44 years (IQR 35.1), and age at GD clinical onset was 23 years (IQR 23.4). Parkinsonism, including Parkinson's disease and Lewy Body dementia, was the most reported neurological manifestation. Other symptoms and signs encompassed oculomotor abnormalities, peripheral neuropathy, seizures, myoclonus, and cerebellar, cognitive and psychiatric symptoms. The genotype N370S/N370S was mostly linked to Parkinsonism and the L444P variant with severe and earlier neurological symptoms.

Conclusions: The findings of this systematic review highlight: 1) the relevance of a comprehensive neurological assessment in GD patients, and 2) the importance of considering possible undiagnosed GD in adult patients with mild systemic symptoms presenting unexplained neurological symptoms [1].

Referemces:

[1] Biegstraaten M, van Schaik IN, Aerts JM, Hollak CE. 'Nonneuronopathic' Gaucher disease reconsidered. Prevalence of neurological manifestations in a Dutch cohort of type I Gaucher disease patients and a systematic review of the literature. J Inherit Metab Dis 2008;3:337–49.
[2] Stirnemann J, Vigan M, Hamroun D, et al. The French Gaucher's disease registry: Clinical characteristics, complications and treatment of 562 patients. Orphanet J Rare Dis 2012;7:77.
[3] Grabowski GA. Phenotype, diagnosis, and treatment of Gaucher's disease. Lancet 2008;372(9645):1263–71.
[4] Riboldi GM, Di Fonzo AB. GBA, Gaucher Disease, and Parkinson's Disease: From Genetic to Clinic to New Therapeutic Approaches. Cells 2019;8:364.

P136

Canvas and sleep disorders: a prospective cross-sectional study

Antonio Funcis[1], S. Rossi[1], F. Madia[1,2], G. Dalla Zanna[1,2], G. Silvestri[1,2], V. Brunetti[1,2]

[1]Institute of Neurology, Catholic University of the Sacred Heart, Rome, Italy
[2]Institute of Neurology, Fondazione Policlinico A. Gemelli, Rome, Italy

Objective: Cerebellar ataxia, neuropathy and vestibular are flexia syndrome (CANVAS) is a recessive late-onset ataxia caused by biallelic AAGGG expansions in the second intron of replication factor complex subunit 1 (RFC1) gene [1,2]. The aim in this study is to characterize, for the first time, sleep and its disorders in patients with genetically confirmed CANVAS.

Methods: Sleep was assessed by means of self-administered questionnaires and home-based polysomnography (PSG). Subjective sleep quality was assessed with Pittsburgh sleep quality index (PSQI), daytime sleepiness was assessed with Epworth sleepiness scale (ESS), and insomnia symptoms were assessed with Insonnia severity index (ISI). The presence of restless leg syndrome (RLS) was investigated with the administration of IRLS diagnostic clinical interview; in case of symptoms consistent with RLS, patients filled the IRLSSG severity scale. Symptoms of anxiety and depression were evaluated by means of Zung Self-Rating Anxiety Scale and Beck Depression Inventory short form, respectively.

Results: Eight patients with genetically confirmed CANVAS were enrolled (5 males, mean age: 64.1±7.3 years) with an average duration of disease of 13.9±7.2 years. Sensory axonal polyneuropathy and chronic spasmodic cough were present in all patients. Dysautonomia was reported in 5/8 patients. For what concern subjective sleep assessment, 5/8 patients complained poor sleep quality, 3/8 complained daytime sleepiness, 4/8 patients reported insomnia symptoms, 5/8 patients met the diagnostic criteria from moderate to very severe RLS. Four out to five patients with subjective poor sleep quality used sleep aids. The anxiety and depressive symptoms were present in 4/8 and 3/8 patients, respectively. PSG results showed a reduction of Slow Wave Sleep (N3/TST=15.2±13.0%) and REM (REM/TST=14.4±7.1%) and an increased wake after sleep onset (WASO=57.3±46.7 minutes). Obstructive sleep apnea (OSA) was present in 7/8 patients, ranging from moderate to severe (mean AHI=29.0±18.7), while 1/8 patients showed significant number of central sleep apnea; only one patient, with shorter disease duration (3 years from onset), did not show sleep-disordered breathing; only 2/7 patients with OSA reported daytime sleepiness. Finally, 3/8 patients showed a periodic limb movement index over the cut-off.

Conclusions: Our data showed that patients with CANVAS have poor sleep quality, altered sleep architecture, and a high prevalence of sleep disorders, particularly of OSA, insomnia, and RLS. Although OSA is the most common disorder, daytime sleepiness was not reported in all patients. Therefore, given the high prevalence of sleep disturbances, sleep assessment should be routinely performed in patients with CANVAS.

References:

[1] Cortese A, Curro' R, Vegezzi E, Yau WY, Houlden H, Reilly MM. Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS): genetic and clinical aspects. Pract Neurol. 2022;22(1):14-18.
[2] Cortese A, Reilly MM, Houlden H. RFC1 CANVAS / Spectrum Disorder. 2020 Nov 25. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2023.

P137

Digital telemedicine in Functional Motor Disorders: data on the health outcomes from a randomized controlled trial

Melania Fasoli[1], M. Gandolfi[1,2,3], A. Sandri[1], Z. Menaspà[1], C. Geroin[4], F. Bombieri[1], F. Schena[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona, Verona, Italy
[4]Department of Surgery, Dentistry, Pediatrics, and Gynecology, University of Verona, Verona, Italy

Introduction: Functional motor disorders (FMDs) are highly disabling conditions associated with long-term disability, poor quality of life, and economic burden on health and social care [1,2]. While both rehabilitation programs and telemedicine have shown to reduce motor and non-motor symptoms, long-term management and monitoring in FMDs remain unmet [3,4,5]. To date, no randomized controlled trials are evaluating the effectiveness of Digital telemedicine in the management of patients with FMD. The Brain Research Foundation Verona ONLUS supports this ongoing study.

Objectives: To report data from a single-blind randomized-controlled trial (RCT) with 2-parallel arms to demonstrate the effectiveness of a 5-days intensive rehabilitation treatment followed by a digital telemedicine program on the motor, non-motor symptoms, self-perception of change and health-related quality of life (QoL) in patients with FMDs.

Methods: All patients underwent a 5-days rehabilitation program (2 hours/day, five days/week, one week) by a qualified physiotherapist at the USD Parkinson's Disease and Movement Disorders Unit of Verona (Italy) [3]. Then, they were randomly assigned to the digital telemedicine group (DT, n=31) or the control group (CG, n=31). The DT program consisted of an individualized self-management program implemented with the Digital Telemedicine platform support (Treatment, as usual, one day, three days/week, 24 weeks). The CG followed the same program without any Digital Telemedicine platform support. Patients were evaluated before treatment (T0), after treatment (T1), at 12-weeks follow-up (T2), and at 24-weeks follow-up (T3).

Results: Overall, both groups showed a favorable trend over time with a progressive reduction in almost all considered variables ($p<0.019$), except for BPI intensity and mental QoL. A significant interaction emerged for the mental health QoL revealing that the CG at T3 reported a significant worsening compared to the DT group ($p<0.033$). No other interactions were significant.

Conclusions: This study provides novel preliminary evidence for a multidisciplinary digital telemedicine program's effect on patients with FMDs. Our data suggest that it may positively affect the patient's perceived mental health.

References:

[1] Perez, D. L. et al. 2021. J Neurol Neurosurg Psychiatry 1–10.
[2] Tinazzi M et al. 2021. Front Neurol 12:786126.
[3] Gandolfi M, 2021. NeuroRehab 48:305–314.
[4] Nielsen G, et al 2017. J Neurol Neurosurg Psychiatry 88(6):484–490.
[5] Gandolfi M, 2022. J Neurol 269(11):5940-5953.

P138

Propriospinal myoclonus in Alzheimer's disease: a case report

Enrico Bergamin[1], E. Del Prete[2], F. Turco[1], E. Unti[2], F. Cignoni[2], L. Giampietri[2], E. Bonanni[1], G. Siciliano[1], G. Tognoni[2], R. Ceravolo[1]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Department of Medical Specialties, Neurology Unit, AOUP, Pisa, Italy

Introduction: Propriospinal myoclonus (PSM) is a rare hyperkinetic movement disorder and often it represents a functional movement disorder (FMD) [1,2]. The recording of polygraphy and Bereitschaftpotential (BP) has been proposed to support clinical diagnosis[2], but sensitivity in studies varies between 25 and 86 %. To improve this sensitivity, the analysis of event-related EEG desynchronization patterns (ERD) has been suggested [3]. Although cases of FMD have been described in patients with neurodegenerative diseases such as Parkinson's Disease (PD), no cases of PSM have been previously described in patients with Alzheimer's Disease (AD).

Objectives: Presenting the case of application of electrophysiological analysis to support the diagnosis of PSM in AD.

Methods: A 61-year-old female patient with diagnosis of AD based on NIA-AA criteria, followed by the Neurology Clinic of University of Pisa, presented a functional PSM. At the time of the examination she presented with arrhythmic involuntary trunk movements that propagated to the shoulders, presented entrainment phenomenon, increased in clinostatism, decreased until disappearing with distraction maneuvers and during gait. After clinical evaluation, she underwent polymyographic recording with research for BP and ERD: no BP was recorded, however, an ERD was found in the beta-gamma frequency prior to the motor event, supporting the electrophysiological evidence of a voluntary cortical genesis of the movement itself. The patient was considerably anxious and the PSM was a very stressful condition that conditioned the quality of her life.

Discussion: Diagnosis and management of FMD is a challenge for the neurologist, furthermore if a cognitive decline is present. The diagnosis of functional PSM is supported by polymyographic findings[2-3], however with variable sensitivity, and growing interest is present to research more sensitive neurophysiological biomarkers.

Conclusions: This is the first case of PSM described in AD. More clinical and electrophysiological data are needed to improve our knowledge of FMD in neurodegenerative disease.

References:

[1] Brown P, Thompson PD, Rothwell JC, Day BL, Marsden CD. Axial myoclonus of propriospinal origin. Brain. 1991 Feb;114 (Pt 1A):197-214. PMID: 1998882.
[2] Erro R, Bhatia KP, Edwards MJ, Farmer SF, Cordivari C. Clinical diagnosis of propriospinal myoclonus is unreliable: an electrophysiologic study. Mov Disord. 2013 Nov;28(13):1868-73. doi: 10.1002/mds.25627. Epub 2013 Sep 18. PMID: 24105950.
[3] Meppelink AM, Little S, Oswal A, Erro R, Kilner J, Tijssen MAJ, Brown P, Cordovari C, Edwards M. Event related desynchronisation predicts functional propriospinal myoclonus. Parkinsonism Relat Disord. 2016 Oct; 31:116-118. doi: 10.1016/j.parkreldis.2016.07.010. Epub 2016 Jul 22. PMID: 27477621; PMCID: PMC5120690.

P139

Anodal transcranial direct current stimulation on the primary motor cortex of patients with multiple system atrophy: a small pilot study

Clara Simonetta[1], M. Conti[1], C. Salimei[2], S. Viscusi[1], J. Bissacco[1], R. Bovenzi[1], D. Mascioli[1], R. Cerroni[1], M. Pierantozzi[1], N.B. Mercuri[1], A. Stefani[1], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]University of Rome Tor Vergata, Rome, Italy

Introduction: Multiple system atrophy (MSA) is a rare and severe neurodegenerative disease characterized by autonomic dysfunction, parkinsonism, and cerebellar ataxia in various combination. To date, there are no effective treatments for MSA, and the symptomatic therapies are almost unsatisfactory. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique allowing for the modulation of cortical excitability [1]. Although the therapeutic application of tDCS is increasing in the field of neurodegenerative diseases, the evidence for MSA is still scarce [2,3].

Objectives: To assess the safety and efficacy of the primary left motor cortex (M1) anodal tDCS in a group of MSA patients.

Methods: We recruited 5 patients with a diagnosis of clinically probable MSA established by MDS-MSA diagnostic criteria [4]. Each patient underwent sham and anodal tDCS, in random order. Anodal tDCS was delivered at 2.0 mA per 20 min for 10 days, through two 25 cm2 electrodes; the anode was placed over the left primary motor cortex (M1) and the cathode over the contralateral supraorbital ridge (Fp2). We assessed clinical outcomes with Unified Multiple System Atrophy Rating Scale part I, UPDRS part III, Scales for Outcomes in Parkinson's disease - Autonomic Dysfunction, Non-Motor Symptoms Scale, Tinetti Performance Oriented Mobility Assessment. The Paired T-test was used to compare clinical outcomes.

Results: The stimulation protocol produced no adverse effects. Both the anodal and sham stimulation did not significantly change clinical scale scores.

Conclusions: Motor impairment in MSA is thought to result from cerebello-thalamocortical circuit dysfunction, which in turn has been associated with decreased M1 excitability (5). However, this small pilot study showed that anodal M1 stimulation was ineffective in MSA patients. Regardless of the sample size, we could hypothesize that the clinical pathological heterogeneity of MSA might prevent substantial improvement due to the isolated M1 stimulation.

References:

[1] Lefaucheur JP, Antal A, Ayache SS, Benninger DH, Brunelin J, Cogiamanian F, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Vol. 128, Clinical Neurophysiology. 2017.
[2] Alexoudi A, Patrikelis P, Fasilis T, Deftereos S, Sakas D, Gatzonis S. Effects of anodal tDCS on motor and cognitive function in a patient with multiple system atrophy. Disabil Rehabil. 2020;42(6).
[3] Ahn JH, Lee D, Kim M, Cho JW, Chang WH, Youn J. M1 and Cerebellar tDCS for MSA-C: a Double-Blind, Randomized, Sham-Controlled, Crossover Study. Cerebellum. 2023;22(3).
[4] Wenning GK, Stankovic I, Vignatelli L, Fanciulli A, Calandra-Buonaura G, Seppi K, et al. The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Vol. 37, Movement Disorders. 2022.
[5] You H, Wang J, Wang H, Zang YF, Zheng FL, Meng CL, et al. Altered regional homogeneity in motor cortices in patients with multiple system atrophy. Neurosci Lett. 2011;502(1).

P140

Creutzfeldt-Jakob disease presenting as corticobasal syndrome

Matteo Alessandro De Rosa[1,2], D. Calisi[1], M. Onofrj[1], A. Thomas[1,2], S.L. Sensi[1,2]

[1]Department of Neuroscience, Imaging and Clinical Sciences, Gabriele d'Annunzio University of Chieti and Pescara, Chieti, Italy
[2]Center for Advanced Studies and Technology (CAST), "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy

Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disease caused by the pathological accumulation of aberrant prion protein (PrP). Early diagnosis can be challenging since CJD can mimic other neurological disorders, but it often fits a pattern of cognitive problems, cerebellar disturbance, behavioral/psychological changes, and perhaps myoclonus [1]. We present a case of sCJD in a 72-year-old woman who presented with alien limb phenomenon, cortical sensory deficit, limb dystonia, and
stimulus-sensitive myoclonus, while cognitive performance was unremarkable (MoCA: 24/30). This clinical picture fitted with corticobasal syndrome according to Amstrong criteria [2]. However, she rapidly worsen and became more bradykinetic, suffered of trunk ataxia without relevant troubles in walking. Thus, we perfomed a lumbar puncture that showed no inflammatory abnormalities whereas RTQuick analysis revealed prionic disease. In just two months her cognitive status changed and developed mild cognitive decline. Lastly, the patient was admitted due to acute urinary retention and she became acutely unresponsive, due to akinetic mutism and worsening of extrapyramidal symptoms. After 5 months since symptoms onset she died from a pulmonary infection. MRI images and EEG were not useful, since they became indicative only after 4 months from symptoms onset, when clinical features were more evident.
This case highlights the clinical heterogeneity of sCJD presentation and the important inclusion of CJD in the differential diagnosis of atypical presentations of neurodegenerative disease. Since CJD is a rare disease and its clinical course is rapidly progressive, an in-depth understanding and awareness of early clinical features are mandatory to enhance the overall diagnostic accuracy in its very early stages [3].

References:

[1] Hermann P, Appleby B, Brandel JP, Caughey B, Collins S, Geschwind MD, Green A, Haïk S, Kovacs GG, Ladogana A, Llorens F, Mead S, Nishida N, Pal S, Parchi P, Pocchiari M, Satoh K, Zanusso G, Zerr I. Biomarkers and diagnostic guidelines for sporadic Creutzfeldt-Jakob disease. Lancet Neurol. 2021 Mar;20(3):235-246. doi: 10.1016/S1474-4422(20)30477-4. Erratum in: Lancet Neurol. 2021 Apr;20(4):e3.PMID: 33609480; PMCID: PMC8285036.
[2] Armstrong MJ, Litvan I, Lang AE, Bak TH, Bhatia KP, Borroni B, Boxer AL, Dickson DW, Grossman M, Hallett M, Josephs KA, Kertesz A, Lee SE, Miller BL, Reich SG, Riley DE, Tolosa E, Tröster AI, Vidailhet M, Weiner WJ. Criteria for the diagnosis of corticobasal degeneration. Neurology. 2013 Jan 29;80(5):496-503. doi: 10.1212/WNL.0b013e31827f0fd1. PMID: 23359374; PMCID: PMC3590050.
[3] Baiardi S, Capellari S, Bartoletti Stella A, Parchi P. Unusual Clinical Presentations Challenging the Early Clinical Diagnosis of Creutzfeldt-Jakob Disease. J Alzheimers Dis. 2018;64(4):1051-1065. doi: 10.3233/JAD-180123. PMID: 30010123.

P141

When the therapy unexpectedly doesn't work and neurological symptoms arise: an unusual case of Wilson's disease

Giulia Bonato[1,2], A. Antonini[1,2], M. Carecchio[1,2]

[1]Parkinson and Movement Disorders Unit, Centre for Rare Neurological Diseases (ERN-RND), Department of Neuroscience, University of Padova, Padova, Italy
[2]Center for Neurodegenerative Disease Research (CESNE), University of Padova, Padova, Italy

Introduction: Wilson's disease (WD) is a rare autosomal recessive disorder caused by mutations in the ATP7B gene, leading to abnormal copper deposition in liver, brain and eyes. It is a treatable disease, whose diagnosis should not be missed at any stage to prevent permanent sequelae [1,2].

Objectives: To describe the neurological features of WD in a patient with a peculiar disease history.

Methods: Video recording

Results: a 28-year-old girl came to our attention due to rapid-onset dystonia-parkinsonism, preceded by with mood and behavioral changes in the previous year. Neurological examination documented jaw opening dystonia with risus sardonicus and dystonic posture of the right hand, bilateral rest and action tremor in the upper limbs, wing-beating tremor in specific postures, and bilateral bradykinesia, with mixed spasticity and rigidity in the left limbs. Speech anarthria, gait ataxia, drooling, dysphagia and brisk reflexes were also observed.
She was diagnosed with Wilson's disease at age 7 due to evidence of increased liver function tests for which she underwent liver biopsy and genetic analysis (H1069Q homozygous mutation in ATP7B); therapy with penicillamine was promptly started and later switched to zinc acetate because of nausea. She was asymptomatic until age 27, when therapy started losing efficacy despite good compliance. Brain MRI showed typical basal ganglia and brainstem copper deposition; blood test and liver ultrasounds both documented disease progression. Symptomatic therapy with levodopa and anticholinergic drugs was started and a liver transplantation was scheduled.

Conclusions: Movement disorders as a consequence of central nervous system involvement in WD on copper chelation therapy is unusual; nevertheless, prompt recognition of neurological WD features is essential to uncover disease progression and change therapeutic strategy if needed.

References:

[1] Mulligan C, Bronstein JM. Wilson Disease: An Overview and Approach to Management. Neurol Clin. 2020;38(2):417-432. doi: 10.1016/j.ncl.2020.01.005
[2] Chaudhry HS, Anilkumar AC. Wilson Disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing; August 7, 2023.

P142

Split syndrome with acute onset hemichorea and contralateral progressive parkinsonism: case report and literature review

Francescantonio Cammarota[1,2], C. Tassorelli[1,2], G. Cosentino[1,3], A. Pichiecchio[1,4], M. Avenali[1,5], M. Todisco[3,5]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]Headache Science and Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy
[3]Translational Neurophysiology Research Unit, IRCCS Mondino Foundation, Pavia, Italy
[4]Advanced Imaging Center and Artificial Intelligence, Department of Neuroradiology, IRCCS Mondino Foundation, Pavia, Italy
[5]Movement Disorders Research Center, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Cerebrovascular diseases cause up to 22% of all secondary movement disorders [1]. Hemichorea is a unilateral hyperkinetic disorder characterized by continuous, non patterned, involuntary movements. Hemichorea may result from ischemic or hemorrhagic stroke affecting the contralateral basal ganglia [2].
Vascular parkinsonism is still debated, being diagnosed in case of clear association of parkinsonism with imaging evidence of cerebrovascular lesions and/or evidence of focal signs due to stroke, when alternative causes of parkinsonism are excluded [3].

Objective: Here, we described an 83-year-old female who had an 8-year progressive history of parkinsonism featured by right-sided bradykinesia and resting tremor, followed by postural instability with recurrent falls. During the disease course, the patient experienced a sudden onset of left-sided hemichorea, predominantly affecting the arm.

Methods: The patient underwent clinical and neuroimaging evaluations. A literature review was performed.

Results: At the age of 77 years, brain MRI revealed a significant cerebral small vessel disease, mainly involving the supratentorial regions, particularly basal ganglia. Notably, one of multiple microbleeds was identified in the cranial portion of the right cerebral peduncle, consistently with the left hemichorea. Parkinsonism mildly improved with dopaminergic therapy. Follow-up clinical evaluations and a scheduled [123I]Ioflupane SPECT aim to provide further insights into the concomitant occurrence of degenerative parkinsonism. Various studies highlighted chorea, including hemiballism, as the most frequent post-stroke movement disorder [1, 4-6]. Ischemic injury was reported to be the predominant underlying mechanism. While contralateral subthalamic nucleus has traditionally been linked to hemichorea, lesions affecting other areas, such as the striatum, have also been reported [2,7].

Conclusions: To our knowledge, this case represents a unique instance of split syndrome, given the coexistence of hyperkinetic and hypokinetic movements disorders on opposite body sides. In this patient, while hemichorea seems to derive from vascular injury, vascular and/or degenerative causes of contralateral parkinsonism are still under investigation.

References:

[1] Suri R, Rodriguez-Porcel F, Donohue K, et al. Post-stroke movement disorders: the clinical, neuroanatomic, and demographic portrait of 284 published cases. J Stroke Cerebrovasc Dis 2018; 27: 2388-2397.

[2] Chung SJ, Im JH, Lee MC, Kim JS. Hemichorea after stroke: clinical-radiological correlation. J Neurol 2004; 251: 725-729.
[3] Vizcarra JA, Lang AE, Sethi KD, Espay AJ. Vascular Parkinsonism: deconstructing a syndrome. Mov Disord 2015; 30: 886-894.
[4] Ghika-Schmid F, Ghika J, Regli F, Bogousslavsky J. Hyperkinetic movement disorders during and after acute stroke: the Lausanne Stroke Registry. J Neurol Sci 1997; 146: 109-116.
[5] Alarcon F, Zijlmans JC, Duenas G, Cevallos N. Post-stroke movement disorders: report of 56 patients. J Neurol Neurosurg Psychiatry 2004; 75: 1568-1574.
[6] Mehanna R, Jankovic J. Movement disorders in cerebrovascular disease. Lancet Neurol 2013; 12: 597-608.
[7] Saris S. Chorea caused by caudate infarction. Arch Neurol 1983; 40: 590-591.

P143

Adult-onset Pantothenate Kinase-Associated Neurodegeneration (PKAN) with long disease duration: a case report and literature review

Sabrine Othmani[1], F. Pinna[1], C. Frau[2], A. Salis[3], V. Floris[1], P. Solla[2], C.F. Bagella[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Unit of Neurology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
[3]Unit of Radiology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Introduction: Pantothenate Kinase-Associated Neurodegeneration (PKAN), related to PANK2 gene mutation, is a rare neurodegenerative disorder characterized by rapidly progressive movement disorders and cognitive impairment. Dystonia and pigmentary retinopathy are prominent symptoms [1]. While clinical presentation is typically in childhood, adult-onset forms have been described. These forms seem characterized by milder clinical manifestations and slower disease progression [2], although data on the long-term outcome are scarce.

Objectives: To describe a novel case of adult-onset PKAN (due to PANK2 gene mutation) with 38 years of follow-up, and review the literature to characterize the long-term outcome of these patients.

Methods: Case report and literature review. Pubmed was searched for cases of adult-onset PKAN with available follow-up details. The clinical characteristics and long-term outcome of included patients were abstracted.

Results: A 30 year-old man presented with slowly progressive speech disturbances and frequent falls. Over years, he had a gradual decline of intellectual functions, behavioral changes, orolingual dystonia with tongue protrusion, and spasticity leading to walking impairment. One brother and one sister (of six total siblings borned from consanguineous parents) had similar clinical manifestations with a slowly progressive course. At the age of 60, brain MRI revealed pathognomonic changes in the basal ganglia due to iron accumulation. Genetic testing showed a homozygous c.965A>G mutation in the PANK2 gene. At 68 years of age, the patient's clinical and radiological manifestations remained stable, without further deterioration compared to the time of the diagnosis. Twenty-six additional cases [3,4,5,6] of adult-onset PKAN with long-term follow-up available (all due to PANK2 gene mutation) were identified in the literature, for a total of 27 cases. The median age at symptoms onset was 30 (range, 20-67) and 9 (33,3%) were female. At last available followup, a median of 12 (range, 2-54) years from onset and 12 (44,4%) patients were alive.

Conclusions: The disease course in patients with adult-onset PKAN seems characterized by early development of symptoms followed by and a subsequent phase of clinical-MRI stability of years.

References:

[1] Kurian, Manju A. (2013). International Review of Neurobiology, Metal Related Neurodegenerative Disease Volume 110. Pantothenate Kinase-Associated Neurodegeneration (PKAN) and PLA2G6-Associated Neurodegeneration (PLAN), 49–71. doi:10.1016/b978- 0-12-410502- 7.00003-x
[2] Tomić A, Petrović I, Svetel M, Dobričić V, Dragašević Mišković N, Kostić VS. Pattern of disease progression in atypical form of pantothenate-kinase-associated neurodegeneration (PKAN) - Prospective study. Parkinsonism Relat Disord. 2015 May;21(5):521-4. doi: 10.1016/j.parkreldis.2015.02.006. Epub 2015 Feb 17. PMID:25724846.

[3] Tomić, Aleksandra; Petrović, Igor; Svetel, Marina; Dobričić, Valerija; Dragašević Mišković, Nataša; Kostić, Vladimir S. (2015). Pattern of disease progression in atypical form of pantothenate-kinaseassociated neurodegeneration (PKAN) – Prospective study. Parkinsonism & Related Disorders, 21(5), 521–524. doi:10.1016/j.parkreldis.2015.02.006
[4] Aysel Milanlıoğlu, Mehmet Nuri Aydın, Alper Gökgül, Mehmet Hamamcı, Temel Tombul, Adult-onset atypical form of Hallervorden- Spatz disease. Eastern Journal of Medicine 18 (2013) 221-223
[5] Thomas, M., Hayflick, S.J. and Jankovic, J. (2004), Clinical heterogeneity of neurodegeneration with brain iron accumulation (Hallervorden-Spatz syndrome) and pantothenate kinase-associated neurodegeneration. Mov. Disord., 19: 36-42. https://doi.org/10.1002/mds.10650
[6] S. Sachin, V. Goyal, S. Singh, G. Shukla, M.C. Sharma, S. Gaikwed, M. Behari. Clinical spectrum of Hallervorden-Spatz syndrome in India. Journal of Clinical Neuroscience, Volume 16, Issue 2, February 2009, Pages 253-258.

P144

Beyond Huntington

Pietro Antenucci[1], F. Colucci[2,3], A. Gozzi[1], M. Neri[4], A. Ferlini[4], M. Sensi[2]

[1]Department of Neurosciences and Rehabilitation, University of Ferrara, Ferrara, Italy
[2]Department of Neurosciences and Rehabilitation, Azienda Ospedaliera Universitaria S. Anna, U.O. Neurologia, Ferrara, Italy
[3]Parkinson and Movement Disorders Unit, Department of Clinical Neurosciences, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Department of Medical Sciences, Unit of Medical Genetics, Università degli Studi di Ferrara, Ferrara, Italy

We herein signpost a case of a 67-year female presented with an insidious onset of short, abrupt, erratic movements initially involving the upper limbs and rapidly spreading to the head and lower limbs... In addition, she complained of depression and episodes of aggressiveness for about two years, in absence of detectable cognitive decline (MMSE 28/30). Her past history was significant for pulmonary thromboembolism with right atrium thrombosi,and thirdstage renal failure.
On depth examination oromandibular and distal corieco-dystonic movements prevalent at the right side were observed. The patient presented motor impersistence, slow saccades, and cautious widened-base ambulation with continuous choric movements to the right hand fingers. For long distance the patient ambulated in a wheelchair. The workup included brain magnetic resonance with evidence of cortical atrophy, subcortical vascular unspecific lesions and ferromagnetic deposits on basal ganglia; a total body CT scan was remarkable only for a splenomegaly. Her blood tests were significant for a known hypertriglyceridemia and a persistent neutrophilic leukocytosis. A genetic panel including TBP-SCA17, PRNP, HTT, C9ORF72, PPP2R2B-SCA12, was negative as the search for Philadelphia Chromosome on peripheral blood. As the neutrophilic leukocytosis was persistent, a hematologic evaluation suggested bone marrow biopsy, detecting primary myelofibrosis. Further genetic testing was performed for the hematologic purpose, and the patient tested positive for the V617FJAK2 mutation.
The patient started a specific therapy with ruxolitinib with a progressive normalization of blood tests. Otherwise, choreic movements remained unchanged and a progressive cognitive declined was detected with attentional and executive impairment and memory difficulties. Considering the absence of other detectable causes, a late onset chorea Jak2 associated was diagnosed.

P145

The genetic landscape of Parkinson's Disease in an Italian cohort and the need for a standardized approach

Angelo Tiziano Cimmino[1], P. Sanginario[1], F. Musso[1], L. Rigon[1], D. Genovese[1], A. De Biase[1], M. Petracca[2], F. Bove[2], C. Piano[1,2], F.D. Tiziano[3], A.R. Bentivoglio[1,2], P. Calabresi[1,2], G. Di Lazzaro[2]

[1]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3]Institute of Genomic Medicine, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Introduction: Advances in genetics have expanded the known spectrum of Parkinson's disease (PD)-related genes. The new techniques have broadened access to genetic analysis, allowing for rapid and simultaneous sequencing of many disease-associated genes, although unraveling a high number of variants with interpretation difficulties and inconsistencies.

Objective: Our study aimed to determine the genetic characteristics and their frequency in an Italian cohort of PD patients.

Methods: PD patients with family history of PD (≥1 affected relative), early onset (≤55 years [1]), and/or atypical phenotype underwent genetic analysis through a next generation sequencing (NGS) panel containing 45 known-PD-causative genes, coupled with MLPA when needed. Variants were interpreted according to ACMG [2] criteria, and reports were categorized as positive (≥1 variant, with definite genetic diagnosis), inconclusive (≥1 variant, insufficient for genetic diagnosis), or negative (no variants reported).
Heterozygous pathogenic/likely pathogenic variants in dominant genes and biallelic pathogenic/likely pathogenic variants in recessive genes were considered positive. GBA1 variants were considered pathogenic [3] and classified based on the risk of PD development [3].
Inconclusive reports underwent reassessment: heterozygous pathogenic variants in recessive genes and variants of unknown significance (VUS) with genotype-phenotype mismatch were considered negative; VUS not otherwise interpretable were clarified through family segregation studies.

Results: We recruited 197 patients. 74 (37.6%) reports revealed ≥1 variant. Of the inconclusive 39 (19.8%) reports, after reinterpretation, 1 (0.5%) was considered positive, while 22 (11.2%) negative. Eventually, positive reports were 36 (18.3%), and inconclusive 16 (8.1%). The most common diagnoses were GBA1 (23, 11.7%), LRRK2 (5, 2.5%), PRKN (4, 2.0%), PINK1 (1, 0.5%) FBXO7 (1, 0.5%). The gene with the most reported variants was GBA1 (28, 27.7%).

Conclusions: Our results contribute to a more in-depth understanding of the genetic spectrum underlying PD in Italian patients and underscore the importance of a standardized approach for the accurate interpretation of genetic findings.

References:

[1] Di Fonzo A, Percetti M, Monfrini E, et al. Harmonizing Genetic Testing for Parkinson's Disease: Results of the PARKNET Multicentric Study. Mov Disord. 2023 ;38(12):2241-2248. doi:10.1002/mds.29617.
[2] Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424. doi:10.1038/gim.2015.30.
[3] Parlar SC, Grenn FP, Kim JJ, Baluwendraat C, Gan-Or Z. Classification of GBA1 Variants in Parkinson's Disease: The GBA1-PD Browser. Mov Disord. 2023;38(3):489-495. doi:10.1002/mds.29314.

P146

Effects of GBA mutations in patients with Parkinson's disease and levodopa-carbidopa intestinal gel: a nation-wide longitudinal multicentre 'real-world' study

Roberto Cilia[1], S. Barca[1,2], E. Cereda[3], F. Colucci[1,4,5], V. Leta[1], M. Zibetti[6,7], M. Carecchio[8], S. Bonvegna[9], G. Calandra Buonaura[10,11], R. Cerroni[12], R. De Micco[13], S. Tamburin[14], L. Magistrelli[9,15], F. Lena[16], M.M. Mascia[17], M. Picillo[18], G. Cossu[19], M. Marano[20], A. Zampogna[21], C. Pellicano[22], V. Fioravanti[23], A. Pilotto[24], R. Zangaglia[25], M. Avenali[26], C. Sorbera[27], F. Di Biasio[28], F. Arienti[29], A. Nicoletti[30], C.F. Bagella[31], M.C. Malaguti[32], A. Ranghetti[33], E. Caputo[34], D. Alimonti[35], E. Torre[36], G. Oggioni[37], A.E. Elia[1], L.M. Romito[1], N. Golfrè Andreasi[1], G. Devigili[1], R. Telese[1], A. Braccia[1], C. Leuzzi[1,38], F. Invernizzi[39], B. Garavaglia[39], G. Imbalzano[6,7], C. Ledda[6,7], P. Antenucci[4,5], A. Gozzi[4,5], G. Bonato[8], M. Percetti[9], G. Giannini[10,11], L. Sambati[10,11], T. Schirinzi[12], M. D'Anna[13], F. Cavallieri[23], M. Liccari[40], A. Priori[37], M. Sessa[35], F. Tamma[34], M. Canesi[33], P. Solla[31], M. Zappia[30], A.B. Di Fonzo[29], L. Avanzino[28], A. Quartarone[27], E.M. Valente[41], C. Pacchetti[25], A. Padovani[24], F. Valzania[23], F.E. Pontieri[22], A. Suppa[16,21], M.T. Pellecchia[18], N. Modugno[16], C. Comi[15], M. Tinazzi[14], A. Tessitore[13], A. Stefani[12], P. Cortelli[10,11], I.U. Isaias[9], A. Antonini[8], M. Sensi[4,5], L. Lopiano[6,7], R. Eleopra[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[2]UO Medicina Interna, Ospedale Nostra Signora delle Mercede di Lanusei, Lanusei, Italy
[3]Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[4]Azienda Ospedaliera Universitaria S. Anna, U.O. Neurologia, Ferrara, Italy
[5]University of Ferrara, Ferrara, Italy
[6]Department of Neuroscience "Rita Levi Montalcini", University of Turino, Turin, Italy
[7]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy
[8]Parkinson and Movement Disorders Unit, Department of Neuroscience, University of Padua, Padua, Italy
[9]Parkinson Institute Milan, ASST G. Pini-CTO, Milan, Italy
[10]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[11]Department of Biomedical and NeuroMotor Sciences, Alma Mater Studiorum, University of Bologna, Bologna, Italy
[12]Parkinson's Disease Unit, University Hospital of Rome "Tor Vergata", Rome, Italy
[13]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[14]Section of Neurology, Department of Neurosciences, Biomedicine, and Movement Sciences, University of Verona, Verona, Italy
[15]Department of Translational Medicine, Movement Disorders Centre, Neurology Unit, University of Piemonte Orientale, Novara, Italy
[16]Parkinson and Movement Disorders Unit, IRCCS Neuromed, Pozzilli, Italy
[17]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[18]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Italy
[19]Neurology Service and Stroke Unit, Department of Neuroscience, AO Brotzu, Cagliari, Italy
[20]Unit of Neurology, Neurophysiology, Neurobiology and Psychiatry, Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Rome, Italy
[21]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[22]IRCCS Santa Lucia Foundation, Rome, Italy
[23]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

[24]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[25]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[26]Department of Brain and Behavioral Sciences, University of Pavia & IRCCS Mondino Foundation, Pavia, Italy
[27]IRCCS Centro Neurolesi “Bonino-Pulejo”, Messina, Italy
[28]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[29]Neurology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[30]Department of Medical, Surgical Sciences and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy
[31]Neurological Unit, AOU Sassari, University of Sassari, Sassari, Italy
[32]Department of Neurology, Santa Chiara Hospital, Trento, Italy
[33]Department of Neurological Rehabilitation, Parkinson's Disease and Movement Disorders Center, Moriggia-Pelascini Hospital, Gravedona ed Uniti, Como, Italy
[34]Department of Neurology, "F. Miulli" General Hospital, Acquaviva delle Fonti, Italy
[35]Neurology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy
[36]Neurology Unit, ASO Santa Croce, Cuneo, Italy
[37]"Aldo Ravelli" Center, Department of Health Sciences, University of Milan Medical School & San Paolo University Hospital, ASST Santi Paolo e Carlo Milano, Italy
[38]D.A.P.S. Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[39]Fondazione IRCCS Istituto Neurologico Carlo Besta, Unit of Medical Genetics and Neurogenetics, Milan, Italy
[40]Neurology Unit, Department of Medical, Surgical and Health Sciences, Cattinara University Hospital, ASUGI, University of Trieste, Trieste, Italy
[41]Department of Molecular Medicine, University of Pavia & IRCCS Mondino Foundation, Pavia, Italy

Introduction: Parkinson's disease carriers of GBA mutations/variants (PD-GBA) progress more rapidly with earlier cognitive dysfunction and psychosis[1]. The long-term outcome of STN-DBS in PD-GBA has been questioned[2,3] increasing interest on the risk-benefit profile of alternative device-aided therapies, including levodopa-carbidopa intestinal gel (LCIG).

Objectives: To investigate the safety and efficacy of LCIG in PD, focusing on the effects of GBA status.

Methods: This multicentre, retrospective ‘real-world’ study (n=31 movement disorders units) included PD patients consecutively treated with LCIG. GBA status was defined as carrier, noncarrier, not available. Data were collected prior to LCIG initiation (baseline), after 1 year and at long-term follow-up (5-year and last visit censored up to 10 years). Early dropouts (<1 year) were included.

Results: A total of 511 patients (males 57.9%, age at LCIG 67.0±8.7ys, PD duration at LCIG 12.9±5.0ys) were included, of whom 297 (58.1%) underwent GBA genotyping. Pathogenic variants were detected in 13.1% (39/297). As of Dec/2023, results were available on a subgroup of n=363 cases. At baseline, GBA-PD had younger age at onset, shorter PD duration at LCIG than noncarriers. Cognitive decline was diagnosed in 57% PD-GBA vs. 36% noncarriers ($p<0.001$). Total LEDD was lower in GBA-PD than noncarriers ($p=0.034$). At 1-year follow-up, LCIG improved motor fluctuations and dyskinesias ($p<0.001$), axial complications (axial dystonia, FOG, recurrent falls), psychosis and ICDs. MDS-UPDRS-II and -IV (fluctuations) scores improved significantly less in PD-GBA than noncarriers (test-forinteraction $p<0.05$). Multivariate analysis on the causes of dropout

and adverse events excluded an effect of GBA status. At long-term follow-up up to 10 years, among predictors of dropout (adjusted Cox regression model) GBA status showed a trend towards significance (p=0.073).

Conclusions: This is the largest cohort of PD with LCIG investigated so far. LCIG is relatively safe and effective in GBA-PD, including those with cognitive decline. Nonetheless, close monitoring is recommended.

References:

[1] Cilia R, Tunesi S, Marotta G, et al. Survival and dementia in GBAassociated Parkinson's disease: The mutation matters. Ann Neurol. 2016;80(5):662-673. doi:10.1002/ana.24777.
[2] Pal G, Mangone G, Hill EJ, et al. Parkinson Disease and Subthalamic Nucleus Deep Brain Stimulation: Cognitive Effects in GBA Mutation Carriers. Ann Neurol. 2022;91(3):424-435. doi:10.1002/ana.26302.
[3] Avenali M, Zangaglia R, Cuconato G, et al. Are patients with GBAParkinson disease good candidates for deep brain stimulation? A longitudinal multicentric study on a large Italian cohort. J Neurol Neurosurg Psychiatry. Published online October 25, 2023. doi:10.1136/jnnp-2023-332387.

P147

Co-influence of sex and GBA genotype on the phenotype of Parkinson disease patients

Micol Avenali[1,2], S.P. Caminiti[1], P. Mitrotti[1], I. Palmieri[3], G. Cuconato[4], L. Gallo[1], R. Calabrese[2], C. Galandra[3], R. Zangaglia[2], C. Tassorelli[1,5], E.M. Valente[3,4], F. Blandini[1,6]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation,Pavia, Italy
[3]Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[5]Neurorehabilitation Unit, IRCCS Mondino Foundation,Pavia, Italy
[6]Ca' Granda IRCCS Foundation, Ospedale Maggiore Policlinico, Milan, Italy

Introduction: GBA mutations are a well-known genetic risk factor for PD. We investigated the potential interaction of sex and GBA mutations on the phenotype of patients with Parkinson disease (PD).

Methods: GBA-relatedPD and nonGBA-PD underwent a comprehensive clinical characterization (MDS-UPDRS-I-IV, MOCA, SCOPAUT, UPSIT, RBDSQ, BDI and HADS-A). Clinical scores were compared between PD groups. Clustering analysis based on genetic status, demographic and clinical measures was applied to delineate new subgroups. Subgroup analysis according to GBA mutations severity was also performed.

Results: 53 GBA-PD (56% males) and 83 nonGBA-PD (64% males) were enrolled. Within GBA-PD, 10 subjects carried mild, 18 severe, 15 risk and 10 unknown variants. GBA-PD were similar to nonGBA-PD expect for significantly younger age at disease onset and higher BDI and HADS-A scores. Comparison analysis stratified by sex showed that GBA-PD males diverged significantly from nonGBA-PD males in terms of depressive symptoms, while females were comparable in the two groups. Cluster analysis based on combined clinical parameters allowed splitting the entire sample into 2 clusters, which discriminated mainly nonGBA-PD males (Cluster1), from the remaining groups (all females and GBA-PD males - Cluster 2). Dysautonomia, mood and sleep disorders were the most relevant features influencing the clustering process. Interestingly, a significantly higher proportion of mild and severe GBA mutations belonged to Cluster 1, while most of risk variants fell in Cluster 2.

Conclusions: This study highlights the intricate interplay between sex, genetic status, and non-motor features of PD. In this cohort, GBA status was associated with distinct non-motor features (particularly mood disorders), with overt sex-related differences. While these data warrant replication in independent cohort, they emphasize that the interplay of sex and genetic status need to be considered when stratifying PD patients, for improving more accurate precision medicine approaches.

P148

Determination of ambroxol in human plasma and cerebrospinal fluid by online solid-phase extraction coupled with liquid chromatography-tandem mass spectrometry in Parkinson's disease patients with GBA mutations

Pierfrancesco Mitrotti[1], V. Franco[2,3], F. Colucci[4], R. De Micco[5], M. Palmisani[2,3], S. Aloisio[5], F. Cazzaniga[8], S. Cerri[3], G. Cuconato[6], G. Devigili[4], D. Franciotta[3], A.E. Elia[4], B. Garavaglia[7], N. Golfrè Andreasi[4], F. Invernizzi[7], V. Leta[4], F. Moda[8], M. Picascia[3], C. Reale[7], L.M. Romito[4], M. Siciliano[5], R. Stiuso[3], R. Eleopra[4], A. Tessitore[5], E.M. Valente[3,6], M. Avenali[1,3*], R. Cilia[4*]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy
[3]IRCCS Mondino Foundation, Pavia, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[5]University of Campania "Luigi Vanvitelli", Naples, Italy
[6]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[7]Fondazione IRCCS Istituto Neurologico Carlo Besta, Unit of Medical Genetics and Neurogenetics, Milan, Italy
[8]Fondazione IRCCS Istituto Neurologico Carlo Besta, Unit of Neurology 5 and Neuropathology, Milan, Italy
*joint senior authorship

Introduction: Heterozygous mutations in the betaglucosylceramidase gene (GBA) are the primary risk factor for Parkinson's Disease (PD). These mutations reduce glucocerebrosidase (GCase) enzymatic function promoting the accumulation of alphasynuclein fibrils (alpha-syn) in the central nervous system (CNS). Administration of ambroxol at dose of 1260 mg per day in humans allows it to reach the CNS, increasing GCase levels in cerebrospinal fluid (CSF) and modifying alpha-syn concentrations [1]. We developed a new method to monitor ambroxol levels in plasma and CSF using automated online solid-phase extraction coupled with liquid chromatography-tandem mass spectrometry (LC-MS).

Methods: Ambroxol was determined by online solid-phase extraction coupled with LC-MS under gradient conditions. The method was applied to monitor plasma samples obtained from PD patients randomized to receive oral ambroxol (1200 mg/day, n=30) or placebo (n=30), collected at 26 and 52 weeks (V3 and V5 respectively) from the beginning of the treatment, at 26 weeks (V6) after the end of the treatment, and CSF at 52 weeks (V5).

Results: The calibration curves for ambroxol were linear (r =0.999) in the range of 50–3000 ng/mL in plasma and 10-300 ng/mL in CSF. Recovery was within 107-113% in plasma and 99-103% in CSF. No significant matrix effect was observed. The intra-day and inter-day precisions were below 12% in both matrices. The intra-day and interday accuracy were within 90-103% in plasma and 96-106% in CSF. Mean ambroxol concentrations were 1174 ng/mL in plasma at V3 (n=25), 1211 ng/mL in plasma at V5 (n=12), not detectable in plasma at V6 (n=12) and 108 ng/mL in CSF at V5 (n=10).

Conclusions: The developed method was successfully validated according to EMA guidelines and its applicability confirmed in a multicenter, randomized, double-blind, placebo-controlled, phase two study to monitor ambroxol levels in plasma and CSF of GBA-PD [2].

References:

[1] Mullin S, et al. Ambroxol for the Treatment of Patients With Parkinson Disease With and Without Glucocerebrosidase Gene Mutations: A Nonrandomized, Noncontrolled Trial. JAMA Neurol. 2020;77(4):427-434.
[2] Colucci F, et al. Ambroxol as a Disease-Modifying Treatment to Reduce the Risk of Cognitive Impairment in GBA-Associated Parkinson's Disease: a Multicentre, Randomised, Double-blind, Placebo-Controlled, Phase II Trial. The AMBITIOUS Study Protocol. BMJ Neurol Open. 2023;5(2):e000535.

P149

NUS1 and progressive myoclonus ataxia: same gene, different pathogenic mechanisms

Luca Magistrelli[1], E. Contaldi[1], S. D'Alfonso[2], L. Corrado[2], F. Biella[3], E. Monfrini[3,4], A.B. Di Fonzo[4], G. Pezzoli[1], I.U. Isaias[1]

[1]Parkinson Institute Milan, ASST G. Pini-CTO, Milan, Italy
[2]Department of Health Sciences, University of Piemonte Orientale, 28100 Novara, Italy
[3]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation University of Milan, Milan Italy
[4]Neurology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan Italy

Introduction: Progressive myoclonus ataxia (PMA) is a rare condition characterized by multifocal myoclonus, gait ataxia and cognitive decline. Mutations in NUS1 have been recognized as possible cause.

Objectives: To describe two patients with NUS1 -related PMA presenting different clinical and genetic characteristics.

Patients: Patient 1: Fifty-five-year-old woman with ataxic gait and myoclonic jerks in the upper limbs started at forty. Her mother presented a similar condition (no assessment available). Brain MRI: unremarkable. Neurological examination: wide based gait, myoclonic jerks in upper, lower limbs and trunk increased by the tactile stimulus. Ocular movements: lowered saccades in all directions and pursuits fragmentation. Furthermore, ideo-motor apraxia in the upper limbs, impaired left-right recognition and marked cognitive decline. Whole exome sequencing: c.490delT(NM_138459.5) p.Cys164fs frameshift mutation in NUS1. This mutation could introduce a premature translation-termination codon (PTC) prone to the nonsense mediated decay (NMD) mechanisms which recognizes and degrades transcripts harbouring a PTC, thus preventing the production of C-terminally truncated proteins.

Patient 2: Seventy-year-old woman with diffuse myoclonic jerks involving the head and four limbs, started at the age of two, which progressively affected her gait leading to wheelchair. She presented a severe cognitive delay: she never concluded primary school. Neurological examination: myoclonic jerks involving head and four limbs, dysmetria, hypodiadocokynesia in the upper limbs and marked dysarthric speech. Family history: unremarkable. She presented dysmorphic features: broad nasal tip and long philtrum. Brain MRI: mild diffuse cortical atrophy and cerebellar vermis hypoplasia.
Genetic analysis: heterozygous deletion [6q22.1-q22.31 (118,051,261-120,084,595)], located 20 kb downstream NUS1. We assessed gene's transcript level starting from patient's blood mRNA: NUS1 expression was significantly lower compared to healthy controls, suggesting the loss of a regulatory element located across the deleted region.

Conclusions: These cases confirm as NUS1 expression reduction could have a role in PMA. The different clinical manifestations could be related to the impact of the two different genetic mutations. Clinician should be aware of these rare and complex scenarios in suspected PMA.

P150

A new potential pathogenetic mutation of the ADCY-5 gene in an Italian family

Martina Patera[1], A. Zampogna[1], F. Asci[1], M. Falletti[1], G. Pinola[1], R. Campopiano[2], S. Gambardella[2], A. Suppa[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy

Introduction and Objectives: Adenylyl cyclase 5 (ADCY5) related-dyskinesia is a rare disorder characterized by early-onset paroxysmal choreoathetosis, dystonia, myoclonus, with heterogenous phenotype [1,2]. Both sporadic and inherited cases have been reported and most of the familiar syndromes are autosomal dominant. Thanks to advanced sequencing techniques, the genetic spectrum of this disorder is still expanding [3]. We present a new potential pathogenetic mutation of the ADCY-5 gene in an Italian family.

Methods: A 30-years old patient presented to our outpatient clinic complaining about cervical dystonia and blepharospasm, exacerbated by stress and lack of sleep. His symptoms developed in adolescence with head tremor and progressive stiffness of the neck, later evolved in clear cervical dystonia. His mother presented head tremor and mild cervical dystonia since her early adulthood. His grandmother, decease at 83 years old, presented the same phenotype. A thorough clinical evaluation of the patient identified frequent ocular myokymias and segmental cervicobrachial dystonia. Suspecting a genetic-determined dystonia we performed genetic testing for most common dystonic and choreic syndromes, followed by an exome Next Generation Sequencing analysis (NGS).

Results: The NGS revealed a de novo c.2177C>T p.(Ala726Val) mutation in the ADCY5 gene, presented in heterozygosis in both the patient's and his mother's DNA. This missense change involves an amino acid residue at the same position as another pathogenic missense change (p.Ala726Thr). There are no information on its allelic frequency in the dedicated database (GnomAD) and computational software in silico suggests a detrimental effect of the reported mutation on the resulting protein. Therefore, the mutation satisfied the ACMG criteria for a novel potential pathogenetic variant [4].

Conclusions: The spectrum of ADCY5-related disorders is expanding. Herein, we reported a new potential pathogenetic variant of the ADCY-5 gene. Further analysis will be required for pathogenicity confirmation, such as epidemiological or biochemical functional studies.

References:

[1] P. J. Menon et al., "Scoping Review on ADCY5 -Related Movement Disorders," Mov. Disord. Clin. Pract., vol. 10, no. 7, pp. 1048–1059, Jul. 2023, doi: 10.1002/mdc3.13796.
[2] N. Vijiaratnam, K. P. Bhatia, A. E. Lang, W. H. Raskind, and A. J. Espay, "ADCY5–Related Dyskinesia: Improving Clinical Detection of an Evolving Disorder," Mov. Disord. Clin. Pract., vol. 6, no. 7, pp. 512–520, Sep. 2019, doi: 10.1002/mdc3.12816.
[3] A. Ferrini, D. Steel, K. Barwick, and M. A. Kurian, "An Update on the Phenotype, Genotype and Neurobiology of ADCY5-Related Disease," Mov. Disord., vol. 36, no. 5, pp. 1104–1114, May 2021, doi: 10.1002/mds.28495.
[4] S. Richards et al., "Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology," Genet. Med., vol. 17, no. 5, pp. 405–424, May 2015, doi: 10.1038/gim.2015.30.

P151

Is it time for a new clinical entity for Huntington's Disease in intermediate allele carriers? A case report of a 55-yo man with clinical manifestations of HD, a 28 CAG repeats expansion plus and a variant of uncertain significance

Giuliano Fernando Patanè[1], M.A. De Rosa[1,2], D. Calisi[1], P. Quintieri[1], M.V. De Angelis[3], S.L. Sensi[1,2,4]

[1]Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti-Pescara, Chieti, Italy
[2]Molecular Neurology Unit Centre for Advanced Sciences and Technology (CAST) and ITAB - Institute for Advanced Biomedical Technologies, "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy
[3]Stroke Unit, "Santo Spirito" Hospital, Pescara, Italy
[4]Neurology University Unit SS Annunziata Hospital of the "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

Introduction: Huntington's Disease (HD) is a neurodegenerative disorder caused by the expansion of the triplet CAG in the exon 1 of the huntingtin gene (HTT). A length ≥ of 36 CAG repeats is pathogenic, while a reduced penetrance occurs for expansion with 36-39 units. However, there is an increasing literature, albeit limited, describing intermediate allele (IA, i.e., 27-35 CAG repeats) carriers with a clinical presentation overlapping that of the pathogenic allele carriers [1,2].

Case report: A 55-year-old man came to our attention for worsening axial dystonia. The patient has a positive history of type 1 bipolar disorder treated with antipsychotics. He presented mild extrapyramidal signs and episodes of head-neck dystonia. Choreic movements were also present, and a genetic test for HD was therefore performed. The test revealed the presence of an intermediate allele, particularly with 28±1 CAG repeats in the gene HTT and a variant of uncertain significance (VUS) in the Juctophilin 3 gene (JPH3).

Discussion: Our report supports the growing literature on a new HD related clinical entity [3]. Given the relatively young age of our patient, the case poses new questions on the inverse correlation between length expansion and age at onset in the context of contributing factors like VUS. Finally, the case unravels new ethical issues associated with genetic testing in relatives of IA carriers.

References:

[1] Jevtic SD, Provias JP. Case report and literature review of Huntington disease with intermediate CAG expansion. BMJ Neurol Open. 2020;2(1):e000027.
[2] Langbehn DR, Brinkman RR, Falush D, Paulsen JS, Hayden MR, International Huntington's Disease Collaborative Group. A new model for prediction of the age of onset and penetrance for Huntington's disease based on CAG length. Clin Genet. 2004 Apr;65(4):267–77.
[3] Savitt D, Jankovic J. Clinical phenotype in carriers of intermediate alleles in the huntingtin gene. J Neurol Sci. 2019 Jul 15;402:57–61.

P152

An uncommon clinical presentation of GBA mutation in an Italian family

Cristiano Sorrentino, G. Dati, S. Cuoco, P. Barone, M.T. Pellecchia

Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Salerno, Italy

Introduction: Heterozygous mutations in GBA gene are known as the most common genetic risk factor for Parkinson's disease (PD) [1]. The protein transcribed by GBA is GCase [2] and increase of glucosylceramide, the GCase substrate, may lead to asynuclein accumulation [3].

Objectives: We herein describe a family carrying a mutation of GBA with several affected members presenting different phenotypes resembling both synucleinopathies and non-synucleinopathies.

Methods: Patients underwent to neurological and neuropsychological evaluation, structural and functional imaging, followed by genetic analyses.

Results: The first patient, a 76 year-old woman referred to our movement disorders outclinic for 2-year history of gait impairment, falls and motor slowness, already treated with levodopa with partial response. The neurological examination showed an asymmetric parkinsonism with vertical supranuclear gaze palsy (VSNGP), left alien limb phenomenon and cognitive impairment. Her MRI showed a diffuse corticosubcortical and midbrain atrophy while FDG-PET showed right fronto-temporo-parietal hypometabolism. She presented a positive familiar history for movement disorders and cognitive deterioration. Her deceased older sister had been diagnosed with CBS and clinical reports were collected; the younger brother had been diagnosed with Parkinson's disease-dementia with good response to levodopa. We visited another sister only reporting depressive symptoms and found she had a clear dementia (MMSE 18/30) assessed by comprehensive neuropsychological battery, gait apraxia and VSNGP. In the case index NGS panel was run showing the presence of heterozygous variant c.882T>G of GBA gene. Enzymatic activity of GCase resulted in the pathological range (2.5 nmol/h/ml). The same variant has been demonstrated with Sanger sequencing in the two affected living siblings.

Conclusions: This case series remarks the phenotypic heterogeneity of the GBA mutation. CBS associated to GBA mutation has been rarely described, however, to our knowledge this is the first family showing such an intra-familiar variability ranging from CBS to PDD to dementia as the presenting phenotype.

References:

[1] Beavan MS et al. Glucocerebrosidase mutations and the pathogenesis of Parkinson disease. AnnMed 2013
[2] Liou B et al. Analyses of variant acid beta-glucosidases: effects of Gaucher disease mutations. J Biol Chem. 2006.
[3] Mazzulli JR et al. Gaucher disease glucocerebrosidase and alphasynuclein form a bidirectional pathogenic loop in synucleinopathies. Cell. 2011.

P153

Progranulin and neurodegenerative diseases: the clinical case of a patient diagnosed with Parkinson's disease and heterozygous mutation for the progranulin gene

Francesca Piattellini[1,2], S. Valente[1,2], D. Greco[1,2], G. Grigioni[1,2], A. Iacono[1,2], A. Govoni[1], L. Caremani[1], A. Caciotti[3], F. Feo[3], R. Tonin[3], A. Morrone[2,3], S. Ramat[1]

[1]Parkinson Unit, Department of NeuroMuscular–Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[2]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[3]Laboratory of Molecular Biology of Neurometabolic Diseases, Neuroscience Department, Meyer Children's Hospital, IRCCS, Florence, Italy

Introduction: Progranulin (PGRN) is a secretory glycoprotein encoded by the granulin (GRN) gene. Mutations in the GRN gene can cause reduction of protein levels. Heterozygous mutations are related to familial frontal temporal lobar degeneration, while homozygous mutations cause the complete loss of PGRN which lead to a lysosomal storage disease (LSD) known as neuronal ceroid lipofuscinosis (NCL). Mutations that reduce progranulin levels are generally associated with an increased risk of developing neurodegenerative diseases, such as Amyotrophic lateral sclerosis, Parkinson's Disease and Alzheimer Disease.

Objectives: We present the case of a 75-year-old woman diagnosed with Parkinson's disease and carrying heterozygous mutation in the GRN gene.

Methods: Patient was enrolled in the Lysolate study designed to identify late onset lysosomal storage diseases in subjects with neurodegenerative disorders. Blood samples from enrolled patients are studied using a Next Generation Sequencing (NGS) panel including more than 65 genes involved in LSD.

Results: Patient arrived at our attention at the age of 64-years-old for extrapyramidal signs characterized by a recent appearance of generalized motor slowing, hindrance to fine movements with the right hand and micrography; she reported also to suffer from diabetes mellitus, depressive syndrome, IgG3 deficit, allergic asthma, pulmonary emphysema, fibrinous pericarditis, Hashimoto's thyroiditis and diffuse osteoarthritis. Brain-MRI showed nonspecific point-like changes in the bilateral white matter, while 123Ioflupane SPECT revealed a reduction in the putamen uptake, more pronounced on the left side. Interestingly the NGS analysis revealed heterozygous c.893G>A, p.(Arg298His) mutation in the GRN gene, for which there is a known association with neurodegenerative disorders.

Conclusions: The association between GRN mutation and parkinsonism is documented in literature, and different extrapyramidal phenotypes associated with the same GRN mutation are reported. The following case shows an association between Parkinson's disease and GRN gene mutation, increasing the knowledge of possible phenotypic spectrum.

P154

ABCD1-related Hereditary Spastic Paraparesis: a case report

Giulia Pinola[1], A. Zampogna[1], F. Asci[1], M. Patera[1], M. Falletti[1], R. Campopiano[2], S. Gambardella[2], A. Suppa[1,2]

[1]Dipartimento di Neuroscienze Umane, Sapienza Università di Roma, Roma, Italy
[2]IRCSS Neuromed, Pozzilli, Italy

Introduction: Adrenoleukodystrophy, an X-linked neurometabolic disorder associated with mutations in the ABCD1 gene, leads to impaired betaoxidation and peroxisomal accumulation of very long-chain fatty acids. The disease manifests with many different phenotypes based on patients' age and gender [1,2]. We here report a Moldavian family including 4 women manifesting adult-onset spastic paraparesis [3].

Objective: The patients experienced dysesthesias and paraesthesia in lower limbs since the average age of 38, progressively accompanied by limb weakness, postural instability, and varying degrees of urinary urgency. Two of them had undergone surgery for orthopedic issues associated with gait disturbances and their family history revealed male infant cousins who succumbed during fever episodes. Neurological examination showed mild spastic paraparesis, brisk lower limb reflexes, lower limb extremity hypopallesthesia or pain, and bilateral Babinski sign.

Methods: An investigatory work up for the differential diagnosis of spastic paraparesis was conducted, including genetic testing. A cognitive and psychological evaluation was also performed in three of them, revealing the presence of depression and anxiety.

Results: Brain and spinal MRI, laboratory tests, and cerebrospinal fluid analysis were unremarkable. Conversely, nerve conduction studies and motor evoked potentials indicated mild sensorimotor axonal neuropathy and increased central motor conduction. Lastly, the c.1661G>A (p.Arg554His) mutation in the ABCD1 gene was identified, confirming the diagnosis of adrenoleukodystrophy [4].

Conclusion: Adrenomyeloneuropathy (AMN) stands as the primary clinical phenotype associated with ABCD1 gene mutations in women. A meticulous medical history investigation is essential to reach the correct diagnosis in women presenting with spastic paraparesis. Specifically, the different impact of ABCD1 gene mutations in males versus females and the role of infections as precipitating factors in male children serve as crucial diagnostic clues for X-linked metabolic disorders. Furthermore, neuropsychological assessment should also be conducted since psychiatric symptoms may also be expression of the AMN-like phenotype.

References:

[1] Engelen M, Barbier M, Dijkstra IM, Schür R, de Bie RM, Verhamme C, Dijkgraaf MG, Aubourg PA, Wanders RJ, van Geel BM, de Visser M, Poll-The BT, Kemp S. X-linked adrenoleukodystrophy in women: a cross-sectional cohort study. Brain. 2014 Mar;137(Pt 3):693-706. doi: 10.1093/brain/awt361. Epub 2014 Jan 29. PMID: 24480483.
[2] Jangouk P, Zackowski KM, Naidu S, Raymond GV. Adrenoleukodystrophy in female heterozygotes: underrecognized and undertreated. Mol Genet Metab. 2012 Feb;105(2):180-5. doi: 10.1016/j.ymgme.2011.11.001. Epub 2011 Nov 10. PMID: 22112817.
[3] Campopiano R, Femiano C, Chiaravalloti MA, Ferese R, Centonze D, Buttari F, Zampatti S, Fanelli M, Amatori S, D'Alessio C, Giardina E, Fornai F, Biagioni F, Storto M, Gambardella S. A Large Family with p.Arg554His Mutation in ABCD1: Clinical Features and Genotype/Phenotype Correlation in Female Carriers. Genes (Basel). 2021 May 19;12(5):775. doi: 10.3390/genes12050775. PMID: 34069712; PMCID: PMC8160645.

[4] Coll MJ, Palau N, Camps C, Ruiz M, Pàmpols T, Girós M. X-linked adrenoleukodystrophy in Spain. Identification of 26 novel mutations in the ABCD1 gene in 80 patients. Improvement of genetic counseling in 162 relative females. Clin Genet. 2005 May;67(5):418-24. doi:10.1111/j.1399-0004.2005.00423.x. PMID: 15811009.

P155

The possible role of progranulin mutations in the development of Parkinson's disease: a case report

Giulia Grigioni[1,2], A. Govoni[1], L. Caremani[1], F. Piattellini[1,2], S. Valente[1,2], D. Greco[1,2], A. Iacono[1,2], A. Caciotti[3], F. Feo[3], R. Tonin[3], A. Morrone[2,3], S. Ramat[1]

[1]Parkinson Unit, Department of NeuroMuscular–Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[2]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[3]Laboratory of Molecular Biology of Neurometabolic Diseases, Neuroscience Department, Meyer Children's Hospital, IRCCS, Florence, Italy

Introduction: Progranulin, encoded by GRN gene, is a protein that regulates lysosomal function, inflammation and stress response and so plays a role in the development, survival and function of neurons and microglia. Homozygous and heterozygous GRN loss-of-function mutations cause ceroid lipofuscinosis neuronal type 11 and frontotemporal dementia respectively, while mutations that reduce progranulin levels increase risk for developing other neurodegenerative diseases such Alzheimer's disease and Parkinson's disease.

Objectives: To present the case of a patient with extrapyramidal syndrome, myositis and sensitivity disorders enrolled in a the Lysolate study. This research project is funded by Tuscany Region.

Methods: The Lysolate study investigates the presence of late onset lysosomal storage diseases (L S D s) in patients with neurodegenerative symptoms and multiorgan involvement. Patients enrolled in the study were analysed using a Next Generation Sequencing (NGS) panel including more than 65 genes involved in LSDs.

Results: We present the case of a woman who suffers from extrapyramidal syndrome since she was 58, which began with postural and rest tremor exacerbated by emotional stress. Neurological symptoms progressively worsened to include widespread muscle pain, hypoesthesia and paresthesias in left hemisome, dysphagia and postural instability which leaded to walking impairment. She also suffered from recurrent headache, mood disorders, bronchial asthma, Sjogren's syndrome, fibromyalgia, multidistrict arthrosis, osteoporosis, discopathy, maculopathy and retinal infarction, an acute cardiac infarction, vescicouterine prolapse, dolichocolon and contact eczema. Brain MRI highlighted microlacunar vascular lesions, cortical atrophy and frontal hyperostosis. Bran 123I-Ioflupane SPECT showed a degeneration of the nigrostriatal system. Electromyography revealed a chronic myositis. The NGS analysis showed that she was heterozygous for the known pathogenic c.796G>C variant in the GRN gene leading to p. (Ala266Pro).

Conclusions: This case confirms the role of progranulin in the development of neurodegenerative diseases and increases knowledge of the phenotypic manifestations associated with GRN mutations.

P156

Parkinson's disease and chronic inflammatory demyelinating polyneuropathy: broadening the clinical spectrum of VCP mutations?

Francesca Vignaroli[1], S. Gallo[2], F. Colombatto[1], E. Contaldi[3], C. Comi[4], L. Magistrelli[3]

[1]Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[2]Neurology Unit, SS. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy
[3]Movement Disorders Centre, Gaetano Pini-CTO Hospital, Milano, Italy
[4]Neurology Unit, S. Andrea Hospital, Department of Translational Medicine, University of Piemonte Orientale, Vercelli, Italy

Introduction: Valosin-containing protein (VCP) mutation is associated to a multiorgan disease called inclusion body myopathy associated with Paget disease and frontotemporal dementia and, more rarely, to Charcot-Marie-Tooth disease type 2, hereditary spastic paraplegia and Parkinson's disease (PD) [1].

Objectives: We present a case of a patient with a co-occurrence of an early-onset PD and chronic inflammatory demyelinating polyneuropathy (CIDP) in which a new mutation in VCP has been detected. So far only another case of CIDP due to VCP mutation has been described [2].

Methods: A 40 years-old man with a progressive onset of cramps, fasciculations and weakness of the lower limbs that leads to gait difficulties, was evaluated in the Movement Disorders Centre of Novara.

Results: Neurological examination showed a mild reduction of bilateral legs strength, normal sensitivity and bilaterally reduced ankle jerk. The electroneurography revealed a motor symmetric demyelinating neuropathy of lower limbs sparing the sensitive branches and the upper arms. CSF analysis detected albumincytological dissociation. Accordingly, a diagnosis of atypical definite CIDP [3] was made. The muscular biopsy confirmed a neurogenic chronic pattern without myopathic signs. After an unsuccessful steroid therapy, a monthly intravenous immunoglobulin therapy was started with moderate benefit. The clinical and electromyographical picture worsened over the years with a diffuse muscular atrophy and a progressive worsening of the demyelinating polyneuropathy with sensorial involvement and conduction blocks that after 14 years involved the upper limbs. When the patient was 49 years old, a parkinsonian syndrome appeared. He presented with hypomimia, mild bilateral bradykinesia, minimal resting tremor and plastic rigidity. A 123I-FP-CIT SPECT confirmed the depletion of dopaminergic pathways supporting the diagnosis of clinically established PD. The Whole Exome Sequencing examination showed a novel mutation in the VCP gene: c.1106T>C.

Conclusions: We described a case of a patient carrying a novel VCP mutation presenting with CIDP and early-onset PD broadening the clinical spectrum of possible VCP gene mutations phenotypes.

References:

[1] C. C. Weihl, A. Pestronk, and V. E. Kimonis, "Valosin-containing protein disease: Inclusion body myopathy with Paget's disease of the bone and fronto-temporal dementia," Neuromuscular Disorders, vol. 19, no. 5, pp. 308–315, May 2009, doi: 10.1016/j.nmd.2009.01.009.
[2] T. Ando et al., "The wide-ranging clinical and genetic features in Japanese families with valosin-containing protein proteinopathy," Neurobiology of Aging, vol. 100, p. 120.e1-120.e6, Apr. 2021, doi: 10.1016/j.neurobiolaging.2020.10.028.

[3] R. A. C. Hughes et al., “European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society,” Eur J Neurol, vol. 13, no. 4, pp. 326–332, Apr. 2006, doi: 10.1111/j.1468-1331.2006.01278.x.

P157

Biallelic expansion of an intronic repeat in RFC1: a common cause of late-onset ataxia

Martina D'Anna[1], R. De Micco[1], E.N. Mosca[1], M. Cirillo[1], A. Tessa[2], G. Tedeschi[1], F.M. Santorelli[2], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]Molecular Medicine for Neurodegenerative and Neuromuscular Diseases Unit, IRCCS Fondazione Stella Maris, Pisa, Italy

Introduction: We report a case of Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia Syndrome (CANVAS).

Objectives: A 73-years-old woman referred to our outpatient clinic for a 20-years history of slowly progressive gait ataxia and postural instability. She also referred episodic dizziness (triggered by rapid head movements), distal numbness and cramps in the lower limbs, and dry cough. Familiar history was positive for gait disorder in her brother. Neurological examination showed wide based ataxic gait, positive Romberg sign with retropulsion and tendency to fall at eye closure, mild bilateral limb ataxia, horizontal/rotatory nystagmus in lateral gaze, lower limbs areflexia, bilateral decreased quantitative vibration below the iliac crest, bilateral distal decreased tactile sensitivity in the lower limbs, positive head impulse test.

Methods: Brain MRI showed cerebellar atrophy, particularly of vermis. MRI of the spinal cord demonstrated abnormal hyperintense signal changes on T2-weighted imaging of the posterior columns in the cervical spine. Neurophysiological assessment showed severe sensory axonal polyneuropathy. Halmagyi test revealed bilateral vestibular dysfunction. Genetic testing for most frequent genetic ataxia was performed.

Results: Genetic testing revealed a biallelic AAGGG expansions in the second intron of replication factor complex subunit 1 (RFC1) supporting the diagnosis of CANVAS.

Conclusions: CANVAS is one of the most frequent autosomal recessive late-onset ataxia [1]. It is characterized by slowly progressive ataxia with associated sensory neuropathy and vestibular impairment [1]. Chronic cough is also frequently reported [1]. This case highlights the relevance of clinical history and examination to drive the diagnostic work-up of rare genetic disorders [2]. In the presence of late-onset gait ataxia it is important to look for the presence of supportive signs and symptoms, such as chronic cough, peripheral nervous system involvement and vestibular dysfunction, in order to consider the diagnosis of CANVAS [3].

References:

[1] "Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS): genetic and clinical aspects"; Andrea Cortese, Riccardo Curro', Elisa Vegezzi, Wai Yan Yau, Henry Houlden, Mary M Reilly; Pract Neurol 2022; 22:14–18. Neurol Clin Pract 2016; 6:61–68.
[2] "Update on Cerebellar Ataxia with Neuropathy and Bilateral Vestibular Areflexia Syndrome (CANVAS)"; Mathieu Dupré, Ruben Hermann & Caroline Froment Tilikete; The Cerebellum 2021; 20:687–700.
[3] "Proposed diagnostic criteria for cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS)"; David J. Szmulewicz, Leslie Roberts, Catriona A. McLean, Hamish G. MacDougall, G. Michael Halmagyi, and Elsdon Storey.

P158

Expanding phenotype of LRRK2 G2019S mutation: case description of two sisters showing peculiar phenomenological traits

Sandy Maria Cartella, S. Neri, G.M. Foti, G. Cartella

Movement Disorders Centre, Department of Neurology, Policlinico "Madonna della Consolazione", Reggio Calabria, Italy

Introduction: LRRK2 is the most common risk gene for Parkinson's disease (PD) [1,5]. Its typical phenomenology is indistinguishable from idiopathic PD, except for a milder course and a less common non-motor involvement [1-4].

Objectives: The aim of this report is to describe LRRK2 phenomenology, including clinical presentation and disease course. We describe two sisters, one presenting with cervical dystonia (CD) and the other one presenting with typical parkinsonian features, although showing prominent non-motor fluctuations.

Case reports: A 80-year old lady was referred to our outpatient clinic due a 2-year history of head tremor. She showed cervical dystonia characterized by head tremor, inclination to the left side, left shoulder elevation, head rotation to the right, antecollis, retrocaput and limitation of range of motion. She had mirror movements and overflow while performing tasks with both upper limbs, dystonic posture and postural tremor of the upper limbs. Her gait was characterized by normal stride length and reduced velocity, with no arm swing on the righthand side. She had positive family history for Parkinson's disease (two of her mother's siblings, one of her father's and 5 of her own). Her sister was a 83-year old lady, who had been diagnosed with Parkinson's disease 8 years previously. Her major complaints were related to her non-motor fluctuations: her OFF phases were characterized by severe anxiety, pain and crying crisis. We run genetic testing for both patients and found the CD one to be a heterozygotic carrier of G2019S mutation and the PD sister to be a homozygotic carrier of the same mutation. We added safinamide and duloxetine to the treatment of the PD sister, with a major impact on non-motor fluctuations and QoL, and decided to treat the CD sister with levodopa/carbidopa, with considerable clinical improvement.

Conclusions: Our cases show that LRRK2 G2019S may have variable clinical presentation, including CD, and it can show prominent non-motor fluctuations. Our data may contribute to expanding LRRK2 phenotype and providing insights on its clinical course and treatment.

References:

[1] Ito G, Utsonomyia-Tate N, Overview of the impact of pathogenic LRRK2 mutations in Parkinson's Disease, Biomolecules 2023, 13, 845. https://doi.org/10.3390/biom13050845.
[2] Kestenbaum M, Alcalay RN, Clinical features of LRRK2 carriers with Parkinson's Disease, Advances in Neurobiology 14, DOI 10.1007/978- 3-319-49969-7_2.
[3] Saunders-Pullman R, Raymond D, Elango S, LRRK2 Parkinson's Disease, [Updated 2023 Jul 6]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023.
[4] Shu L, Zhang Y, Pan H, Xu Q, Guo J, Tang B, Sun Q, Clinical heterogeneity among LRRK2 variants in Parkinson's Disease: a metaanalysis, Front. Aging Neurosci. 10:283. doi: 10.3389/fnagi.2018.00283.
[5] Simpson C, Vinikoor-Imler L, Nassan FL, Shirvan J, Lally C, Dam T, Maserejian N, Prevalence of ten LRRK2 variants in Parkinson's Disease: a comprehensive review, Park Rel Dis 98 (2022) 103-113.

P159

Increased neurosteroids serum levels in Parkinson's disease patients with heterozygous GBA mutation compared to idiopathic Parkinson's disease patients: a case control study

Francesco Cavallieri[1], C. Lucchi[2], E. Monfrini[3], S. Grisanti[4], V. Fioravanti[1], G. Toschi[1], G. Di Rauso[1,4], J. Rossi[1,4], T. Trenti[5], A.B. Di Fonzo[3], G. Biagini[2], F. Valzania[1]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USLIRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[3]Neurology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[4]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[5]Department of Laboratory Medicine and Pathological Anatomy, NOCSAE Hospital, AUSL Modena, Modena, Italy

Introduction: Neurosteroids are pleiotropic molecules produced by neurons and glial cells which play an important role in modulating several central nervous system functions including neuronal growth, brain development, synapse formation, neural transmission, myelination, neurogenesis, dendritic growth, neuronal survival, and neuroinflammation.

Objectives: To assess and compare levels of serum neurosteroids in a cohort of consecutive Parkinson's Disease (PD) patients with heterozygous glucocerebrosidase (GBA) mutation (GBA-PD) compared with an age, sex, disease stage, and comorbidity-matched cohort of consecutive idiopathic (I) PD patients (I-PD).

Methods: A consecutive cohort of GBA-PD patients has been paired for age, sex, disease duration, Hoehn & Yahr stage, and comorbidities (Charlson Comorbidity Index) with a cohort of consecutive I-PD patients. Clinical assessment included the MDS-UPDRS scale and the Montreal Cognitive Assessment (MoCA). Serum samples were processed to remove endogenous phospholipids and eluates were analyzed by liquid chromatography coupled with triple quadrupole mass spectrometry. Clinical scores and neurosteroid levels were compared by the Fisher'sexact test and the Student's t-test. Correlation analyses were performed by calculating the respective Spearman's ρ values and their significance level.

Results: Twenty-two GBA-PD (age: 63.68 years; MDS-UPDRS III: 35.41; MoCA: 22.73) and 22 I-PD (age: 63.05 years; MDS-UPDRS III: 29.68; MoCA: 21.82) patients were included. Compared to I-PD, GBA-PD patients showed more hallucinations and psychosis ($p<0.05$), higher MDS-UPDRS part II score ($p<0.05$), and higher PIGD subscores ($p<0.05$). Levels of almost all the evaluated neurosteroids were significantly higher in the GBA-PD cohort when compared to I-PD ($p<0.05$ t-test). This finding was associated with a statistically significant correlation between disease duration and allopregnanolone ($p<0.05$, $\rho=0.38$) and pregnanolone ($p<0.01$, $\rho=0.58$) levels in GBA-PD.

Conclusions: This pilot study shows for the first time the presence of significantly higher neurosteroids peripheral levels in the GBA-PD cohort. Their possible involvement in the psychiatric symptoms deserves further attention.

P160

Evidence of predominant parasympathetic dysautonomia in GBA associated Parkinson's disease

Tiziana De Santis[1], A. Cocco[1], P. Polverino[1], S. Lalli[1], E.M. Valente[2,3], A. Albanese[1,4]

[1]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Italy
[2]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[3]Neurogenetics Research Center, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Neuroscience, Catholic University, Milano, Italy

Introduction: There is scattered evidence that Parkinson's disease (PD) patients carrying variants in the GBA gene (GBA-PD) have an increased risk of autonomic disturbances [1-4].

Objectives: To objectively assess cardiovascular autonomic function in GBA-PD patients compared to patients with no variants in any PD-related gene (I-PD).

Methods: All patients underwent a battery of autonomic tests including head-up tilt test, deep breathing, and Valsalva maneuver. The occurrence and the severity of dysautonomia were graded using the cardiovascular section of the Composite Autonomic Severity Score (cv-CASS) [5]. 123I-MIBG was retrospectively assessed. The analysis of Heart Rate Variability was performed on ECG recordings [6]. Sympathetic noradrenergic and parasympathetic indexes were compared in the two groups.

Results: The parasympathetic autonomic scores from the autonomic battery were more impaired in the GBA-PD group. Heart rate variability indexes confirmed these results.

Conclusions: This study confirms that GBA-PD patients have a higher incidence of cardiovascular autonomic involvement compared to I-PD patients and specifically points to impairment of the parasympathetic branch.

References:

[1] Cilia R, Tunesi S, Marotta G, et al. Survival and dementia in GBAassociated Parkinson's disease: The mutation matters. Ann Neurol 2016;80:662-673.
[2] Carandina A, Lazzeri G, Rodrigues GD, et al. Dysautonomia inParkinson's Disease: Impact of Glucocerebrosidase Gene Mutations on Cardiovascular Autonomic Control. Frontiers in Neuroscience 2022;16:842498.
[3] Usnich T, Hanssen H, Lohmann K, et al. Pronounced Orthostatic Hypotension in GBA-Related Parkinson's Disease. J Parkinsons Dis 2022;12:1539-1544.
[4] Devigili G, Straccia G, Cereda E, et al. Unraveling Autonomic Dysfunction in GBA-Related Parkinson's Disease. Mov Disord Clin Pract 2023
[5] Low PA. Composite autonomic scoring scale for laboratory quantification of generalized autonomic failure. Mayo Clin Proc 1993;68:748-752.
[6] Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Eur Heart J 1996;17:354-381.

P161

Adult-onset dystonic opisthotonus associated with DLG4-related synaptopathy

Tiziana De Santis[1], P. Polverino[1], A. Cocco[1], S. Lalli[1], E.M. Valente[2,3], A. Albanese[1,4]

[1]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Italy
[2]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[3]Neurogenetics Research Center, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Neuroscience, Catholic University, Milano, Italy

Introduction: DLG4 -related synaptopathy is a rare autosomal dominant brain disorder associated with pathogenic variants of the DLG4 gene [1]. The clinical phenotype encompasses epilepsy, developmental delay, intellectual disability, behavioral problems, autism, dysmorphic and marfanoid features [2]. Dystonia has been described as occurring in this condition, but not well characterized.

Objectives: To describe the clinical features associated with a novel DLG4 -variant.

Case presentation: A 31-year-old male, born at term to healthy no-consanguineous parents, presented symptoms onset in early infancy, when delayed language emergence and poor school performances were noticed. At age eight generalized tonic-clonic seizures occurred. At age 27 generalized dystonia emerged, mainly affecting the trunk and leading to walking-induced opisthotonus. Neuropsychological assessment revealed mild cognitive impairment and obsessive-compulsive traits. Brain MRI was unremarkable. The following genetic analyses were not diagnostic: array-CGH for chromosomal abnormalities, NGS-based panel assessing genes related to dystonia and NBIA, and PCR of the FMR gene. A multigene development delay panel revealed a de novo heterozygous variant (c.1435delC) of the DLG4 gene.

Conclusions: Dystonic features of DLG4- related synaptopathy may include adultonset dystonic opisthotonus.

References:

[1] Kassabian B. Developmental epileptic encephalopathy in DLG4-related synaptopathy. Epilepsia. 2023 Dec 22. doi: 10.1111/epi.17876.
[2] Rodríguez-Palmero A. DLG4-related synaptopathy: a new rare brain disorder. Genet Med. 2021 May;23(5):888-899. doi: 10.1038/s41436-020-01075-9.

P162

Pathogenic GRN variants in Parkinson's disease patients

Vidal Yahya[1], F. Cogiamanian[2], L. Borellini[2], F. Arienti[3], E. Monfrini[1,3], A.B. Di Fonzo[3]

[1]Dino Ferrari Center, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurophyisiology Unit, Milan, Italy
[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy

Introduction: Heterozygous loss-of-function variants in GRN (Progranulin) are the second most common monogenic cause of frontotemporal dementia [1–3] Extrapyramidal symptoms often follow cognitive disturbances. Lewy body pathology may be present in combination with classical TDP-43 pathology [4–6]. Recent evidence linked pathogenic GRN variants to Lewy body dementia and other atypical parkinsonisms. In addition, levodopa-responsive parkinsonism resembling idiopathic PD has been reported as an atypical presentation of pathogenic GRN variants [7–10].

Objectives: To integrate the clinical, genetic, and biochemical features of two patients with PD carrying pathogenic GRN variants.

Methods: Two patients with PD underwent complete neurological and neuroradiological assessment, genetic testing (whole-exome sequencing [WES] and multiplex ligation-dependent amplification), and plasmatic progranulin dosage.

Results: Patient 1 is a 64-year-old woman with PD onset at 57 years. After an optimal response to dopaminergic therapy, she developed motor fluctuation and levodopa-induced dyskinesias. Brain MRI resulted normal while DAT-SPECT was positive at onset. After six years and an unremarkable neuropsychological evaluation, bilateral subthalamic nucleus deep brain stimulation was successfully started. WES revealed the heterozygous pathogenic c.813_816del p.Thr272SerfsTer [10] GRN variant [11]. Patient 2 is a 30-year-old man with a levodopa-responsive parkinsonism accompanied by mild cervical dystonia and action upper limbs' tremor since adolescence, and familiarity for PD (maternal grandmother). Brain MRI showed mild fronto-parietal atrophy, DATSPECT was positive, brain PET-FDG and neuropsychological testing resulted normal. WES revealed the heterozygous likely pathogenic c.415T>C p.Cys139Arg GRN variant [12–16]. Plasma progranulin resulted 52 ng/ml (threshold 71) highlighting a mild functional haploinsufficiency for the p.Cys139Arg variant [14]. No other pathogenic variants in PD genes were detected in both patients [17].

Conclusions: Pathogenic G R N variants may represent a monogenic cause of a phenotype strikingly similar to PD and should be investigated in patients with a high suspect of genetic parkinsonism even in absence of cognitive decline, considering the relevant prognostic impact and the ongoing therapeutic advancements on progranulin.

References:

[1] Baker M, Mackenzie IR, Pickering-Brown SM, et al. Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. Nature. England; 2006;442:916–919.
[2] Gass J, Cannon A, Mackenzie IR, et al. Mutations in progranulin are a major cause of ubiquitin-positive frontotemporal lobar degeneration. Hum Mol Genet. England; 2006;15:2988–3001.
[3] Greaves C V, Rohrer JD. An update on genetic frontotemporal dementia. J Neurol. Germany; 2019;266:2075–2086.
[4] Le Ber I, Camuzat A, Hannequin D, et al. Phenotype variability in progranulin mutation carriers: a clinical, neuropsychological, imaging and genetic study. Brain. England; 2008;131:732–746.

[5] van Swieten JC, Heutink P. Mutations in progranulin (GRN) within the spectrum of clinical and pathological phenotypes of frontotemporal dementia. Lancet Neurol. England; 2008;7:965–974.
[6] Reho P, Koga S, Shah Z, et al. GRN Mutations Are Associated with Lewy Body Dementia. Mov Disord. 2022;37:1943–1948.
[7] Nalls MA, Blauwendraat C, Sargent L, et al. Evidence for GRN connecting multiple neurodegenerative diseases. Brain Commun. 2021;3:1–5.
[8] Brouwers N, Nuytemans K, Van Der Zee J, et al. Alzheimer and Parkinson diagnoses in progranulin null mutation carriers in an extended founder family. Arch Neurol. 2007;64:1436–1446.
[9] Carneiro F, Saracino D, Huin V, et al. Isolated parkinsonism is an atypical presentation of GRN and C9orf72 gene mutations. Park Relat Disord. 2020;80:73–81.
[10] Biagioli N, Cavallieri F, Marti A, et al. Levodopa responsive asymmetric parkinsonism as clinical presentation of progranulin gene mutation. J Neurol Sci [online serial]. 2023;451:120737. Accessed at: https://linkinghub.elsevier.com/retrieve/pii/S0022510X23001983.
[11] Smith KR, Damiano J, Franceschetti S, et al. Strikingly different clinicopathological phenotypes determined by progranulin-mutation dosage. Am J Hum Genet. 2012;90:1102–1107.
[12] Brouwers N, Sleegers K, Engelborghs S, et al. Genetic variability in progranulin contributes to risk for clinically diagnosed Alzheimer disease. Neurology. United States; 2008;71:656–664.
[13] Bernardi L, Tomaino C, Anfossi M, et al. Novel PSEN1 and PGRN mutations in early-onset familial frontotemporal dementia. Neurobiol Aging. 2009;30:1825–1833.
[14] Wang J, Van Damme P, Cruchaga C, et al. Pathogenic cysteine mutations affect progranulin function and production of mature granulins. J Neurochem. England; 2010;112:1305–1315.
[15] Antonell A, Gil S, Sánchez-Valle R, et al. Serum progranulin levels in patients with frontotemporal lobar degeneration and Alzheimer's disease: detection of GRN mutations in a Spanish cohort. J Alzheimers Dis. Netherlands; 2012;31:581–591.
[16] Gómez-Tortosa E, Guerrero-López R, Gil-Neciga E, et al. Plasma progranulin levels in cortical dementia phenotypes with asymmetric perisylvian atrophy. Eur J Neurol. England; 2013;20:1319–1324.
[17] Di Fonzo A, Percetti M, Monfrini E, et al. Harmonizing Genetic Testing for Parkinson's Disease: Results of the PARKNET Multicentric Study. Mov Disord. United States; Epub 2023 Sep.

P163

Abnormalities of the descending inhibitory nociceptive pathway in functional motor disorders

Christian Geroin[1], G. Squintani[2], A. Pasquali[1], E. Cavazzana[1], A. Segatti[2], M. Lippolis[2], E. Antelmi[1], M. Tinazzi[1]

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neurology and Neurophysiology Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy

Introduction: Pain is a common disabling non-motor symptom affecting patients with Functional Motor Disorders (FMD) [1,2].

Objectives: We aimed to study ascending and descending nociceptive pathways with Laser evoked potentials (LEPs) in FMD.

Methods: We applied a conditioned pain modulation (CPM) protocol [2,3] and recorded N2/P2 amplitude in 21 FMD and 20 controls following stimulation of both right arm and leg at baseline (BS), during heterotopic noxious conditioning stimulation (HNCS) with ice test and post-HNCS.

Results: We found a normal ascending pathway but reduced CPM response (lower reduction of the N2/P2 amplitude) in FMD patients, by stimulating both upper and lower limbs. The N2/P2 amplitude ratio*100 (between the HNCS and BS) was significantly higher in patients with FMD than HC.

Conclusions: Our results suggest that pain in FMD possibly reflects a descending pain inhibitory control impairment, thus providing a novel venue to explore the pathophysiology of pain in FMD.

References:

[1] Tinazzi M, Morgante F, Marcuzzo E, et al. Clinical Correlates of Functional Motor Disorders: An Italian Multicenter Study. Mov Disord Clin Pract. 2020;7(8). doi:10.1002/mdc3.13077.
[2] Morgante F, Matinella A, Andrenelli E, et al. Pain processing in functional and idiopathic dystonia: An exploratory study. Mov Disord. 2018;33(8). doi:10.1002/mds.27402.
[3] Antelmi E, Squintani GM, Sandri A, Lippolis M, Segatti A, Tinazzi M. Defect of the Endogenous Inhibitory Pain System in Idiopathic Restless Legs Syndrome: A Laser Evoked Potentials Study. Mov Disord. 2023;38(9):1688-1696. doi:10.1002/mds.29509.

P164

Glutamatergic alterations and gait parameters in de novo Parkinson's disease patients: a TMS-based study using mobile health technology assessment

Andrea Rizzardi[1,2,3,] A. Benussi[1,3], A. Pilotto[1,3], A. Galli[1], C. Tirloni[1], C. Zatti[1], M. Catania[1], C. Hansen[4], R. Romijnders[4], B. Borroni[1,3], W. Maetzler[4], A. Padovani[1,3]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Laboratory of Digital Neurology and Biosensors, University of Brescia, Brescia, Italy
[3]Department of Continuity of Care and Frailty, Neurology Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[4]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany

Introduction: Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation technique able to detect the impairment of specific neurotransmitter circuits in vivo. The use of mobile health technologies (MHT) has become increasingly effective in detecting and quantifying gait alteration in early PD phases. The aim of this study was to evaluate the correlations between cortical glutamatergic profile in de Novo PD (NAIVE) Parkinson's disease patients and motor severity.

Backgrounds: Several studies found changes of glutamatergic circuitries in patients with PD [1-2]. To date, no studies evaluated the relationship between TMS-cortical changes and clinical phenotype, as well as motor, cognitive and gait performances in drug-naïve PD patients. [3]

Methods: The study included 45 de novo patients with PD without dopaminergic treatment (68.9+7.8 years). Each subject underwent an extensive motor and cognitive assessment, and MHT assessment in supervised condition in which patients perform a 20mt straight walk in selected pace, fast pace and during dual tasking. A TMS pairedpulse protocol evaluating glutamatergic circuits (ICF) was performed in all subjects and in a group of 25 Healthy control subjects.

Results: TMS assessment showed different glutamatergic profiles in PD vs HC. In PD, ICF values correlated with total UPDRS-III ($r=0.412$, $p=0.018$), rigidity ($r=0.483$, $p=0.006$) and bradykinesia subscore ($r=0.433$, $p=0.011$) but not with tremor and Step time variability correlates with ICF peak and ICF mean values ($r=0.529$; $r=0=534$, both $p<0.02$) in both normal and fast pace.

Conclusion: Glutamatergic alterations assessed by TMS in PD drug naïve patients correlated with the severity of symptoms and gait alterations, suggesting an ongoing compensations mechanisms. Ongoing longitudinal studies including advanced imaging and TMS techniques are necessary to evaluate the complex relationship between glutamatergic and dopaminergic changes and their relevance for progression and response to treatment in PD patients.

References:

[1] Leon-Sarmiento FE, et al. Novel mechanisms underlying inhibitory and facilitatory transcranial magnetic stimulation abnormalities in Parkinson's disease. Arch Med Res. 2013;44(3):221–228.
[2] Lefaucheur JP. Motor cortex dysfunction revealed by cortical excitability studies in Parkinson's disease: influence of antiparkinsonian treatment and cortical stimulation. Clin Neurophysiol. 2005;116(2):244–253.
[3] Nardone R, et al. Functional evaluation of central cholinergic circuits in patients with Parkinson's disease and REM sleep behavior disorder: a TMS study. J Neural Transm (Vienna). 2013;120(3):413–422.

P165

Tremor during walking in Parkinson's disease: a neurophysiological assessment

Francesco Marchet[1], M. Costanzo[2], C. Cutrona[1], G. Leodori[1,2], M.I. De Bartolo[2], G. Vivacqua[3,4], M. Mancuso[1], A. Conte[1,2], G. Fabbrini[1,2], A. Berardelli[1,2], D. Belvisi[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Deparment of Experimental Morphology and Microscopy, Integrated Research Center (PRAAB), Campus Biomedico University of Rome, Rome, Italy
[4]Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Sapienza University of Rome, Rome, Italy

Introduction: Distal upper limb tremor during walking (TW) is frequently observed in Parkinson' disease (PD) [1]. Recent evidence has shown that TW displays similar clinical features of resting (RT) and reemergent tremor (RET), suggesting that these tremors share common pathophysiological mechanisms [2,3].

Objectives: To delineate the neurophysiological features of TW and to compare with those of RT and RET. To test the hypothesis that TW, like RT and RET, is a "stability" tremor whose appearance is related to reduced automatic arm movements during walking.

Methods: Twenty-five tremulous PD patients were studied using a wearable wireless gyroscope to measure hand tremor frequency during resting, wrist extension posture holding, and walking. Pendular movement amplitude was evaluated through an angular sensor attached to the proximal arm region. Tremor frequency and pendular movements angular displacement magnitude were measured using a Fourier transform.

Results: TW, RT and RET frequencies were similar (TW:4.26 ± 0.61 Hz. RT: 4.13 Hz ± 0.55; RET: 4.30 ± 0.54 Hz; p values > 0.05). A significant positive correlation existed between RT, RET, and TW frequency on the same body side. TW was bilateral in 36% of patients and shared a similar distribution with RT in 92% and RET in 68% of the cases. In cases of unilateral TW, it manifested on the side with lesser pendular movements in 28% of the cases and on the other side in 36%.

Conclusions: The observation that TW has a similar frequency and body distribution of RT and RET confirms the hypothesis that similar pathophysiological mechanisms underlie these parkinsonian tremors. The lack of relationship between TW and reduced arm swing challenges the hypothesis that TW arises from decreased automatic arm movements. TW may emerge due to the absence of ongoing voluntary hand movements during automatic arm swing.

References:

[1] Costanzo M, Cutrona C, Leodori G, De Bartolo MI, Fabbrini A, Vivacqua G, Conte A, Fabbrini G, Berardelli A, Belvisi D. Distal Upper Limb Tremor during Walking in Parkinson's Disease. Mov Disord Clin Pract. 2023 Jun 22;10(8):1198-1202.
[2] Helmich RC, Dirkx MF. Pathophysiology and Management of Parkinsonian Tremor. Semin Neurol. 2017 Apr;37(2):127-134.
[3] Leodori G, Belvisi D, De Bartolo MI, Fabbrini A, Costanzo M, Vial F, Conte A, Hallett M, Berardelli A. Re-emergent.

P166

An electroencephalographic study on motor imagery of usual and complex gait in early-stage Parkinson's disease

Martina Putzolu[1], J. Samogin[2], G. Bonassi[3], C. Cosentino[3], S. Mezzarobba[3,4], A. Botta[4], S. Terranova[3], E. Ravizzotti[3], L. Avanzino[1,4], D. Mantini[2], A. Vato[5,6,7], E. Pelosin[3,4]

[1]Department of Experimental Medicine (DIMES), Section of Human Physiology, University of Genoa, Genoa, Italy
[2]Movement Control and Neuroplasticity Research Group, KU Leuven, Leuven, Belgium
[3]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal, and Child Health, University of Genoa, Genoa, Italy
[4]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[5]Department of Biomedical Engineering, The Catholic University of America, Washington, D.C., USA
[6]National Center for Adaptive Neurotechnologies, Stratton VA Medical Center, Albany, NY, USA
[7]College of Engineering and Applied Sciences, University at Albany – SUNY, Albany, NY, USA

Introduction: Gait relies on higher-order cognitive control, particularly during complex walking conditions. Individuals with Parkinson's Disease (PD) commonly experience motor and cognitive deficits, that can lead to additional challenges in walking performance, increasing fall risk [1]. Understanding the neurophysiological mechanisms of gait has become crucial and motor imagery (MI), which consists in mentally simulating an action, is frequently used given the neural overlap between simulated and executed movements [2].

Objective: Our aim was to assess gait imagery related activations in a population of PD patients and age-matched healthy controls.

Methods: A total of 14 patients with early-stage PD (Hoehn and Yahr stage: 1-2.5) and 13 elderly were recruited. During high-density electroencephalography registration, they were asked to visually imagine walking on a straight pathway (UW MI) and on a straight pathway while crossing a hurdle in the middle (DT MI). We selected regions of interest from a large cortical-subcortical network, and we registered and analyzed q, a, and β bands Event Related Desynchronizations (ERDs).

Results: The right superior frontal, precentral and supplementary areas were always active during MI (i.e., in both groups, in all bands and tasks). In both populations, a greater range of frontal regions were engaged during DT MI in respect to UW task. Regarding PD population only, bilateral insula and various frontal, parietal, temporal and occipital regions were never recruited during UW MI, but were then activated during DT MI. These results were particularly evident in low frequency bands.

Conclusions: By uncovering disparities in gait imagery related activations between the two groups, this protocol could potentially help in better understanding walking pathophysiological mechanisms in the early stages of PD.

References:

[1] Peterson DS, Horak FB. Neural Control of Walking in People with Parkinsonism. Physiology. 2016;31(2):95–107.
[2] Decety J. The neurophysiological basis of motor imagery. Behav Brain Res. 1996;77(1–2):45–52.

P167

Using illusions to understand hallucinations: differences in perceptual performances on illusory figures underscore specific visuoperceptual impairments in Parkinson's Disease

Sophie Rangan[3], A. Cucca[1,2], C.V. Manara[1], M. Catalan[3], M. Liccari[3], L. Antonutti[3], T. Lombardo[3], V. Cenacchi[3], S. Mingolo[1], C. Crisafulli[4], F. Dore[4], M. Murgia[1], T. Agostini[1], P. Manganotti[3]

[1]Department of Life Sciences, University of Trieste, Trieste, Italy.
[2]Department of Neurology, New York University School of Medicine, New York, USA.
[3]Neurology Clinic, Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy.
[4]Nuclear Medicine, Imaging Diagnostic Department University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy

Introduction: Visual hallucinations are prevalent, potentially disabling symptoms of Parkinson's Disease (PD). Multiple impairments in bottom-up sensory processing and top-down perceptual modulation are implicated in hallucinations' pathophysiology. In healthy individuals, visual illusions are elicited by illusory figures through parametric manipulations of geometrical configurations, contrast, color, or spatial relationships between stimuli. These illusory percepts provide insight on the physiologic processes subserving perception.

Objectives: To investigate the perceptual performance of both hallucinating (PD_Hal) and non-hallucinating PD patients (PD_NonHal) on illusory figures and to compare it with that of age-matched healthy individuals (HC).

Materials and Methods: In this exploratory, cross-sectional, controlled study, the Delboeuf illusion and the size shrinkage due to amodal completion were used to assess perceptual performance of 11 PD_Hal, 10 PD_NonHal, and 10 HC.
Clinical assessments were performed on PD patients by means of MDS-UPDRS. Patients' brain metabolic patterns on ^{18}FDG-PET were analyzed to characterize potential neural substrates of perceptual performances.

Results: On the size estimation task of the Delboeuf illusion, PD_NonHal performed significantly better than healthy controls. Perceptual performance on the amodal completion illusion was significantly worse in PD_Hal patients as compared to HC.
General motor impairment was comparable between PD groups, but a trend towards a worse axial involvement was found in PD_Hal. Hallucinating PD patients showed a relative hypermetabolism at the level of left medial prefrontal cortex compared to a mild hypometabolism of non-hallucinating patients.

Conclusions: The impairment of high order visuoperceptual functions occurring in PD is linked to different profiles of vulnerability to illusory biases. Illusions relying on attentional modulation and global perception were attenuated in PD_NonHal. Conversely, illusory effects normally counteracted by figure to background segregation and overlapping figures recognition were enhanced in PD_Hal. ^{18}FDG-PET findings further suggest that perceptual differences between PD patients might be linked to abnormal top-down perceptual modulation.

P168

Combined effect of computerized cognitive training and tDCS in early Parkinson's disease

Alfonsina D'Iorio[1], A. Barbaro[1], R. De Micco[2], F. Ambrosio[2], M. Galietti[1], G. Santangelo[1], A. Tessitore[2]

[1]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy

Introduction: Parkinson's disease (PD) is characterized by motor and nonmotor symptoms such as cognitive decline, apathy, social withdrawal and mood disturbances. Albeit pharmacological therapy is the main choice when treating PD symptoms, it becomes less effective with time. Moreover, nonmotor symptoms like cognitive impairment do not effectively respond to medication [1-3]. Therefore, PD patients require new therapeutic approaches capable of providing them a better quality of life. Among non-pharmacological interventions, a combination of transcranial direct current stimulation (tDCS), that modulates cortical excitability, and computerized cognitive training (CCT) could be able to improve the non-motor symptoms of PD.

Objectives: The main aim is to investigate the effects of active tDCS combined with CCT on cognition and mood disturbances in early PD patients.

Methods: 10 early PD patients were randomly assigned to 2 groups: a control group (5) and an experimental group (5), the latter being treated with a combination of CCT and tDCS with anodal stimulation in F3. The treatments were administered twice a week for 30 minutes over a period of 8 weeks. Each participant underwent a neuropsychological assessment and an evaluation for motor and non-motor PD feature at baseline (T0) and at the end of the trial (T1).

Results: The two PD groups didn't differ at T0 for demographic, clinical, cognitive and behavioral features. The experimental group showed a significant improvement ($p < .05$) in the phonemic fluency test at T1.

Conclusions: This study provides preliminary evidence for a non-pharmacological treatment able to improve cognitive performance in early PD patients. The anodal stimulation of the left DLPFC in combination with a CCT led to an improvement in a cognitive flexibility task. These results are in line with previous evidence showing positive effect of tDCS and CCT on the deficit in verbal fluency attributed to frontal lobe dysfunctions in PD [4,5] and suggest a new protocol to improve cognitive function in early PD patients.

References:

[1] Jankovic, J. (2000). Parkinson's disease therapy: tailoring choices for early and late disease, young and old patients. Clinical neuropharmacology, 23(5), 252- 261. https://doi.org/10.1097/00002826-200009000-00003.
[2] Voon, V., Fernagut, P. O., Wickens, J., Baunez, C., Rodriguez, M., Pavon, N., Juncos J. L., Obeso J. A., & Bezard, E. (2009). Chronic dopaminergic stimulation in Parkinson's disease: from dyskinesias to impulse control disorders. The Lancet Neurology, 8(12), 1140-1149. https://doi.org/10.1016/S1474-4422(09)70287-X.
[3] Nonnekes, J., Timmer, M. H., de Vries, N. M., Rascol, O., Helmich, R. C., & Bloem, B. R. (2016). Unmasking levodopa resistance in Parkinson's disease. Movement Disorders, 31(11), 1602- 1609. https://doi.org/10.1002/mds.26712.

[4] Pereira, J. B., Junqué, C., Bartrés-Faz, D., Martí, M. J., Sala-Llonch, R., Compta, Y., Falcón, C., Vendrell, P., Pascual-Leone, A., Valls-Solé, J., & Tolosa, E. (2013). Modulation of verbal fluency networks by transcranial direct current stimulation (tDCS) in Parkinson's disease. Brain stimulation, 6(1), 16-24. https://doi.org/10.1016/j.brs.2012.01.006.
[5] Manenti, R., Cotelli, M. S., Cobelli, C., Gobbi, E., Brambilla, M., Rusich, D., Alberici, A., Padovani, A., Borroni, B., & Cotelli, M. (2018). Transcranial direct current stimulation combined with cognitive training for the treatment of Parkinson disease: a randomized, placebo-controlled study. Brain stimulation , 11(6), 1251- 1262. https://doi.org/10.1016/j.brs.2018.07.046.

P169

Direct Current Stimulation (DCS)-induced lipidomic modulation in an in vitro neuroblastoma cell line model: implications for Parkinson's disease (PD)

Natale Vincenzo Maiorana[1], L. Barbato[2], A. Mingione[1], M. Schiepati[3], M. Guidetti[1], M. Manfredi[4,5], F. Raimono[6], F. Cirillo[7], M. Piccoli[7], L. Anastasia[7], T. Bocci[1,8], E. Albi[9], A. Priori[1,8], P. Signorelli[1]

[1]Department of Health Science, Aldo Ravelli Research Center, University of Milan, Milan, Italy
[2]IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy
[3]University of Pavia, Pavia, Italy
[4]Center for Translational Research on Autoimmune and Allergic Diseases, University of Piemonte Orientale, Novara, Italy
[5]Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[6]Clinical Proteomics and Metabolomics Unit, School of Medicine and Surgery, University of Milano - Bicocca, Vedano al Lambro, Italy
[7]Laboratory of Stem Cells for Tissue Engineering, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy
[8]ASST – Santi Paolo e Carlo, Milan, Italy
[9]Department of Pharmaceutical Sciences, University of Perugia, Perugia, Italy

Introduction: Lipids are key signaling mediators, modulating immune regulation, inflammation, and maintenance of homeostasis as "bioactive lipids". There is a bidirectional relationship between the immune and nervous systems, and lipids interact with the aggregation and propagation of pathogenic proteins in neurodegenerative disorders as PD. The possibility of modulating cell lipidomic is therefore an interesting approach for neuroprotection in PD. While evidence indicates electric field modulation of alpha-synuclein in neuroblastoma cells, the impact on lipidomic changes remains unexplored.

Objectives: To evaluate possible lipid-related neuroprotective effect of static electric field in a dopaminergic cellular model by assessing the DCS-induced neuroblastoma cell lipidomic changes in vitro.

Methods: A neuroblastoma dopaminergic cell line, SHSY5Y, was cultured and exposed to single (sDCS) or repeated (n=3) DCS (rDCS) sessions (0.5mA; 0.6 C; electrode size: 0.25 cm^2; 20 mins /5x10^5 cells). rDCS sessions were delivered with 24 hours – interval. Lipid profile was assessed by mass spectrometry. Results in cells exposed to DCS were compared to findings in non-DCS-exposed cells at the same time intervals.

Results: Overall after DCS there were complex changes in neuroblastoma cell lipidomic: sDCS changed cellular lipidome after 24 h and rDCS reverted these changes for several species. rDCS modulated the igher number of lipid species. Overall sDCS reduced the total amount of cellular lipids (including the energy reserve of triglicerides by 28.5%; $p < 0.05$), decreased free fatty acids (66.6; $p < 0.05$) and increased the fatty acid transporter (23%; $p < 0.05$) in the mitochondria. rDCS reduced inflammatory lipid species (ceramides and lysoglycerol lipids by 33.3 % and 44,4 % respectively all $p< 0.05$).

Conclusions: DCS significantly alters dopaminergic neuroblastoma cell lipidomics. Electric field exposure boosts oxidative metabolism, energy production, and reduces inflammatory lipids. The in vitro lipidomic changes induced by DCS suggest potential neuroprotection through non-invasive neuromodulation in PD.

P170

Direct Current Stimulation (DCS) -induced behavioral and transcriptomic effects in Botryllus Schlosseri (BS)

Natale Vincenzo Maiorana[1], C. Anselmi[2,3,4,5], T. Bocci[1,6], L. Consuma[1], M. Guidetti[1], F. La Torre[5], E. De Lisa[5], G. Sabbadin[5], A. Priori[1,6], L. Manni[5]

[1]Department of Health Science, Aldo Ravelli Research Center, University of Milan, Milan, Italy
[2]Hopkins Marine Station, Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Pacific Grove, CA, USA
[3]Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, Stanford, CA, USA
[4]Wu Tsai Neurosciences Institute, Stanford University, Stanford, CA, USA
[5]Department of Biology, University of Padova, Padova, Italy
[6]ASST – Santi Paolo e Carlo, Milan, Italy

Introduction: BS, a marine colonial tunicate ascidian, has been recently proposed as model for human neurodegenerative diseases with the expression of relevant genes [1,2,3]. Transcranial direct current stimulation (tDCS) may induce some benefit in patients with Parkinson's disease and direct current stimulation (DCS) decreases alpha-synuclein in neuroblastoma cell models.

Objectives: To assess DCS-induced changes in BS through behavioral and transcriptomic approaches.

Methods: In this study, five BS genotypes (Stage: 9/8/3) were divided into stimulated ("A") and control ("C"). Heart rate and behavioral responses to micromechanical stimulation before and after DCS at 0.5 mA for 20 minutes, were measured in five zooids per subclone. Genotypes were assessed before and 3, 24, and 48 hours after DCS.

Results: In comparison with control group, DCS (A group) significantly decreased the heartbeat by 10% in the A group after DCS and in the following 3 hours ($t = 3.686$; $p = 0.001$). Also, DCS significantly reduced the response to micromechanical simulation ($t = -8.032$, $p < 0.001$). In comparison with Control group of animals, DCS (A group) also significantly modulated gene expression at different time points: LRP2 ($x = 25.88$, $p < 0.001$) and TUBB2_A ($x = 7.65$, $p = 0.005$) exhibited higher expression after 3 hours, whereas VPS35 displayed lower expression after 48 hours ($x = 122.50$, $p < 0.001$).

Conclusions: DCS induces behavioral and genetic changes in BS. DCS modulates expression of LRP2, TUBB2_A, and VPS35. Because these genes are implicated in the pathogenesis of PD, the DCS-induced changes in their expression may have implications for developing novel neuroprotective approaches for neurodegenerative disease.

References:

[1] Manni, L., Zaniolo, G., Cima, F., Burighel, P., & Ballarin, L. (2007). Botryllus schlosseri: a model ascidian for the study of asexual reproduction. Developmental Dynamics: An Official Publication of the American Association of Anatomists, 236 (2), 335–352. https://doi.org/10.1002/dvdy.21037.
[2] Thompson, S. H., Anselmi, C., Ishizuka, K. J., Palmeri, K. J., & Voskoboynik, A. (2022). Contributions from both the brain and the vascular network guide behavior in the colonial tunicate Botryllus schlosseri. The Journal of Experimental Biology, 225 (22). https://doi.org/10.1242/jeb.244491.
[3] Anselmi, C., Kowarsky, M., Gasparini, F., Caicci, F., Ishizuka, K. J., Palmeri, K. J., Raveh, T., Sinha, R., Neff, N., Quake, S. R., Weissman, I. L., Voskoboynik, A., & Manni, L. (2022). Two distinct evolutionary conserved neural degeneration pathways characterized in a colonial chordate. Proceedings of the National Academy of Sciences, 119 (29). https://doi.org/10.1073/pnas.2203032119.

P171

The effect of monopolar transcranial direct current stimulation on freezing of gait in a patient with Parkinson's disease: a case-study with personalized computational model

Matteo Guidetti[1], E. Concas[2], N.V. Maiorana[1], S. Oliveri[1,2], A. Priori[1,2], T. Bocci[1,2]

[1]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Clinical Neurology Unit, "Azienda Socio-Sanitaria Territoriale Santi Paolo e Carlo", Department of Health Sciences, University of Milan, Milan, Italy

Introduction: Freezing of gait (FOG) is a common motor symptom in Parkinson's disease (PD) defined as an episodic absence or marked reduction in forward progression of the feet despite the intention to walk [1]. The clear underlying mechanisms and effective treatments are still to be defined [1]. Several studies have applied transcranial Direct Current Stimulation (tDCS) over motor cortices with alternating results [2]. However, none have used monopolar montage, which has shown to influence selectively those deep brain structure that might be implied in the development of FOG3.

Objectives: To investigate the effect of monopolar tDCS on FOG in a patient with PD.

Methods: In this case-study report, a subject diagnosed with Parkinson's disease (M, 70yo, disease duration: 13yy, LEDD = 776 mg) underwent bilateral motor cortex anodal tDCS with cathode over right deltoid (2 mA for 20 min, once a day for 5 days a week, 2 weeks). Timed 10-Meter Walk Test (10MWT), Berg Balance Scale (BBS), Timed Up & Go (TUG), Falls Efficacy Scale-International (FES-I), and Freezing of Gait Questionnaire (FOGQ) were used to assess balance, gait performance and FOG (Levodopa ON phase). A personalized finite element method (FEM) head model based on the patient's RMN was developed to describe tDCS-induced electric field distribution.

Results: Objective assessments (i.e., 10MWT and TUG) revealed a worsening of balance, functional mobility and gait performance (ΔTUG = 9.82s; Δ10MWT – self-selected velocity = 6.44s, Δ10MWT – fast velocity = 4.41s), although BBS remained unchanged (Δ BBS = 0) However, subjective scales disclosed an improvement in selfperceived fear of falling (ΔFES-I = -17) and FOG (Δ FOGQ = -5). FEM model confirmed a concentration of electric fields in deep brain structures.

Conclusions: Monopolar tDCS might improve the subjective perception of the gait impairments related to FOG, but not objective evaluation.

References:

[1] Nutt, J.G. et al. Lancet Neurol 10, 734–744 (2011).
[2] Rahimpour, S. et al. Neuromodulation 24, 829–842 (2021).
[3] Guidetti, M. et al. Clinical Neurophysiology (2023).doi:10.1016/j.clinph.2023.08.011.

P172

Exploring the placebo effect in motor domain: behavioral and electrophysiological insights

Miriam Braga[1], I. Lozzi[1], A. Marotta[1], A. Grando[2], C. Miniussi[2], M. Emadi Andani[1], M. Fiorio[1]

[1]Department of Neuroscience, Biomedicine and Movement Science, University of Verona, Verona, Italy
[2]Center for Mind/Brain Sciences (CIMeC), University of Trento, Rovereto, Italy

Introduction: Recent work proposed a predictive coding perspective for functional neurological disorder (FND), positing that expectations-driven processes could be involved in the generation of symptoms [1]. Anticipatory mechanisms can be studied recording event-related potentials (ERPs) before movement onset, which can reflect the predictive nature of cognitive and motor preparation processes. Further investigations are required to test if the manipulation of top-down expectations, which are the key mechanisms of placebo/nocebo effects, can act on the preparatory phase of movement, thus supporting the predictive coding framework [2, 3].

Objectives: In a study on healthy adults, we will explore whether a placebo procedure optimizes preparatory processes by decreasing reaction time (RT) and modulating event-related potentials (ERPs) before movement onset.

Methods: We plan to enroll 45 healthy participants who will perform a simple RT task at baseline and test sessions, interleaved by an intervention or a 5-minutes interval depending on the group assigned. In a placebo group (N = 15), a 10Hz inert stimulation (TENS) will be applied on the right forearm along with verbal suggestions of its efficacy in speeding up RT; one control group (N = 15) will receive the same device with overt information about its inert nature; a second control group (N = 15) will serve as natural history. As behavioral outcome, we will analyze RT, defined as the latency between the presentation of a visual cue and the onset of electromyographic (EMG) activity. The amplitude of the Contingent Negative Variation (CNV) and the Readiness Potential (RP), two cortical waves associated with preparatory processes [3, 4], will be recorded.

Results: We expect to induce a motor placebo effect, with faster RT in the placebo group compared to the control groups. We hypothesize an increase in the amplitude of ERPs components in the placebo group, suggesting that the top-down manipulation of expectations modulates cortical processes during the preparation of movement and supporting the predictive coding perspective of motor placebo effect.

Conclusions: The proposed methodological approach will provide a comprehensive, predictions-based framework for understanding motor placebo effect. Subsequent studies could extend this procedure to FND patients, testing future interventions focused on the reversion of nocebo-like mechanisms in this clinical population.

References:

[1] Fiorio et al., 2022. Nat Rev Neurol; 18 (10): 624-635.
[2] Piedimonte et al., 2015. E J Neurosci; 41(4): 492-497.
[3] Piedimonte et al., 2017. E J Pain; 21 (5): 874-885.
[4] Schurger et al., 2021. Trends Cogn Sci; 25 (7): 558-570.

P173

Striatal dopamine correlates to spatial gait parameters in dual task conditions

Cinzia Zatti[1,2,3], A. Pilotto[1,2,3], A. Rizzardi[1,2], A. Galli[1,2], C. Hansen[4], M. Catania[1,2,3], R. Romijnders[4], W. Maetzler[4], A. Padovani[1,2,3]

[1]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Brescia, Italy
[2]Laboratory of Digital Neurology and Biosensors, University of Brescia, Brescia, Italy
[3]Department of Continuity of care and Frailty, Neurology Unit, ASST Spedali Civili of Brescia, Brescia, Italy
[4]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany

Background: Parkinson's disease (PD) is clinically defined by motor symptoms and the underlying mechanism is determined by loss of dopaminergic neurons in the substantia nigra, leading to dopamine depletion in the basal ganglia circuit. Despite this, the MDS-UPDRS-III, the standard motor assessment, does not correlate with the dopaminergic deficit. The aim of this study was to investigate the relationship between dopamine uptake and motor changes using inertial sensors.

Methods: Forty de novo PD patients were enrolled. They underwent a comprehensive motor assessment including MDS-UPDRS-III and digital assessment of gait parameters in normal, fast and dual-task conditions using mobile health technologies (MHT) in a supervised setting. All patients underwent 123I-FP-CIT-SPECT imaging to quantify dopaminergic uptake. The relationship between motor parameters and dopamine binding was assessed using partial correlations corrected for age, sex and height.

Results: No correlation was observed between MDS-UPDRS-III and dopamine uptake in the striatal circuit. Step length in single and dual task conditions correlates directly with MDS-UPDRS-III (p: 0.001 R: 0.376), while reduced step length in dual task conditions is associated with reduced DAT availability in both putamen and pallidum (p: 0.022 and 0.013 with R: 0.417 and R: 0.428).

Conclusions: Dopamine depletion is known to be the pathological mechanism underlying motor changes in PD. Our study suggests that the use of more sensitive parameters, specifically spatial parameters in dual task conditions, can identify this relationship.

P174

Diagnostic accuracy of "Swallow tail" sign in early Parkinson's disease

Carmelo Alessandro Fogliano, L. Bresciani, B. Savini, M. Campagnolo, A. Antonini

Parkinson and Movement Disorders Unit, Department of Neuroscience, University of Padova, Padova, Italy

Introduction: The 'swallow tail' sign (STS) consists in the normal appearance of the dorsolateral substantia nigra in T2*-weighted MRI images, due to the presence of a hyperintense ovoid area [1]. This aspect is lost in Parkinson's disease (PD) due the degeneration of nigrosome-1, the first zone of the substantia nigra to degenerate in the disease course [2]. STS absence has showed a consistent accuracy as a biomarker of PD [3]. Data are lacking on its validity in early-PD.

Objectives: To measure the diagnostic performance of STS absence in a cohort of patient with early stages PD.

Methods: A set of patients with diagnosis of PD and motor symptoms' onset in the lasts 24 months and a group of controls with no sign of parkinsonism were selected and underwent a 3T Brain MRI scan with SWI sequences, slice thickness <1 mm. Images were reviewed independently by two neurologists, blind to the diagnosis, followed by consensus reading.

Results: 23 PD patients and 25 controls underwent the MRI. 2 MRI were excluded from the analysis because of low quality. The sensitivity of the STS absence was 77.3%, specificity 83.3%, positive predictive value 81%, negative predictive value 80% and accuracy 80.4%, in the diagnosis of early-PD vs control. Kappa coefficient was 0.735 ($p < 0.001$) for inter-rater agreement, supporting a substantial reproducibility for the detection of the sign.

Conclusions: STS absence appears to be a reliable biomarker, suitable for clinical practice implementation to detect PD even at the first visit with the movement disorder specialist. Of note, 2 patients diagnosed with PD, with a suggestive clinical syndrome and a positive 123I-Ioflupane SPECT, had preserved STS and no αSynuclein at the skin biopsy, thus having probable vascular parkinsonisms. Recategorizing those 2 cases, diagnostic performances improve (sens. 85%, spec 84.6%). STS could
then be precious to differentiate vascular parkinsonisms from idiopathic ones, even when 123I-Ioflupane SPECT fails.

References:

[1] Blazejewska et al., 2013. Neurology; 81(6): 534–540.
[2] Damier et al., 1999. Brain; 122(8): 1437–1448.
[3] Toan Chau et al., 2020. Parkinsonism & Related Disorders; volume 78: 12-20.

P175

Insular and limbic abnormal functional connectivity in de novo Parkinson's disease patients with autonomic dysfunction

Matteo Conti, R. Bovenzi, E. Garasto, V. Ferrari, N.B. Mercuri, M. Pierantozzi, T. Schirinzi, C. Rocchi, A. Stefani

Neurology Unit, Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy

Introduction: Autonomic symptoms (AS) in Parkinson's Disease (PD) are critical manifestations including urinary problems, constipation, orthostatic hypotension, swallowing and sweating problems due to the involvement of multiple autonomic nervous system domains and significantly contributing to the disease burden [1]. Despite the recent increase of interest in AS in PD, many aspects remain open questions. The study of functional connectivity (FC) through different techniques allows us improving the understanding of the PD pathophysiology [2].

Objective: To investigate the association between AS and cortical FC in de novo PD, by means of high-density EEG (HD-EEG).

Methods: 44 de novo PD patients (30/14 male/female) were included in the study. Motor impairment was assessed using MDS-UPDRS part III, while AS were evaluated using SCOPA-AUT score. Data were recorded with a 64-channels EEG system. Source reconstruction method based on personal MRI was used to identify brain regions activity. We analysed cortico-cortical FC, based on weighted phaselag index (wPLI) [3], in three bands (θ-α-β). Network-based statistic (NBS) was used to perform linear regression between SCOPA-AUT score and FC in PD patients. Age, sex, disease duration and UPDRS-III were considered as covariates.

Results: We observed significant positive relations between total SCOPA-AUT score and FC in α ($\tau = 2.8$, $p = 0.046$) and in β bands ($\tau = 2.9$, $p = 0.019$). Brain regions with high number of degrees were bilateral insula and limbic lobe, especially bilateral anterior cingulate.

Conclusion: Our results revealed abnormal FC in specific areas in PD patients with greater AS burden since the early stages of the disease. Insula and limbic areas are known to play a significant role in the regulation of the autonomic system. Increased FC in these regions might represent a central compensatory mechanism of a peripheral autonomic dysfunction or reflect a central co-pathology in early stages of PD.

References:

[1] S. C. Gu et al., "Autonomic function and motor subtypes in Parkinson's disease: a multicentre cross-sectional study," Sci Rep, vol. 13, no. 1, 2023, doi: 10.1038/s41598-023-41662-9.
[2] M. Conti et al., "Band-Specific Altered Cortical Connectivity in Early Parkinson's Disease and its Clinical Correlates," Movement Disorders, pp. 1–13, 2023, doi: 10.1002/mds.29615.
[3] T. M. Lau, J. T. Gwin, K. G. McDowell, and D. P. Ferris, "Weighted phase lag index stability as an artifact resistant measure to detect cognitive EEG activity during locomotion," J Neuroeng Rehabil, vol. 9, no. 1, 2012, doi: 10.1186/1743-0003-9-47.

P176

Asymmetry of DAT SPECT imaging in Parkinson's disease according to REM sleep behavior onset

Calogero Edoardo Cicero[1], S. Tabbì[1], R. Garofalo[1], A. Luca[1], G. Mostile[1,2], G. Donzuso[1], M. Zappia[1], A. Nicoletti[1]

[1]Department of Medical, Surgical Sciences and Advanced technologies G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[2]Oasi Research Institute - IRCCS, Troina, Italy

Introduction: Parkinson's Disease (PD) body first subtype is characterized by the prodromal development of REM sleep behavior disorder (RBD), followed by the development of motor symptoms. Body first patients usually display a higher burden of non-motor symptoms and a more symmetrical motor phenotype. Whereas brain first subtype displays a more asymmetrical clinical presentation. Semiquantitative analysis of 123I-FP-CIT DAT SPECT imaging can be used to evaluate the degree of dopaminergic dysfunction.

Objectives: To investigate 123I-FP-CIT DAT SPECT differences between brain-first and body-first PD patients.

Methods: PD patients with an available routinely performed 123I-FP-CIT DAT SPECT were retrospectively selected. Diagnosis of probable RBD was made using the RBD screening questionnaire (cutoff ≥ 6). Patients without RBD were defined as PD-RBD-, whereas patients with RBD were classified into PD-RBDpre ("body first") if RBD onset preceded motor symptoms onset or PD-RBDpost ("brain first") if RBD was developed after motor symptoms onset. Mean caudate and putamen binding values were computed. The asymmetry index of both caudate and putamen binding values was also calculated.

Results: A total of 56 PD patients were recruited. Twenty-seven were PD-RBD-, 10 PD-RBDpre and 19 PD-RBDpost. Comparing SPECT 123I-FP-CIT DAT SPECT semiquantitative analysis values within the three groups, we found a significant difference for mean caudate binding with lower values in PD-RBDpre group compared to PD-RBD post and PD-RBDpatients ($p=0.02$). A significant difference was also found for the putamen asymmetry index with lower values in PD-RBDpre group ($p=0.03$). No differences were found comparing caudate asymmetry index.

Conclusions: PD-RBDpre patients display a more symmetrical putaminal involvement compared to PD patients without RBD or when RBD follows motor symptoms onset. Consequently, SPECT 123I-FP-CIT DAT SPECT semiquantitative analysis could be used as a biomarker in the differentiation of PD subtypes.

P177

Mapping the Impact of White Matter Changes on Non-Motor Symptoms in Parkinson's disease

Carlo Santoro[1], D. Urso[2], V. Gnoni[2], S. Landolfo[1], A. Giugno[2], D. Vilella[2], G. Logroscino[2]

[1]Department of Basic Medical Sciences, Neuroscience and Organ Sense. University "Aldo Moro", Bari, Italy
[2]Center for Neurodegenerative Diseases and the Aging, Department of Clinical Research in Neurology, University of Bari “Aldo Moro”, “Pia Fondazione Cardinale G. Panico”, Tricase, Lecce, Italy

Introduction: Managing Parkinson's Disease (PD) presents a considerable challenge due to the prevalence of non-motor symptoms (NMS), including cognitive impairment (CI). While the impact of Lewy-Body and Amyloid pathology on PD-related CI is known, the role of vascular co-pathology, especially cerebral small vessel disease (cSVD), remains uncertain. This study explores potential links between white matter damage in specific brain regions and NMS prevalence in PD, including cognitive impairment.

Methods: A cohort of 66 PD patients underwent comprehensive assessments, including clinical motor evaluations, NMS scale (NMSS) and neuropsychological testing. Magnetic Resonance Imaging (MRI) visually rated cSVD burden, emphasizing white matter hyperintensities (WMH) total burden and their impact on specific brain regions assessed using Fazekas and Scheltens scales.

Results: PD subjects showed diverse demographics and clinical characteristics. Visual rating of WMH burden revealed associations with cognitive decline, executive dysfunction, and language impairment. Associations between NMS, particularly urinary dysfunction, and WHM were observed, particularly in the frontal and parietal lobes.

Conclusions: Our findings underscore white matter pathology's impact on cognitive and non-motor domains in PD. The association between deep lobar WMH and urinary dysfunction suggests a vascular contribution to the dopaminergic fronto-striatal pathway.

P178

Predicting cognitive phenotypes in de novo Parkinson's disease: an fMRI data-driven approach

Maria Ilenia De Bartolo[1], A. Ojha[2], G. Leodori[1,2], C. Piervincenzi[2], S. Pietracupa[1,2], G. Vivacqua[3], M. Costanzo[2], F. D'Antonio[2,4], S. Barbetti[2], R. Margiotta[2], G. Bruno[2], A. Conte[1,2], A. Berardelli[1,2], P. Pantano[1,2], D. Belvisi[1,2], G. Fabbrini[1,2]

[1]IRCCS Neuromed, Pozzilli, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]Department of Microscopic and Ultrastructural Anatomy, Campus Biomedico University of Rome, Rome, Italy
[4]Cognitive and Motor Rehabilitation and Neuroimaging Unit, IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Cognitive decline is one of the most common and disabling non-motor symptoms in Parkinson disease (PD) [1,2]. The dorsolateral prefrontal cortex (DLPC) and the Precuneus (PCun) represent two central hubs in networks underlying respectively fronto-executive [3] and visuospatial functions [4].

Objective: Here, we aimed to investigate whether early functional connectivity changes in the DLPC and the PCun can predict cognitive phenotypes in cognitively intact de novo PD patients using a data-driven approach.

Methods: Resting-state functional connectivity (rsFC) of the DLPC and the PCun has been assessed in 68 de novo PD patients and 31 healthy controls (HC). Mean values of altered rsFC have been used to perform a non-hierarchical cluster analysis, which assigned PD patients to 3 different clusters. Differences in neuropsychological, motor and non-motor scales among the 3 clusters have been investigated at T0 and after a 3.5 year follow-up (T1).

Results: Patients displayed reduced rsFC of both DLPC (right and left) and PCun with several cortical and subcortical areas in comparison to HC. Patients assigned to cluster 1 showed extended lower values of rsFC in comparison to patients assigned to cluster 2 and 3, which respectively exhibited extended higher and intermediate values of rsFC in all investigated ROIs. Furthermore, cluster 1 was characterized by older age and lower performance in global cognition, fronto-executive and memory domains in comparison to cluster 2 and 3 at T0. At T1, a more evident worsening in global cognition, fronto-executive and visuo-spatial functions and non-motor symptoms was observed in cluster 1 and 3 in comparison to cluster 2.

Conclusions: Early rsFC alterations of the DLPC and the PCun can predict cognitive phenotypes in cognitively intact de novo PD patients. Our study opens to potential disease-modifying therapies, as neuromodulation protocols, to limit the development of dementia in PD.

References:

[1]. Litvan I, Goldman JG, Tröster AI, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord 2012;27(3):349–356.
[2] Goldman JG, Sieg E. Cognitive Impairment and Dementia in Parkinson Disease. Clinics in Geriatric Medicine 2020;36(2):365– 377.
[3] Panikratova YR, Vlasova RM, Akhutina TV, et al. Functional connectivity of the dorsolateral prefrontal cortex contributes to different components of executive functions. International Journal of Psychophysiology 2020;151:70–79.
[4] Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. Brain 2006;129(Pt 3):564–583.

P179

Intravoxel incoherent motion (IVIM) MRI imaging in iNPH: a noninvasive way to look into basal ganglia involvement in iNPH

Enrico Belgrado[2], D. Bagatto[1], F. Tuniz[3], M.C. De Colle[1], D. Piccolo[3], M. Valente[4]

[1]Department of Neuroradiology, University of Udine, Udine, Italy
[2]Department of Neurology, Udine University Hospital, Udine, Italy
[3]Department of Neurosurgery, University of Udine, Udine, Italy
[4]Department of Medicine (DAME), Neurologic Clinic, University Hospital, Udine, Italy

Objectives: To determine the relationship between intravoxel incoherent motion (IVIM) MRI parameters and clinical changes post-tap test (TT) in idiopathic normal-pressure hydrocephalus (iNPH) patients.

Methods: 44 probable iNPH patients underwent 3T MRI before and after TT. IVIM parameters were calculated from eight different bilateral regions of interest in basal ganglia, centrum semiovale, and corona radiata. Patients were categorized based on TT response into positive (group 1) and negative (group 2) groups. A Welch Two Sample t-test was used to compare differences in D, D*, f, and ADC between the two groups, while a paired t-test was employed to assess the changes within each group before and after TT. These parameters were then correlated with clinical results.

Results: In the lenticular and thalamic nuclei, the D value was significantly lower in the group 1 compared to group 2 both pre- and post-TT ($p=0.002$ and $p=0.007$ respectively). Post-TT, the positive response group exhibited a notably reduced D* value ($p=0.012$) and significantly higher f values ($p=0.028$). In the corona radiata and centrum semiovale, a significant post-TT reduction in D* was observed in the positive response group ($p=0.017$). Within groups, the positive response cohort showed a significant post-TT increase in ADC ($p<0.001$) and a decrease in D* ($p=0.007$).

Conclusions: IVIM permits the acquisition of important non-invasive information about tissue and vascularization in iNPH patients. Enhanced perfusion in the basal ganglia region may suggest the role of re-established microvascular and glymphatic pathways, potentially elucidating the functional improvement in motor function after TT in iNPH patients.

References:

[1] Paschoal AM, Leoni RF, Dos Santos AC, Paiva FF. Intravoxel incoherent motion MRI in neurological and cerebrovascular diseases. NeuroImage Clin. 2018;20:705-714. doi:10.1016/j.nicl.2018.08.030.
[2] Ziegelitz D, Arvidsson J, Hellström P, Tullberg M, Wikkelsø C, Starck G. In Patients With Idiopathic Normal Pressure Hydrocephalus Postoperative Cerebral Perfusion Changes Measured by Dynamic Susceptibility Contrast Magnetic Resonance Imaging Correlate With Clinical Improvement. J Comput Assist Tomogr. 2015;39(4):531-540. doi:10.1097/RCT.0000000000000254.
[3] Tuniz F, Vescovi MC, Bagatto D, et al. The role of perfusion and diffusion MRI in the assessment of patients affected by probable idiopathic normal pressure hydrocephalus. A cohort-prospective preliminary study. Fluids Barriers CNS. 2017;14(1):24. doi:10.1186/s12987-017-0072-3.

P180

Modulation of response times in early-stage Parkinson's disease during emotional processing of embodied and non-embodied stimuli

Alessandro Botta[1], E. Pelosin[1,2], G. Lagravinese[1], R. Marchese[1], F. Di Biasio[1], G. Bonassi[2], S. Terranova[3], E. Ravizzotti[2], M. Putzolu[3], S. Mezzarobba[2], C. Cosentino[2], L. Avanzino[1,3]

[1]IRCCS, Ospedale Policlinico San Martino, Genoa, Italy
[2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Genoa, Italy
[3]Department of Experimental Medicine (DIMES), Section of Human Physiology, University of Genoa, Genoa, Italy

Introduction: Valence (positive and negative) and content (embodied vs. non-embodied) characteristics of visual stimuli have been shown to influence motor readiness, as tested with response time paradigms. Both embodiment and emotional processing are affected in Parkinson's disease (PD) due to basal ganglia dysfunction.

Objective: Here we aimed to investigate, using a two-choice response time paradigm, motor readiness when processing embodied (emotional body language [EBL] and emotional facial expressions [FACS]) vs non-embodied (emotional scenes [IAPS]) stimuli with neutral, happy, and fearful content.

Methods: We enrolled twenty-five patients with early-stage PD and 25 age matched healthy participants. Motor response during emotional processing was assessed by measuring response times (RTs) in a home-based, forced two-choice discrimination task where participants were asked to discriminate the emotional stimulus from the neutral one. Rating of valence and arousal was also performed. A clinical and neuropsychological evaluation was performed on PD patients.

Results: Results showed that RTs for PD patients were longer for all conditions compared to HC and that RTs were generally longer in both groups for EBL compared to FACS and IAPS, with the sole exception retrieved for PD, where in discriminating fearful stimuli, RTs for EBL were longer compared to FACS but not to IAPS. Furthermore, in PD only, when discriminating fearful respect to neutral stimuli, RTs were shorter when discriminating FACS compared to IAPS.

Conclusions: This study shows that PD patients were faster in discriminating fearful embodied stimuli, allowing us to speculate on mechanisms involving an alternative, compensatory, emotional motor pathway for PD patients undergoing fear processing.

P181

Unraveling the biological bases of menopause-related vulnerability to Parkinson's disease

Roberta Bovenzi[1], M. Conti[1], C. Simonetta[1], J. Bissacco[1], D. Mascioli[1], A. Stefani[1,2], N.B. Mercuri[1], M. Pierantozzi[1], T. Schirinzi[1]

[1]Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]UOSD Parkinson Centre, Tor Vergata University Hospital, Rome, Italy

Introduction: Menopause might increase the risk for Parkinson's disease (PD) [1]. In this regard, there are compelling findings from animal models [2]; conversely, human-based evidence is still scarce.

Objective: To deepen into menopause-related vulnerability to PD by analyzing the relationships between reproductive life factors, sex hormones, clinical features, and CSF biomarkers in a cohort of postmenopausal PD patients.

Methods: The study involved 35 patients with post-menopausal PD onset afferent to the Neurology Unit of Tor Vergata University Hospital (Rome - Italy) and 38 post-menopausal controls (CTLs). A complete clinical evaluation, including motor, non-motor and cognitive scores, was coupled to CSF biomarkers assay and blood sex hormone levels measurement. CSF levels of total α-synuclein (αSyn), amyloid-β-42 (Aβ42), amyloid-β-40 (Aβ40), total tau (t-tau), and phosphorylated- 181-p tau (p-tau) were quantified in PD patients and CTLs. Aβ42/Aβ40 ratio was also calculated. Serum sex hormone levels, including total testosterone, estradiol, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were determined in each subject.

Results: PD patients had lower estradiol levels than CTLs, and the residual estradiol production was associated with milder motor disturbances and lower dopaminergic requirements. In PD but not in controls, FSH and LH levels correlated with worse cognitive scores and CSF markers of amyloidopathy and neuronal loss. In PD patients, a longer fertile life span correlated with less severe motor impairment in terms of the H&Y stage. On the other hand, greater length and higher number of pregnancies were associated with worse global clinical impairment.

Conclusions: Menopause-related hormonal changes might differentially contribute to clinical-pathological trajectories of PD, accounting for the peculiar vulnerability to the disease. While the lowering of estradiol levels might be critical in the pathophysiology of motor disturbances, the increase in gonadotropins could contribute to the complex neurodegenerative pathways underlying PD-related cognitive deterioration.

References:

[1] Cerri S, Mus L, Blandini F. Parkinson's Disease in Women and Men: What's the Difference? J. Parkinsons. Dis. (2019).
[2] Kompoliti K. Estrogen and Parkinson's disease. Front. Biosci (2003).

P182

Role of estrogens in motor fluctuations in a young female parkinsonian patient

Simone Valente[1,2], F. Piattellini[1,2], D. Greco[1,2], G. Grigioni[1,2], A. Iacono[1,2], L. Caremani[2], A. Govoni[2], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Department of NeuroMuscular-Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

Introduction: There are clear gender-related differences in the clinical features and response to pharmacological therapies in Parkinson Disease (PD). Most reports suggest that there is a PD symptoms' worsening and related need to increase L-Dopa during menstruation, when blood estrogens levels are lower. Estrogens may have a symptomatic benefit modulating dopaminergic transmission via prepost and perisynaptic mechanisms, modulating dopamine (DA) synthesis and release, stimulating dopaminergic synaptic contacts and decreasing COMT gene transcription and COMT and MAO activity.

Objectives: We present the case of a 46-years old parkinsonian woman who has a worsening of extrapyramidal symptoms during her premenstrual phase, when estrogens levels decrease.

Methods: Patient underwent MRI and SPET scans, gene screening and regular neurological evaluations.

Results: The patient has been suffering from PD since the age of 37, when she started to have tremor and bradykinesia in her right upper limb. L-Dopa and Pramipexole therapy was started with benefit, but she was complaining OFF periods always during premenstrual phase, characterized by more severe tremor and bradykinesia, early morning dystonia and anxiety. Melevodopa therapy was not tolerated: despite resolving OFF periods, it caused disturbing dyskinesias. Opicapone was then started with a good clinical response in the motor fluctuations control. Therapy with progestin-only pill was attempted, but this strategy worsened the extrapyramidal symptoms apart from the phase of her period, leading her to stop it.

Conclusions: This is an explicative example of how fluctuating estrogens levels may have effects on the dopaminergic pathways, severity of symptoms and therapeutical response. Further understanding of the role of sex hormones may lead to novel therapeutic strategies, combining L-Dopa with other molecules, in order to give a tailored therapy which could control these hormone and symptom fluctuations.

P183

RAPIDO (teleRehabilitation for pAtient with ParkInson's Disease at any mOment): preliminary results

Giulia Bonardi[1], M. Gandolfi[1], L. Pepa[2], A. Antoniello[3], A. Sabatelli[2], S. Valenti[2], L. Spalazzi[2], E. Andrenelli[3], S. Vada[3], M. Capecci[3], G. Farabolini[3], M. Tinazzi[1], M.G. Ceravolo[3]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of Information Engineering- Politecnica delle Marche University, Ancona, Italy
[3]Department of Experimental and Clinical Medicine - Politecnica delle Marche University, Ancona, Italy

Introduction: The current COVID-19 pandemic has revealed how fragile is the territorial care system dedicated to Parkinson's disease (PD). Thus, telemonitoring and telerehabilitation techniques are significant approaches for these people to improve their clinical health status. However, a greater integration of the existing systems is warranted. In the RAPIDO (teleRehabilitation for pAtient with ParkInson's Disease at any mOment) project, a remote monitoring system for physical exercises is proposed to enhance patients' rehabilitation [1]. At the same time, wearable devices collect health parameters throughout the day. These parameters are then stored on a remote server, facilitating subsequent analysis [2].

Objectives: The main objective of this study is to assess the acceptability and feasibility of an integrated telerehabilitation and telemonitoring system in patients with PD at any stage of the disease. Secondary objectives include evaluating the impact of the telerehabilitation and telemonitoring system on both motor and non-motor symptoms, the patient's quality of life, and the caregiver's burden.

Methods: Sixteen adults with PD at any stage of the disease were enrolled and equipped with smartwatches and tablets to independently perform an increasingly complex exercise program tailored to their motor profile for 12 weeks. Three evaluations were performed: at study entry (T0), after 3 months (T1), and after six months (T2). Wearable devices were used to collect 24-hour health parameters that were successively stored on a remote server and then analyzed.

Results: Sixteen PD patients were recruited in this study (37.5% women, age 70.19 ± 8.48) with an average Hoehn & Yahr Scale of 2.19 ± 0.36). Regarding system feasibility, patients completed an average of 92.00% of the expected sessions. System usability and subjective perception reported promising results. No statistically significant differences in health quality measures and motor and non-motor symptoms existed between T0 and the subsequent evaluations.

Conclusions: The treatment of PD patients through an integrated telerehabilitation system brought benefits in terms of patient satisfaction and improved quality of life and symptoms, in absence of any significant change in motor function and disease severity. Further information is expected at the completion of follow-up for the whole study sample.

References:

[1] A. Antoniello, A. Sabatelli, S. Valenti, M. Di Tillo, L. Pepa, S. L. et al., "A low-cost telerehabilitation and telemonitoring system for people with parkinson's disease: the architecture," 2022.
[2] A. Sabatelli, S. Valenti, A. Antoniello, M. Di Tillo, L. Pepa, L. Spalazzi et al., "Parkinson's disease telemonitoring and telerehabilitation based on commercial wearable sensor data analysis: a pilot study," 2022.

P184

The whistle-smile reflex in Parkinson's disease

Adriana Martini[1], G. Paparella[1,2], A.S. Grandolfo[1], D. Costa[1], D. Birreci[1], L. Balestrucci[1], M. De Riggi[1], L. Angelini[1], M. Passaretti[1], A. Cannavacciuolo[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: In Parkinson's disease (PD), facial movements alterations stand out as prominent features of the disease [1]. Interestingly, the lack of the whistle-smile reflex in PD has been anecdotally described in two reports [2,3] (Hanes 1943 and Monteiro et al., 2022). However, no experimental studies have investigated the whistle-smile reflex in a relatively large sample of PD patients to determine whether it constitutes a clinically useful sign.

Objectives: To assess whether the absence of whistle-smile reflex differentiates PD patients compared to age- and gender-matched healthy controls (HC).

Methods: We enrolled twenty-one PD patients (ON medication) and twenty-one HC. We recorded participants while they whistled and during neutral facial expressions for 30 seconds. Four raters, blinded to participants' status, evaluated the videos and identified whether subjects smiled or not after whistling. Raters also scored facial expressions using the MDS-UPDRS-III (item 3.2). We calculated inter-rater agreement using Fleiss' K and compared PD and HC data with non-parametric tests.

Results: We found substantial agreement among raters in video evaluation (Fleiss' K=0.66). As expected, MDS-UPDRS 3.2 scores were higher in PD than in HC (P=0.01 by Mann-Whitney U test). Eleven out of 21 PD patients (52.4%) did not smile after whistling and only 2 HC (9.5%) did not smile after the whistle according to all raters (P=0.0027 by Chisquare). Four patients (19.0%) were recognized to smile after whistling and 11 out of 21 HC (52.4%) smiled after the whistle according to all four raters (P=0.024 by Chisquare). Sensitivity, specificity, a n d positive and negative predictive values of t h e whistle-smile reflex absence in differentiating PD from HC were 0.73%, 0.85%, 0.85%, and 0.73%, respectively.

Conclusions: We demonstrate the substantial reduction of thewhistle-smile reflex in PD. Further investigations will be necessary to delineate the clinical correlates and utility of this alteration in clinical practice.

References:

[1] Bologna M, Fabbrini G, Marsili L, Defazio G, Thompson PD, Berardelli A. Facial bradykinesia. J Neurol Neurosurg Psychiatry. 2013 Jun;84(6):681-5. doi: 10.1136/jnnp-2012-303993. Epub 2012 Dec 12. PMID: 23236012.
[2] Hanes FM. Two clinically useful signs: 1. the whistle-smile reflex in the parkinsonian syndrome 2. the 'nephritic stare" in chronic nephritis. JAMA. 1943;121(14):1152–1153. doi:10.1001/jama.1943.62840140003007a
[3] Monteiro MD, Brustolin GT, Carvalho Neto EG, Rieder CRM. The whistle-smile reflex: a missed sign. Arq Neuropsiquiatr. 2022 Oct;80(10):1075-1076. doi: 10.1055/s-0042-1758396. Epub 2022 Dec 19. PMID: 36535292; PMCID: PMC9770076.

P185

Validity and Reliability of the Italian version of Short Parkinson's Evaluation Scale (SPES/SCOPA)

Ilaria Ruotolo[2], G. Sellitto[2], A. Berardi[2], R.S. Pisaltu[1], R. Simeon[1], F. Panuccio[1], E. Amadio[1], A. Marini Padovani[1], G. Fabbrini[2,3], G. Galeoto[2]

[1]Sapienza University of Rome, Rome, Italy
[2]Sapienza University of Rome, Department of Human Neuroscience, Rome, Italy
[3]IRCCS Neuromed, Pozzilli, IS, Italy
[4]Sapienza University of Rome, Department of Public Health and Infectious Disease, Rome, Italy

Background: In the medical and rehabilitative field, it is essential to employ tools such as evaluation scales and performance tests to assess the impact of Parkinson's disease on QoL of affected individuals. The Short Parkinson's Evaluation Scale (SPES) is a reliable and valid tool, applicable both in research and clinical practices (26), useful in assessing motor damage, activities of daily living, and motor complications in patients with Parkinson's disease. The aim of the study is to investigate the psychometric properties of the Italian version of the SPES-SCOPA scale.

Methods: Translation and cultural adaptation were performed. Included patients had diagnosis of Parkinson's disease, no concurrent pathologies, MiniMental test score above 2 and signed informed consent; they were recruited at the Department of Human Neurosciences in Sapienza University of Rome, from February 2023 to November 2023. Test-retest reliability was evaluated through Intraclass Correlation Coefficient (ICC), internal consistency was assessed using Cronbach's Alpha and construct validity using Pearson's correlation between SPES-SCOPA and the gold standard PDQ-39.

Results: 101 patients were recruited. Inter-rater evaluation was conducted on 62 patients, while 39 underwent an intra-rater assessment. The analysis showed statistically significant data with a Cronbach's Alpha value of 0.89 for the entire scale; test-retest reliability results are statistically significant for all subscales. Correlation between PDQ-39 domains and SPES/SCOPA subscales were statistically significant for most measurements.

Conclusion: This research shows that the Italian version of SPESSCOPA scale has excellent psychometric properties.

P186

Real-life, long-term evaluation of the use of opicapone as add-on therapy in Parkinson's disease

Anna Covolo[1,2], D. Rinaldi[3], P. Pacilio[3], M.G. Rizzone[1,2], M. Zibetti[1,2], A. Romagnolo[1,2], G. Imbalzano[1,2], C. Ledda[1,2], M.M. Tangari[1,2], L. Lopiano[1,2], C.A. Artusi[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy
[3]Department of Neuroscience, Mental Health and Sense Organs (NESMOS), Sapienza University of Rome, Rome, Italy

Introduction: Opicapone is a single-dose, potent COMT inhibitor used as add-on to levodopa to improve motor fluctuations in Parkinson's disease (PD) [1,2].

Objectives: To analyze long-term, real-life use of opicapone.

Methods: Retrospective observational study on data from PD patients followed by four movement disorder experts of the Cittádella- Salute-e-della-Scienza-di-Torino starting opicapone since October 2018. We analyzed: changes in dopaminergic therapy at opicapone prescription and at the following visit; timing and causes of opicapone interruptions.

Results: We included 69 patients (males 66.7%; age 61.2±9 years; disease duration 10.1±5.1 years, levodopa-Levodopa Equivalent Daily Dose (LEDD) 718.8 mg). The visit before opicapone prescription was not available for 14 patients. Dopaminergic therapy was modified in 58.2% (n=32/55) of patients at opicapone start, with a mean reduction of levodopa-LEDD of 15.6% (795.5 mg vs. 671.8 mg); 37.5% of these patients made a further minimal levodopa-LEDD reduction at the successive visit (637.5 mg vs. 632.6 mg). 30.4% (n=21/69) of patients interrupted opicapone after a mean of 24.3±17.3 months (42.9% for dyskinesia, 28.6% for transition to device-aided therapies, 23.8% for behavioral changes, 9.5% for persistent wearing-off, 4.8% for hallucinations). Among patients interrupting opicapone for dyskinesia for which we have available baseline data (n=6), 50% did not receive change of levodopa-LEDD at opicapone start, and 50% had minimal increase in levodopa-LEDD (419.2 mg vs. 441.7 mg). 57.1% (n=12/21) of patients interrupting opicapone resumed opicapone for worsening in motor fluctuations after a mean withdrawal of 9.6±11.9 months. At the last available visit (follow-up 34±18 months), 87% of patients had opicapone ongoing.

Conclusions: In real life, opicapone showed high rate of maintenance over a mean follow-up of 3 years. Data suggest the need for a reduction of levodopa-LEDD in most patients, being dyskinesia the main cause of interruption. Interestingly, >50% of patients interrupting opicapone resumed it later in the disease course.

References:

[1] Ferreira JJ, Lees A, Rocha JF, Poewe W, Rascol O, Soares-da-Silva P; Bi-Park 1 investigators. Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: a randomised, double-blind, controlled trial. Lancet Neurol. 2016 Feb;15(2):154-165. doi: 10.1016/S1474-4422(15)00336-1. Epub 2015 Dec 23. PMID: 26725544.
[2] Lees AJ, Ferreira J, Rascol O, Poewe W, Rocha JF, McCrory M, Soares-da-Silva P; BIPARK-2 Study Investigators. Opicapone as Adjunct to Levodopa Therapy in Patients With Parkinson Disease and Motor Fluctuations: A Randomized Clinical Trial. JAMA Neurol. 2017 Feb 1;74(2):197-206. doi: 10.1001/jamaneurol.2016.4703. PMID: 28027332.

P187

Mediterranean diet adherence in patients with Parkinson disease and glucocerebrosidase mutations

Luca Gallo[1], M. Avenali[1,2], P. Mitrotti[1], I. Palmieri[1], G. Cuconato[4], R. Calabrese[2], C. Galandra[1], C. Pasquini[1], R. Zangaglia[1], F. Valentino[1], E.M. Valente[3,4], F. Blandini[1,6], C. Tassorelli[1,2]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[5]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[6]Ca' Granda IRCCS Foundation, Ospedale Maggiore Policlinico, Milan, Italy

Introduction: In recent years, Mediterranean diet (MD) has been widely studied for its potential protective effects against several chronic diseases [1], including Parkinson Disease (PD)[2]. However, the relationship between PD, GBA mutations and the adherence to Mediterranean diet has still not been explored.

Objectives: To investigate a possible correlation between PD clinical features and MD adherence in a group of GBA-related PD (GBA-PD) patients compared to non mutated (NM-PD).

Methods: We analyzed clinical motor and non-motor features (UPDRS part I-IV; SCOPA-AUT, BDI-II, HADS-D, HADS-A, RBDSQ, UPSIT, MoCA and LEDD) and dietary habits (MEDAS questionnaire) in 52 GBA-PD and 84 NMPD patients. PD groups were also stratified by low/high adherence to the MD using the MEDAS cut-off score of 8. Within group analyses according to low/high diet adherence and between PD groups comparison were also performed.

Results: GBA-PDs showed an earlier age of disease onset and higher scores at UPDRS part I, BDI-II, HADS-D, HADS-A, compared to NM-PDs. No significant differences were found in MEDAS scores as well as UPDRS (part II, III and IV), MoCA, SCOPA-AUT, RBDSQ, LEDD and UPSIT scores between the two groups. GBA-PD patients with low diet adherence showed higher BDI-II and HADS-A scores as compared to GBA-PD patients with high diet adherence, while no difference was detected when comparing low diet adherence vs high diet adherence in the NM-PD group. We also report a significant correlation between a low MD adherence and higher scores in BDI-II ($p=0.0312$) in the GBA-PD group.

Conclusions: These findings show an interesting association between adherence to the Mediterranean diet and mood disorders in PD-GBAs. Further studies are needed to confirm these results and to investigate the underlying mechanisms of this association. If confirmed, these findings may have important implications for the development of personalized dietary interventions for PD patients with genetic mutations.

References:

[1] Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. BMJ. 2008 Sep 11;337:a1344. doi: 10.1136/bmj.a1344. PMID: 18786971; PMCID: PMC2533524.
[2] Solch RJ, Aigbogun JO, Voyiadjis AG, Talkington GM, Darensbourg RM, O'Connell S, Pickett KM, Perez SR, Maraganore DM. Mediterranean diet adherence, gut microbiota, and Alzheimer's or Parkinson's disease risk: A systematic review. J Neurol Sci. 2022 Mar 15;434:120166. doi: 10.1016/j.jns.2022.120166. Epub 2022 Jan 26. PMID: 35144237.

P188

Psychometric properties of the Parkinson's Disease Questionnaire – 39 and its Short Form Parkinson's Disease Questionnaire - 8: a systematic review and meta-analysis

Ilaria Ruotolo[1], A. Berardi[1], G. Sellitto[1], R. Simeon[2], F. Panuccio[2], E. Amadio[2], A. Ugolini[3], G. Fabbrini[1,4], G. Galeoto[1,4]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Sapienza University of Rome, Rome, Italy
[3]Private Practice, Empoli (FI), Italy
[4]IRCCS Neuromed, Pozzilli, IS, Italy

Background: Parkinson's disease (PD) significantly affects Quality of Life (QoL), since it is responsible for cognitive impairment, non-motor, and motor symptoms. The outcome measures are fundamental for evaluating treatment's effect on QoL over time

Objective: This systematic review aimed to identify the psychometric properties of the PDQ-39 and the PDQ-8 in the different populations in which they were validated.

Methods: The electronic databases that were systematically searched are: MEDLINE (via PubMed), CINAHL, SCOPUS, and Web of Science; the research was conducted in July 2023. The psychometric properties considered were those of the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) study design checklist. Risk of bias was assessed using the COSMIN checklist.

Results: The search identified 1306 articles. 398 duplicates were eliminated; 908 articles were analyzed reading title and abstract; 799 were finally excluded because were studies using the PDQ-39 and the PDQ-8 as outcome measures or were not dealing with psychometric properties; 66 articles were excluded after reading the full text. At the end, 43 articles were included in the review.

Conclusion: PDQ-39 demonstrated to be a specific HRQoL questionnaire that is correlated with generic HRQoL questionnaires, in fact in many studies included in the review, correlations with SF-36 were found. In the last studies about psychometric properties of PDQ- 8 emerged that it is a practical and informative instrument that can be easily used in clinical settings, especially in busy ones, but also in large-scale studies in which a brief instrument would be preferred.

P189

Gastrointestinal dysfunction entails peculiar clinical-biological features in Parkinson's disease

Jacopo Bissacco[1], R. Bovenzi[1], C. Simonetta[1], D. Mascioli[1], R. Cerroni[1], A. Stefani[1,2], N.B. Mercuri[1], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, Tor Vergata University of Rome, Rome, Italy
[2]UOSD Parkinson, Tor Vergata University Hospital, Rome, Italy

Introduction: Gastrointestinal dysfunctions (GIDs) are a critical issue in Parkinson's disease (PD), occurring in any phase of the disease course, from the premotor to the advanced ones. Recently, GIDs have also been considered a marker for specific clinical-pathological trajectories suitable for targeted interventions. In this regard, the novel Movement Disorders Society (MDS)-sponsored Gastrointestinal Dysfunction Scale for Parkinson's Disease (GIDS-PD) [1] allows for an accurate assessment of GIDs in PD patients.

Objective: To assess GIDs in a heterogenous PD cohort through the GIDS-PD and examine correlations with CSF biomarkers of neurodegeneration, blood-brain barrier (BBB) permeability, and clinical parameters.

Methods: We recruited 116 PD patients, including 57 de novo (DN) and 59 middle-advanced (MA) patients assessed with GIDS-PD, MDS-UPDRS III, Non-Motor Symptoms Scale (NMSS), MoCA, and levodopa equivalent daily dose (LEDD). For each patient we collected CSF amyloid-β42 (Aβ42), Aβ42/Aβ40 ratio, total-tau, phosphorylated-181-tau, total α-synuclein, CSF/serum albumin ratio. Clinical parameters and biomarkers were correlated, adjusting for main covariates separately in DN and MA groups.

Results: GIDS-PD inversely correlated with CSF amyloid-β42, and directly correlated with total-tau and CSF/serum albumin ratio in both DN and MA groups. GIDS-PD also inversely correlated with Aβ42/Aβ40 ratio, and directly correlated with phosphorylated-181-tau and α-synuclein only in the DN group. Finally, GIDS-PD directly correlated with MDS-UPDRS III and NMSS in both groups. No correlations resulted with MoCA and LEDD instead.

Conclusions: In both DN and MA PD patients, GIDs were proportionally associated with clinical burden and, from the biological perspective, with brain amyloidopathy, neural injury and blood-brain-barrier impairment. In DN group, patients with worse GIDs had higher CSF α-synuclein levels suggesting a minor load of central synucleinopathy, as described for the "body first" PD subtype [2]. Overall, we found that comorbid GIDs can precipitate the clinical-pathological profile of PD patients independently from the disease stage, identifying a frailer phenotype.

References:

[1] Camacho M, Greenland JC, Williams-Gray CH. The Gastrointestinal Dysfunction Scale for Parkinson's Disease. Movement Disorders [online serial]. John Wiley & Sons, Ltd; 2021;36:2358–2366.
[2] Grillo P, Sancesario GM, Mascioli D, et al. Constipation distinguishes different clinical-biochemical patterns in de novo Parkinson's disease. Parkinsonism Relat Disord [online serial]. Parkinsonism Relat Disord; 2022;102:64–67.

P190

Gait analysis may distinguish discrete phenotypes in newly diagnosed Parkinson's disease patients

Antonio Volzone[1], C. Ricciardi[2], M. Russo[2], M. Romano[2], F. Amato[2], A. Iavarone[3], C. Vitale[4], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry ″Scuola Medica Salernitana″, University of Salerno, Baronissi, Italy
[2]Department of Electrical Engineering and Information Technology, University of Naples ″Federico II″, Naples, Italy
[3]Neurological and Stroke Unit, CTO Hospital, AORN ″Ospedali dei Colli″, Naples, Italy
[4]Department of Motor Science and Wellness, University Parthenope, Naples, Italy

Introduction: Parkinson's Disease (PD) phenotypes have been generally based on motor symptoms [1], despite a clinical heterogeneity in non-motor symptoms since early stage [2]. Cluster analysis is a method of unsupervised Machine Learning (ML) algorithms, which do not require labelled dataset [3].

Objective: The aim was identifying different phenotypes in de novo PD patients through a clustering method based on gait parameters.

Methods: Thirty-six de novo PD patients were consecutively enrolled before starting dopaminergic therapy and clinically assessed. In addition, they were evaluated by Gait Analysis, using an optoelectronic system (BTS Bioengineering). An unsupervised approach of ML was implemented on spatial-temporal parameters through k-means clustering algorithm. After obtaining the clustered data, a statistical analysis was performed on the achieved groups to find the clinical profile associated with each cluster.

Results: K-means algorithm clustered the data into two groups: Cluster 1 and Cluster 2 including 15 and 21 patients, respectively. When comparing the two clusters, Cluster 1 versus Cluster 2 showed increase in mean cycle duration, mean support duration, mean swing duration, mean support phase (p-value <0,001) and reduction in mean swing phase, mean single support phase, mean velocity, cadence, mean cycle duration (p-value <0,001). When comparing demographical and clinical variables of the two groups, Cluster 1 versus Cluster 2 showed worse scores on the Part I and Part II of the MDS-UPDRS scale (p-value 0,02, 0,013, respectively). The two Clusters were comparable on age, H&Y scale and Part III of the MDS-UPDRS scale.

Conclusions: Cluster Analysis was able to identify two discrete PD phenotypes in newly diagnosed patients, based on a data-driven approach implemented with gait parameters. Therefore, subclinical gait impairment could identify a worse PD phenotype characterized by more severe non-motor symptoms, despite apparently similar motor impairment, since the onset of the disease.

References:

[1] Hendricks RM et al., 2021. Aging Dis; 12 (7):1567-1586.
[2] Liu P et al., 2011. J Zhejiang Univ Sci B.; 12 (9):694-703.
[3] S.M. van Rooden et al., 2010. Mov. Disord; vol. 25, fasc 8, pp. 969-978.

P191

Dysautonomia and cognitive impairment as clinical predictors of disease progression in patients with Parkinson's disease

Francesco Pirone[1,2], G. Di Rauso[3,4], F. Arienti[1], G. Franco[1], I. Trezzi[1], E. Monfrini[1,2], A.B. Di Fonzo[1]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[2]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy.
[3]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[4]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

Introduction: Parkinson's disease (PD) is a neurodegenerative disease with heterogeneous clinical manifestation and progression.

Objectives: To identify clinical factors at disease onset that may influence the type of PD course.

Methods: We enrolled a cohort of patients with PD, followed at Policlinico di Milano Fondazione IRCCS Ca' Granda. Selection criteria were 1) a follow-up of at least 10 years and 2) genetic investigation assessed. We collected clinical data, genetic tests, and levodopa equivalent daily dose (LEDD) at onset, 5 years and 10 years follow-up. Patients were classified according to the interquartiles of the percentage variation in LEDD between 10 and 5 years as "slow" (first interquartile), "intermediate" (second and third interquartiles), and "fast" in the fourth interquartile. Then we compared the three groups in terms of prevalence of different motor and non-motor clinical symptoms at onset and distribution of the associated genetic findings.

Results: The total population included in the study was 93 PD patients, of which 24 were fast progressors, 46 intermediate progressors and 23 slow progressors. The fast progressor patients had a higher prevalence of dysautonomia (8.33%) and cognitive impairment (8.33%) at onset than slow and intermediate progressor patients. In terms of motor symptoms, the prevalence of tremor and dystonia was higher in the intermediate group, 56.52% and 23.9% respectively. Finally, we observed an association between that genetic status and the disease progression.

Conclusions: Fast progressor PD patients have a higher prevalence of dysautonomia and cognitive impairment at onset. The elucidation of clinical and genetic factors that predict the disease progression will be useful to better stratify, manage and treat patients with PD.

P192

Peripheral immune and inflammatory dysregulation in Parkinson's disease patients

Tommaso Ercoli[2,4], A.R. Carta[1], A.F. Vega Benedetti[1], C. Porcedda[1], M.F. Palmas[1], C. Burgaletto[3], P. Solla[4], A. De Simone[5], G. Cantarella[3], V. Sogos[1], G. Defazio[2,6,1]

[1]Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy
[2]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[3]Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy
[4]Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy
[5]Department of Pharmacy, Federico II University of Naples, Naples, Italy
[6]Department of Translational Biomedicine and Neuroscience, Aldo Moro University of Bari, Bari, Italy

Introduction: Parkinson's disease (PD) displays clinical heterogeneity, presenting with motor symptoms and non-motor symptoms originating in the central nervous system or in periphery, which may reflect distinct clinical phenotypes. The immune system plays a prominent role in both central and peripheral pathology, reacting to misfolded α-synuclein (αSyn) with dysregulated inflammatory responses [1-2].

Objectives: To characterize the inflammatory profile and immunephenotype of peripheral blood mononuclear cells (PBMCs) in PD, after exposure to αSyn monomer (αSynM) or oligomer (αSynO) [3], and to investigate correlations with clinical scores.

Methods: 18 healthy subjects (HS) and 21 patients with Parkinson (PWP) were enrolled and PWP evaluated by motor (HY and UPDRS) and non-motor (NMSS and MoCA) scales. PBMCs were exposed to PBS, αSynO or αSynM, cytokines/chemokines release was measured by Multiplex Elisa, immune-phenotype was studied by FACS-flow cytometry. The inflammatory and immune profiles of PWP were correlated with clinical scores.

Results: PWP exhibited a dysregulated PBMCs-cytokine profile, which remained unaltered after exposure to αSynO or αSynM, and correlated with UPDRS, HY and the NMSS score. Both αSyn species significantly increased the cytokine/chemokine release by PBMCs from HS, leveling them up to PWP values. PWP and HS exhibited distinct PBMCs immune phenotypes, which were unaffected by exposure to αSyn species. Within the monocytes (Mos) subpopulations, frequency of classical Mos negatively correlated with disease duration and the non-motor item olfactory deficit. NKs from PWP showed a decrease in the CD56Dim/CD16+ mature fraction, and an increase in the unconventional CD56-/CD16+ fraction, which correlated with the non-motor item constipation. Stratification of PWP for olfactory deficits or constipation confirmed significant differences respectively in Mos and NKs subpopulations between the two groups of patients.

Conclusions: The inflammatory profile and immune phenotype was dysregulated in PBMCs from PWP. NK and Mos showed substantial correlations with peripheral or CNS-related PD symptoms respectively, suggesting that alterations in specific PBMCs fractions may support the diagnosis of different clinical phenotypes of PD.

References:

[1] Terkelsen MH, Klaestrup IH, Hvingelby V, Lauritsen J, Pavese N, Romero-Ramos M. Neuroinflammation and Immune Changes in Prodromal Parkinson's Disease and Other Synucleinopathies. J Parkinsons Dis. 2022;12(s1):S149-S163. doi: 10.3233/JPD-223245.

[2] El-Agnaf OM, Salem SA, Paleologou KE, Curran MD, Gibson MJ, Court JA, Schlossmacher MG, Allsop D. Detection of oligomeric forms of alpha-synuclein protein in human plasma as a potential biomarker for Parkinson's disease. FASEB J. 2006 Mar;20(3):419-25. doi: 10.1096/fj.03-1449com.
[3] Fusco G, Chen SW, Williamson PTF, Cascella R, Perni M, Jarvis JA, Cecchi C, Vendruscolo M, Chiti F, Cremades N, Ying L, Dobson CM, De Simone A. Structural basis of membrane disruption and cellular toxicity by α-synuclein oligomers. Science. 2017 Dec 15;358(6369):1440-1443. doi: 10.1126/science.aan6160.

P193

Salivary biomarkers for the differential diagnosis of Parkinson's disease and atypical parkinsonism

Alice Gualerzi[1], F.L. Saibene[1], S. Picciolini[1], L. Forleo[1], R. Martino[1], A. Mangolini[1], V. Mangolini[1,2], F. Rodà[1,3], S. Gobbo[1], A. Salvatore[1], A. Castagna[1], M. Meloni[4], P. Arcuri[1], P.I. Banfi[1], J.S. Navarro[1], M. Bedoni[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano, Italy
[2]Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, Brescia, Italy
[3]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[4]Azienda Ospedaliero- Universitaria di Cagliari, Cagliari, Italy

Introduction: The rapid identification and the differential diagnosis of subjects with Parkinson's disease (PD) and atypical parkinsonism is still an unmet clinical need. The identification of measurable, easily accessible biomarkers would allow to promptly identify the optimal pharmacological and rehabilitative therapy for each subject, leading to a significant improvement in the quality of life for the patient and, in the future, an increased probability slowing the progression of the disease.

Objectives: The objective of this project is the validation of Raman spectroscopy as diagnostic tool for the discrimination of people with PD from those with atypical parkinsonism through the analysis of a non invasive biological fluid, saliva. The main aim is the evaluation of the diagnostic potential of the Raman molecular signature of saliva and salivary extracellular vesicles (EVs).

Methods: Saliva collection and Raman analysis of whole saliva was performed following a previously published protocol [1]. Saliva samples were used for the isolation of salivary EVs as previously described [2]. Raman spectra were acquired from saliva and salivary EVs using an Aramis Raman microscope (Horiba). Data analysis included the correlation between the clinical profiling of people with PD and the spectral modification of salivary content and salivary EVs.

Results: Preliminary data obtained on the characterization of saliva and salivary EVs from people with PD and with atypical Parkinsonism support the use of Raman spectroscopy as a valuable tool for PD differential diagnosis. Besides, the proposed operating procedure was demonstrated to be feasible in a clinical scenario, thanks to the limited time requested for sample collection, the easy storage of salivary samples and the minimal invasiveness of collection.

Conclusions: The Raman spectrum of saliva and salivary EVs represents a promising biomarker for PD, that can fill the current lack of a measurable biomarker for rapid differential diagnosis and for monitoring the evolution of the diseases. Besides, it would help to personalize the pharmacological and rehabilitation intervention identifying the optimal pharmacological and rehabilitative therapy for each subject.

References:

[1] Carlomagno, C.; Bertazioli, D.; Gualerzi, A.; Picciolini, S.; Andrico, M.; Rodà, F.; Meloni, M.; Banfi, P.I.; Verde, F.; Ticozzi, N.; et al. Identification of the Raman Salivary Fingerprint of Parkinson's Disease Through the Spectroscopic–Computational Combinatory Approach. Front. Neurosci. 2021, 15, doi:10.3389/fnins.2021.704963.
[2] Mangolini, V.; Gualerzi, A.; Picciolini, S.; Rodà, F.; Del Prete, A.; Forleo, L.; Rossetto, R.A.; Bedoni, M. Biochemical Characterization of Human Salivary Extracellular Vesicles as a Valuable Source of Biomarkers. Biology 2023, 12, 227, doi:10.3390/biology12020227.

P194

Cognitive and behavioural changes in relation to the presence and reversion of impulse control disorder in patients with Parkinson's disease

Valeria Sant'Elia[1], M. Siciliano[1,2], R. De Micco[1], S. Aloisio[1], E.N. Mosca[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Introduction: Around 14% of patients with Parkinson's disease (PD) suffer from an impulse control disorder (ICD), which consists of a loss of voluntary control that leads to repetitive and excessive behaviors. The exposure to dopamine agonists is known as the main risk factor of ICD in PD patients. A few studies have compared cognitive and behavioral features of patients with and without ICD, suggesting that their development is related to the presence of deficits in executive functions, such as set shifting and working memory. However, no study has investigated the effect of ICD reversion on cognitive and behavioral features in PD patients.

Objectives: To investigate the cognitive and behavioural changes occurring in PD patients before and after ICD reversion following dopamine agonists dose reduction or discontinuation.

Methods: Ten patients with PD (10% male; age 62±5.67 years) with ICD were consecutively enrolled. The ICD was screened by means of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) (cut off≥1). Patients were assessed at baseline, when ICD were actively present. Dopamine-agonists regimen was modified after clinical assessment which was re-acquired after complete ICD reversion (follow-up duration 2.66±1.5 months). We assessed changes in cognitive functioning in by using the two parallel versions of Montreal Cognitive Assessment (MoCA) and we evaluated changes in sleepiness, fatigue, depression, anxiety, and apathy. We used the Wilcoxon test to evaluate these changes.

Results: Compared to baseline, we found that the performance of the MoCA total score (Cohen's d= 0.74, p=0.011) and its memory domain (Cohen's d= 0.76, p=0.041) improved after ICD reversion.

Conclusions: We provided preliminary evidence that in PD patients the shift from ICD presence to recovery is associated with improved cognitive functioning, especially global cognition and memory. Our findings may foster the development of early combined therapeutic approaches for cognitive and behavioural disturbances.

P195

The role of T lymphocytes subtypes as possible poor outcome predictors in Parkinson's disease

Federico Colombatto[1], F. Vignaroli[1], S. Gallo[1], E. Contaldi[1], R. Cantello[1], L. Magistrelli[1], C. Comi[2]

[1]Neurology Unit, Department of Traslational Medicine, University of Piemonte Orientale, Novara, Italy
[2]Neurology Unit, S. Andrea Hospital, Department of Translational Medicine, University of Piemonte Orientale, Vercelli, Italy

Introduction: Peripheral immune system plays a key role in the pathophysiology of PD. In fact, patients display a pro-inflammatory phenotype characterized by increased Th1 and Th17 cells, decreased Th2 cells and dysregulation of Treg compartment. Whether it may be considered a predictor of clinical outcome has not yet been investigated.

Objectives: To evaluate, in a cohort of Parkinson's disease (PD) naïve patients, whether peripheral immunological parameters may correlate with long-term disease outcome.

Methods: 8 idiopathic PD patients were evaluated with UPDRS part III scale and a semantic fluency test, (the animal fluency test). Based upon the prognostic model proposed and validated by Velseboer at al [1], we calculated the probability of an unfavorable outcome, intended as the development of dementia or postural instability (Hoehn and Yahr ≥ 3) at 5 years from disease onset. Furthermore, we correlated this probability with lymphocyte count, cytofluorimetric T cell subsets and the expression of transcription factors involved in lymphopoiesis (such as STAT1, STAT3, STAT4, STAT6, RORC, TBX21, GATA3, NR4A2 and FOXP3). Statistical analyses were conducted using Pearson correlation coefficient (r) and t-student test.

Results: Positive correlation was found between a poor outcome and CD4+ T cells absolute count ($r=0.62$, $p<0.05$), while no correlation was found with CD3+ nor with CD8+. Subsequently, we evaluated CD4+ T cell subsets: T helper (Th)1 were positively correlated with a poorer outcome ($r=0.60$, $p<0.05$), while a negative correlation was found between Th2 and an unfavourable outcome ($r=-0.41$, $p<0.05$). No correlation was found with Treg nor Th17, even if RORC expression had a significant correlation with the poor outcome ($r=0.67$, $p<0.05$). No additional correlation was found with the transcription factors analysed.

Conclusions: Even considering the small sample size, in the present study we identified a possible correlation between Th1 cells and poor outcome, suggesting that a greater pro-inflammatory state from the beginning may influence disease course.

References:

[1] Velseboer DC, de Bie RM, Wieske L, Evans JR, Mason SL, Foltynie T, Schmand B, de Haan RJ, Post B, Barker RA, Williams-Gray CH. Development and external validation of a prognostic model in newly diagnosed Parkinson disease. Neurology. 2016 Mar 15;86(11):986-93. doi: 10.1212/WNL.0000000000002437. Epub 2016 Feb 17. PMID: 26888991; PMCID: PMC4799715.

P196

Motor and non-motor correlates of hyposmia detected by the Italian Olfactory Identification Test (IOIT) in an italian cohort of Parkinson's disease patients

Alessandro Mechelli[1], S. Simoni[2], P. Nigro[1], E. Cresta[3], G. Susca[3], A. Tufo[3], C. Maremmani[4], N. Tambasco[1], L. Parnetti[3]

[1]Movement Disorders Center, Neurology Department, Perugia General Hospital and University of Perugia, Perugia, Italy
[2]Neurology Unit-Stroke Unit, Città di Castello Hospital, USL Umbria 1, Perugia, Italy
[3]Neurology Department, Perugia General Hospital and University of Perugia, Perugia, Italy
[4]Neurology Department, Apuane Hospital, Massa, Italy

Introduction: Olfactory dysfunction is one of the earliest and most frequent non-motor symptoms (prevalence >90%) in PD. However, hyposmia correlation with motor or other non-motor symptoms still lacks a full characterization [1].

Objectives: To characterize olfaction in a cohort of PD patients and to investigate the relationship between olfactory impairment with both motor and non-motor features and other clinical characteristics (duration, stage and severity).

Methods: One-hundred fifty-four patients with idiopathic PD without dementia (Mini-Mental State Examination score >25) were included. Odor identification ability was tested using the validated Italian Olfactory Identification Test (33-testers), specifically designed for the Italian population [2]. A comprehensive spectrum of motor (tremor, bradykinesia, rigidity, postural stability, gait, masked face, speech, voice, posture) and non-motor features (urinary symptoms, depression, sleep disorders, constipation) was assessed. Patients were divided into 3 clinical phenotypes: tremor-dominant type (TDT), akinetic-rigid type (ART) and mixed type (MXT) [3].

Results: Hyposmia was found in 141/154 (93%) patients (mean H&Y:1.99±0.6, mean UPDRS-partIII score:23.4±11.56, mean age 66.96±9.2 years, mean disease duration 5.57±4.9 years). Hyposmic patients were older than those with normal olfaction ($p=0.012$). H&Y score≥2 was associated with a higher probability of being hyposmic (OR=1.18, $p=0.01$). IOIT score did not significantly differ between TDT, ART and MXT PD patients. IOIT score directly correlated with patients' age ($p<0.001$), disease duration ($p=0.01$) and H&Y score≥2($p<0.05$). Clinical features associated with higher IOIT score were freezing of gait (FOG) (+2.38, $p=0.027$) and camptocormia (+2.31, $p=0.022$).

Conclusions: Assessing olfactory dysfunction through IOIT may help identify PD patients at higher risk of developing severe motor features (camptocormia and FOG). Overall, IOIT may be a useful tool not only for supporting PD diagnosis but also for providing prognostic information about motor function. Follow-up studies are warranted to confirm IOIT's ability to predict more sever motor symptoms in PD patients.

References:

[1] Roos DS, Twisk JWR, Raijmakers P, Doty RL, Berendse HW. Hyposmia as a marker of (non -)motor disease severity in Parkinson's disease. J Neural Transm (Vienna). 2019;126(11):1471-8.
[2] Maremmani C, Rossi G, Tambasco N, Fattori B, Pieroni A, Ramat S, et al. The validity and reliability of the Italian Olfactory Identification Test (IOIT) in healthy subjects and in Parkinson's disease patients. Parkinsonism Relat Disord. 2012;18(6):788-93.
[3] M.C. Schiess, H. Zheng, V.M. Soukup, J.G. Bonnen, H.J.W. Nauta, Parkinson's disease subtypes: clinical classification and ventricular cerebrospinal fluid analysis, Parkinsonism Relat. Disord., 6 (2) (2000), pp. 69-76.

P197

The chronic use of serotonin norepinephrine reuptake inhibitors facilitates dyskinesia priming in early Parkinson's disease

Massimo Marano[1,2], A. Magliozzi[1,2], A. Pilotto[3,4,5], G. Vivacqua[6], M. Carta[7], M. Meloni[7]

[1]Unit of Neurology, Neurophysiology, Neurobiology and Psychiatry; Department of Medicine; Università Campus Bio-Medico di Roma, Roma, Italy
[2]Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[3]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[4]Laboratory of Digital Neurology and Biosensors, University of Brescia, Brescia, Italy
[5]Neurology Unit, Department of Continuity of Care and Frailty, ASST Spedali Civili Brescia Hospital, Brescia, Italy
[6]Laboratory of Microscopic and Ultrastructural Anatomy; Università Campus Bio-Medico di Roma, Roma
[7]Neurology Unit, Azienda Ospedaliera Universitaria di Cagliari, Cagliari, Italy

Introduction: Parkinson's disease (PD) patients are frequently exposed to antidepressant medications (ADMs), acting on the norepinephrine (NE) and serotonin (5HT) systems. Both these ADMs, according to the preclinical evidence, have a role in the pathophysiology of levodopa induced dyskinesias (LID) [1,2,3].

Objectives: To evaluate the role of ADMs on dyskinesia development.

Methods: We evaluated the longitudinal data of the PPMI cohort, including patients naïve to dopamine replacement therapies (DRTs), who are progressively exposed to DRT and L-DOPA. The main outcome was the development of LID within the fourth year of follow-up and the association with ADMs.

Results: 251 subjects with full available longitudinal data were selected. The prevalence of LID at 4 years of treatment was 16% (42/251). Patients who developed LID were more likely women (26 vs 45%, p=0.01), had higher motor scores at baseline (20.3 ± 8.7 vs 24.1 ± 8.6, p<0.001), geriatric depression scores at baseline (2 ± 1.9 vs 3.4 ± 2.7, p=0.01) and follow-up (2.7 ± 2.8 vs 3.9 ± 3.6, p=0.03) and putaminal DAT binding ratio at baseline (0.80 ± 0.26 vs 0.70 ± 0.24, p=0.04) and follow-up (0.53 ± 0.19 vs 0.44 ± 0.19, p=0.01). The presence of LID was associated with the exposure time to L-DOPA (2.2 ± 1.07 vs 2.6 ± 0.9, p=0.02) and the exposure to ADMs, in particular to SNRI (4.8% vs 21.4%, p<0.001) and NDRI (5.2% vs 16.7 %, p<0.01). Univariate and multivariate analysis confirmed the association between SNRI and LID, and that such an association occurred independently by other known factors able to influence the LID risk (sex, disease duration, cognitive status, motor impairment, ^{123}I-I-FP-CIT data).

Conclusions: This study supports the presence of an effect of SNRI on LID priming in patients with early PD. Independent cohorts are under recruiting to replicate such finding.

References:

[1] Carta M, Carlsson T, Muñoz A, Kirik D, Björklund A. Involvement of the serotonin system in L-dopa-induced dyskinesias. Parkinsonism Relat Disord. 2008;14 Suppl 2:S154-8. doi: 10.1016/j.parkreldis.2008.04.021. Epub 2008 Jun 24.
[2] Mazzucchi S, Frosini D, Ripoli A, Nicoletti V, Linsalata G, Bonuccelli U, Ceravolo R. Serotonergic antidepressant drugs and L-dopa-induced dyskinesias in Parkinson's disease. Acta Neurol Scand. 2015 Mar;131(3):191-5.

[3] Chotibut, T., Fields, V., and Salvatore, M. F. (2014). Norepinephrine transporter inhibition with desipramine exacerbates L-DOPA-induced dyskinesia: role for synaptic dopamine regulation in denervated nigrostriatal terminals. Mol. Pharmacol. 86, 675–685.

P198

HDL-cholesterol serum levels are associated with the clinical-biological profile of Parkinson's disease patients

Davide Mascioli, R. Bovenzi, J. Bissacco, C. Simonetta, A. Stefani, N.B. Mercuri, T. Schirinzi

Unit of Neurology, Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy

Introduction: Recent evidence indicates a link between the serum lipid profile and Parkinson's disease (PD). In particular, the lower serum high-density lipoprotein levels increase the risk to develop the disease. However, the biological bases of such association have not been clarified yet [1].

Objectives: To analyze the correlations between serum lipid profile and CSF biomarkers of neurodegeneration in a well characterized cohort of PD patients.

Methods: We conducted a cross-sectional study including 84 PD patients and 71 sex/age-matched controls (CTRLs). Serum levels of HDL (HDL-C), low-density lipoprotein (LDLC), total cholesterol (TC-C) and triglycerides (TG-C) were measured and correlated with CSF levels of total α-synuclein (α-syn), amyloid-β-42 (Aβ42), total and phosphorylated tau separately in each group by using appropriate covariates. In patients, lipids were correlated with MDS-UPDRS part III, H&Y scale, Non-Motor Symptom Scale (NMSS), MMSE, and MoCA scores.

Results: Compared to controls, PD patients had lower CSF α-syn and lower serum TR-C. In PD, but not in controls, lipids had significant associations with CSF biomarkers and clinical parameters. In particular, HDL-C directly correlated with α-syn and Aβ42; TG-C inversely correlated with Aβ42. In addition, HDL-C was inversely correlated with NMSS and and directly correlated with MMSE scores.

Conclusions: This study provided evidence for the association between serum lipid profile and central neurodegeneration in PD. Specifically, we found that lower HDL-C levels may account either for greater brain synucleinopathy and amyloidopathy, or widespread neurotransmitter impairment, as the higher non-motor symptoms burden and cognitive impairment suggest. These data are consistent with the antioxidant and anti-inflammatory functions of HDL or the anti- α-synuclein aggregation properties of the apolipoproteins constituting the HDL complex, providing the biological substrate of the greater vulnerability to PD of people with lower HDL-C.

References:

[1] Park, Joo-Hyun et al. "Association of High-Density Lipoprotein Cholesterol Variability and the Risk of Developing Parkinson Disease." Neurology vol. 96,10 (2021): e1391-e1401.

P199

Parkinson disease: the importance of advanced skills in neuroscience nursing. A review

Federico Cortese[2,3], M. Ruggeri[1], S. Scaroni[2], A. Sollami[2,3]

[1]Casa di Cura "Città di Parma", Parma, Italy
[2]Dipartimento Testa-collo, Azienda Ospedaliero Universitaria di Parma, Parma, Italy
[3]Dipartimento Medicine Specialistiche, Azienda Ospedaliero Universitaria di Parma, Parma, Italy
[4]Dipartimento Professioni Sanitarie, Azienda Ospedaliero Universitaria di Parma, Parma, Italy

Introduction: Parkinson's disease is a neurodegenerative disease that affects about 1-2% of people over 65 and about 4% of people over 80 years old. People with Parkinson's disease may have motor and non-motor symptoms that worsen as disease progresses, causing a reduction in their autonomy. Nowadays there are no specific guide lines about Parkinson's for nurses. In order to improve care in Parkinson's, in several countries such as German and United Kingdom, it has been introduced a trained nurse with advanced skills: the Parkinson's Disease Nurse Specialist.

Objectives: The Objective of this study is to define and measure the advanced skills of the specialist in neuroscience nursing and Evaluate the impact of the nurse specialist in the care pathway.

Methods: The review of national and international literature was conducted by examining 23 articles found in the following databases: Pubmed, Cinahl and Cochrane Library.

Results: The competences of the Parkinson's Disease Nurse Specialist (P.D.N.S.): providing information, education and education for the patient and his caregiver; supporting the caregiver and caregiver during the promotion of self-care activities; providing psychological support; implement actions aimed at prevention; provide specialized diagnostic strategies and nursing therapeutic interventions; collaborate within a multidisciplinary team. The treatments provided by the Parkinson Disease Nurse Specialist show a significant improvement in the well-being of the patients and their caregivers without increasing health costs. In addition, this figure is the first point of reference for people suffering from this pathology and relieves the work pressure that weighs on neurologists and geriatricians.

Conclusions: The Parkinson's Disease Nurse Specialist has proven to be a valuable resource in assisting people with Parkinson's disease.

References:

[1] Balestrino, R., & Schapira, A. H. (2020). Parkinson disease. European Journal of Neurology , 27(1), 27-42. https://doi.org/ 10.1111/ene.14108.
[2] Bhidayasiri, R., Boonpang, K., Jitkritsadakul, O., van Laar, T., Calne, S. M., Henriksen, T., . . . Ray Chaudhuri, K. (2016). Understanding the role of the Parkinson's disease nurse specialist in the delivery of apomorphine therapy. Elsevier, 33(1), 49-55. https://doi.org/ 10.1016/j.parkreldis.2016.11.014.
[3] Brown, S., Dalkin, S. M., Bate, A., Bradford, R., Allen, C., Brittain, K. Hand, A. (2020). Exploring and understanding the scope and value of Parkinson's nurse in the UK (The USP Project): a realist economic evaluation protocol. BMJ Open, 10(10), 1https://doi.org/ 10.1136/bmjopen-2020-037224.
[4] Fabbri, M., Coelho, M., Garon, M., Biundo, R., Mestre, T. A., & Antonini, A. (2022). Personalized Care in Late-Stage Parkinson's Disease: Challenges and Opportunities. Personalized Medicine, 12(5), 1-10. https://doi.org/10.3390/jpm12050813.
[5] Flinkman, M., Leino-Kilpi, H., Numminen, O., Jeon, Y., Kuokkanen, L., & Meretoja, R. (2017). Nurse Competence Scale: a systematic and psychometric review. Journal of Advanced Nursing, 73(5), 1035-1050. https://doi.org/10.1111/jan.13183.
[6] Hand, A., & Martin , A. (2015). Assessing quality of life in Parkinson's: the nuerse specialist's role. British Journal of Neuroscience Nursing , 11(4), 166-169. https://doi.org/10.12968/bjnn.2015.11.4.166.

[7] Hellqvist, C., & Berterö , C. (2015). Support supplied by Parkinson's disease specialist nurses to Parkinson's disease patients and their spouses. Elsevier, 28(2), 86-91. https://doi.org/10.1016/j.apnr.2014.12.008 .

P200

Fashion and clothing challenges for people with Parkinson's disease: an international survey

Elena Berti[1], S. Della Morte[2], F. De Bartolomeis[3], F. Morgante[4], L. Ricciardi[4]

[1]Clinical Psychologist, CM Trainer, Mindfulness Instructor; ParkinZone Onlus, Rome, Italy
[2]Psychotherapist, Mindfulness Instructor, CF Therapist, ParkinZone Onlus, Rome, Italy
[3]Psychomotor Therapist; Parkinson No Limits, Fuerteventura, Canary Islands, Spain
[4]Neurosciences Research Center, Molecular and Clinical Sciences Research Institute, St George's University of London, UK; Medical Research Council Brain Network Dynamics Unit, Nuffield, Department of Clinical Neurosciences, Oxford, UK

Introduction: People with Parkinson's disease (PD) often have reduced dexterity and they may experience difficulty in getting dressed or with personal hygiene. Little is known about the changes in the way people with PD dress and what adjustments they adopt in their style to overcome the difficulties they face due to their disease.

Objectives: Aim of the present study was to explore the way people with PD perceive their image in the mirror and the challenges they face with clothes and accessories.

Methods: A online survey (26 questions) was sent via email; questions were focused on quantifying the difficulties in wearing clothes or accessories. In 54% of the questions, the answer was based on a Likert scale (0=no difficulty, 4=not able to do it without help). 33% of the questions required an open answer and the remaining were multiple choice options.

Results: 99 people with PD completed the survey (63 female and 36 male; mean disease duration=10.3 yrs ds=10.1, mean age= 58.9 yrs ds=8.4). Prevalent motor symptoms reported were walking difficulties, tremor, bradykinesia. 88% of the participants defined themselves as interested in fashion, 59.6% reported a change in the way they dress because of the disease. They all see themselves changed in the mirror (abnormal posture, facial expression, body shape). The 3 most difficult tasks detected were in order: back zip, buttons, shoelaces.

Conclusions: People with neurodegenerative disorders face challenges with getting dressed and wearing accessories. They also experience changes in their self-image perception and their usual dressing habits because of the disease. Fashion should address these challenges and take action in order to be more inclusive and supportive.

P201

Cognitive Reserve and its subcomponents in people with Parkinson's disease: possible effects on cognitive domains

Anna Salvatore[1], S. Di Tella[1,2], S. Gobbo[1], P. Arcuri[1], A. Castagna[1], E. Farina[1], M. Alberoni[1], E. Calabrese[1], J.S. Navarro[1], M. Meloni[1,3], F.L. Saibene[1]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy
[3]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy

Introduction: The concept of cognitive reserve was proposed to explain the differences among individuals in their ability to cope with physiological or pathological cognitive decline and suggests that the brain actively attempts to cope with damage by using pre-existing cognitive processes or using compensatory strategies. Several studies investigated cognitive reserve (CR) in people with Parkinson's disease (PwPD) [1].

Objectives: The aim of this study was to investigate the effects of CR and its subcomponents (CRI-Education, CRI-WorkingActivity, CRI-LeisureTime) on cognitive functioning in PwPD.

Methods: 73 PwPD (Age:69.97±6.49; H&Y:1.50-3; 39M/34F). Cognitive functioning was assessed through the administration of a global cognitive functioning test (MoCA Test) [2] and a complete neuropsychological battery while CR was investigated through the CRI-q [3].

Results: Regression analyses showed an effect of CR in the following test: MoCA Test and its domains (except visuo-spatial abilities and orientation), Attentive Matrices, Alternating Verbal Fluency, Phonemic Verbal Fluency, Raven's Matrices, Copy and Recall of Rey's Figure and Imitation Gesture Test. A significant effect of CRI-LeisureTime was found in TMT-B, TMT-B-A, Alternating Verbal Fluency, Phonemic Verbal Fluency, Raven's Matrices and Copy of Rey's Figure. Furthermore, a significant interaction effect was found between CRI-Education *Gender: females with higher- CR-Education, unlike men, show a better performance than females with lower- CRI-Education in Recall of Rey's Figure test.

Conclusions: CR has a positive impact on global cognitive functioning and on several cognitive domains. In particular, CRI-q-LeisureTime seems to have a positive impact especially on attentional-executive functions. Thus, high CR may help to cope with initial cognitive difficulties in PwPD. Furthermore, this could be important in preventive and rehabilitative perspective, as CRI-LeisureTime can be enhanced by cognitively stimulating activities. Further studies are necessary to investigate how CR and its subcomponents modulate cognitive impairment in PwPD.

References:

[1] Hindle, J. V., Martyr, A., & Clare, L. (2014). Cognitive reserve in Parkinson's disease: a systematic review and meta-analysis. Parkinsonism & related disorders, 20(1), 1-7.
[2] Santangelo, G., Siciliano, M., Pedone, R., Vitale, C., Falco, F., Bisogno, R., ... & Trojano, L. (2015). Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36, 585-591.
[3] Nucci, M., Mapelli, D., & Mondini, S. (2012). Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. Aging clinical and experimental research , 24, 218-226.

P202

Effects of dopaminergic therapy on swallowing physiology: electrokinesigraphic study in patients with Parkinson's disease

Francesca Valentino[1], A. Kapidiani[2], M. Rossi[3], G. Belluscio[1,2], S. Malaspina[1,2], M. Avenali[1,2], C. Pacchetti[1], R. Zangaglia[1], G. Cosentino[2,3]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[3]Translational Neurophysiology Research Unit, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Though dopaminergic therapy is the gold-standard treatment for PD, its effects on the swallowing function are still debated and both beneficial and detrimental effects have been described so far. The high variability of PD-related dysphagia response to levodopa suggests that swallowing abnormalities in PD are not solely related to dopamine deficiency.

Objective: To assess the swallowing function through an electrokinesigraphic approach in a group of non-dysphagic PD patients with motor complications evaluated both in off- and ontherapy.

Methods: The repeated swallowing (8 swallowing acts) of a liquid bolus (12 cc of water) was performed while recording the following parameters: i) surface electromyographic activity of the submentalsuprahyoid muscles (sh-EMG), involved both in the oral and pharyngeal phases of swallowing); ii) intraswallowing apneic pause (AP); iii) pharyngo-laryngeal mechanogram (PLM). Amplitude, duration and area of the recorded signals and time intervals were calculated using the Matlab platform. All patients were assessed twice, i.e. both in on- and off-medication state.

Results: 11 patients (64 ±6.4, 4F/7M) were enrolled and completed the experimental assessments. A significant ($p<.05$) shortening of the interval between the inspiratory and expiratory peaks and the end of the AP was observed in the on- vs. off-medication state. Better but not statistically significant swallowing performances were also observed in patients when on-medication, in particular we observed a shorter oro-pharyngeal dealy ($p=.11$) and a larger area of the PLM ($p=.017$).

Conclusion: Dopamine therapy can improve the synergy between breathing and swallowing in accordance to previous findings that dopaminergic treatment can improve pulmonary function tests. However, based on these preliminary results in a small group of nondysphagic PD patients, no significant changes in the other aspects of the oral and pharyngeal phases of swallowing were observed.

P203

Pisa syndrome and botulinum toxin injection in paraspinal muscle ipsilateral to the bending site regardless of EMG signals: a pilot study

Tiziana Maria Isabella Lombardo, V. Cenacchi, G. Bellavita, V. Tommasini, M. Catalan, L. Antonutti, M. Liccari, P. Manganotti

Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy

Introduction: PS consists of a lateral flexion on the spine and is a common dystonic posture in patients with PD. It is possibly due to muscle hyperactivity, ipsi- or contralateral to the bending side [1]. One of the possible therapies in dystonic issues, botulinum toxin (BoNT), acts in PS by blocking the presynaptic release of acetylcholine at the neuromuscular junction level [2].

Objective: The aim of our study was to evaluate the clinical and electromyographical effects of botulinum toxin injections in patients with Parkinsons's disease (PD) suffering from Pisa syndrome (PS) after one and three months.

Methods: This pilot study involved 16 patients with PD and PS, recruited from the Movement Disorders Unit of Trieste (Italy) between March 2021 and March 2023. Each patient was evaluated at baseline, 1 month and 3 months after BoNT injection, which was always ipsilateral to the bending site regardless of EMG activation. We recorded demographic, PD- and PS-related clinical variables, including measure of selfperceived health (PDQ-8 and PGIC scales), and back pain evaluation (VAS scale). Muscular hypo- and hyperactivity patterns were assessed using superficial EMG recording. Lateral bending angle of the spine was calculated on the planar view photographs as the angle between the vertical axis and a line connecting the fulcrum of the bent spine with the C7 spinous process.

Results: Sixteen outpatients (44% females; aged 73±6; disease duration 6±3 years; 56% mixed-phenotype PD; LEDD 572±346) showed an initial reduction in bending degrees followed by a reversion (6.5±3, 5±1.5, 6.7±6 degrees at baseline, 1 and 3 months respectively; there was a trend toward significance between baseline and 1 months with p .12316), a substantial stability in PDQ-8 scores (4±3.2, 3.3±2.8, 4±3.9), and a reduction in back pain (3.9±3.2, 2.1±2.3, 2.9±3.4; the difference between baseline and 1 month resulted significant with p .004392, between baseline and 3 months p .447019). Accordingly to 91 and 100% of the patients at 1 and 3 months respectively, their condition globally improved (considering "improvement" as PGIC scores ≥3). Qualitative EMG signal analysis showed an almost uniform improvement in global paraspinal muscle activation.

Conclusion: Our study shows an efficacy in bending angle reduction after 1 month from the treatment with a reversion after 3 months (as expected from BoNT pharmacodynamic), and a subjective clinical improvement extending also after this time limit. This may indicate a benefit deriving from ipsilateral injection regardless of EMG activity.

References:

[1] Doherty KM, van de Warrenburg BP, Peralta MC, Silveira-Moriyama L, Azulay JP, Gershanik OS, Bloem BR. Postural deformities in Parkinson's disease. Lancet Neurol. 2011 Jun;10(6):538-49. doi: 10.1016/S1474-4422(11)70067-9. Epub 2011 Apr 22. PMID: 21514890.

[2] Tassorelli C, De Icco R, Alfonsi E, Bartolo M, Serrao M, Avenali M, De Paoli I, Conte C, Pozzi NG, Bramanti P, Nappi G, Sandrini G. Botulinum toxin type A potentiates the effect of neuromotor rehabilitation of Pisa syndrome in Parkinson disease: a placebo controlled study. Parkinsonism Relat Disord. 2014 Nov;20(11):1140-4. doi: 10.1016/j.parkreldis.2014.07.015. Epub 2014 Aug 13. PMID: 25175601.

P204

Predicting the clinical diagnosis of Parkinson's disease using machine learning approaches on linguistic measures

Cinzia Palmirotta[1], S. Aresta[1,2], S. Tagliente[1], G. Lagravinese[1], C. Gelao[2], D. Mongelli[1], R. Falcone[1], P. Fiore[2,3], I. Castiglioni[4], F. Tamma[5], B. Minafra[2], P. Battista[1,6], C. Salvatore[7,8]

[1]Istituti Clinici Scientifici Maugeri IRCCS, Laboratory of Neuropsychology, Bari Institute, Bari, Italy
[2]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Bari Institute, Bari, Italy
[3]Department of Physical and Rehabilitation Medicine, University of Foggia, Foggia, Italy
[4]Department of Physics G. Occhialini, University of Milan-Bicocca, Milan, Italy
[5]Neurology Unit, Miulli Hospital, Acquaviva delle Fonti, BA, Italy
[6]Global Brain Health Institute (GBHI), University of California, San Francisco, CA, USA
[7]Department of Science, Technology and Society, University School for Advanced Studies IUSS Pavia, Pavia, Italy
[8]DeepTrace Technologies S.R.L., Milan, Italy

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disease caused by the loss of nigrostriatal dopaminergic neurons, causing motor and non-motor symptoms [1]. Furthermore, PD patients can experience difficulties with linguistic production at basic and complex levels, particularly in tasks requiring action words or fluency. Given the evidence supporting the classification of patients with Alzheimer's disease, studies on the application of machine learning (ML) to linguistic data are becoming more popular.

Objectives: We systematically reviewed the current literature regarding the application of ML and linguistic measures to classify PD patients.

Methods: The protocol was designed according to the PRISMA statement. The literature search was conducted in MEDLINE, CINAHL, and PsycINFO databases considering only studies written in full-text English in a peer-reviewed journal. Inclusion criteria were: patients with PD, linguistic measures, and ML performance metrics. A wide variety of information was extracted, including linguistic analysis methods, linguistic tasks, ML classifiers, classification performances, and optimal linguistic predictors.

Results: Initially 102 papers were retrieved; following duplicate removal and verified inclusion criteria, 10 papers were included in the study. Tasks used to elicit language were connected or spontaneous speech, retelling tasks, or semi-structured interviews; only one study adopted a custom-made task. Transcriptions were mostly analysed using Natural Language Processing (NLP) techniques. Support Vector Machine was the ML model most frequently used for classification. The classification accuracy (%) ranged from 43 to 94, sensitivity (%) from 8 to 95, specificity (%) from 3 to 100, and AUC (%) from 32 to 97. The most frequent optimal linguistic measures were lexicosemantic (40%), followed by NLP-extracted features (40%) and morphosyntactic features (20%).

Conclusions: Linguistic measures and ML algorithms can be useful tools for the automated classification of PD and to better investigate the clinical linguistic profile of patients.

References:

[1] Braak, Heiko, et al., 2004. Cell and tissue research 318: 121-134.

P205

Clinical differences among Parkinson's disease patients carrying heterozygous GBA gene mutation compared with matched idiopathic PD patients: a case-control study

Sara Grisanti[1], G. Di Rauso[1,2], F. Cavallieri[2], V. Fioravanti[2], G. Toschi[2], G. Portaro[2], J. Rossi[1,2], R. Sabadini[2], V. Ferrari[2], A. Melpignano[3], M. Scarano[4], A. Groppi[2], M. Napoli[5], R. Pascarella[5], A. Castellucci[6], A. Ghidini[6], C. Lucchi[7], G. Biagini[7], A. Fraternali[8], A. Versari[8], I. Campanini[9], A. Merlo[9], A. Scaglioni[10], F. Valzania[2]

[1]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3]Presidio Ospedaliero Fidenza AUSL Parma, Fidenza, Italy
[4]Dipartimento di Cure Primarie, Azienda Unità Sanitaria Locale (AUSL) Modena, Modena, Italy
[5]Neuroradiology Service, Department of Diagnostic Imaging and Laboratory Medicine, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[6]Otolaryngology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[7]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[8]Nuclear Medicine Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[9]LAM-Motion Analysis Laboratory, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS Reggio Emilia, Reggio Emilia, Italy
[10]Centro S. Maria ai Servi, Fondazione Don Gnocchi, Parma, Italy

Introduction: When compared to I-PD, GBA-PD patients might manifest a different PD phenotype, characterized by a relative earlier disease onset, a greater cognitive impairment and, overall, a more aggressive disease progression [1].

Objectives: To compare the clinical characteristics of a cohort of consecutive GBA-PD patients with an age, sex, disease stage, and comorbidity-matched cohort of consecutive idiopathic PD (I-PD) patients.

Methods: A consecutive cohort of GBA-PD patients has been paired for age, sex, disease duration, Hoehn & Yahr stage, and comorbidities (Charlson Comorbidity Index [CCI]) with a cohort of consecutive I-PD patients. Clinical assessment included the four parts of the MDS-UPDRS scale, and the Montreal Cognitive Assessment (MoCA). Several subscores of the MDS-UPDRS were also calculated including tremor, bradykinesia, rigidity, speech, gait, freezing of gait [FOG] and axial subscores. The Mann–Whitney test and the Chi-square test were performed to compare the two cohorts for continuous and categorical variables.

Results: 56 GBA-PD (males: 31; age: 64.48 years; disease duration: 7.46 years, MDSUPDRS III: 35.29; MoCa: 21.77, CCI: 2.61) and 56 I-PD (age: 64.66 years; disease duration: 7.76 years, MDS-UPDRS III: 28.80; MoCa: 22.73, CCI: 2.47) were included. Compared to I-PD, GBA-PD patients showed more hallucinations and psychosis ($p<0.05$), higher MDS-UPDRS part III score ($p<0.05$), higher rigidity ($p<0.005$) and FOG ($p<0.05$) subscores.

Conclusions: This cohort study confirms the presence of significant differences in clinical characteristics between GBA-PD and I-PD. If compared with age, sex, disease stage, and

comorbidity-matched I-PD, GBA-PD showed a more severe motor involvement characterized by higher rigidity and FOG, and increased psychiatric symptoms.

References:

[1] Petrucci S, Ginevrino M, Trezzi I, Monfrini E, Ricciardi L, Albanese A, Avenali M, Barone P, Bentivoglio AR, Bonifati V, Bove F, Bonanni L, Brusa L, Cereda C, Cossu G, Criscuolo C, Dati G, De Rosa A, Eleopra R, Fabbrini G, Fadda L, Garbellini M, Minafra B, Onofrj M, Pacchetti C, Palmieri I, Pellecchia MT, Petracca M, Picillo M, Pisani A, Vallelunga A, Zangaglia R, Di Fonzo A, Morgante F, Valente EM; ITA-GENE-PD Study Group. GBARelated Parkinson's Disease: Dissection of Genotype-Phenotype Correlates in a Large Italian Cohort. Mov Disord. 2020 Nov;35(11):2106-2111. doi: 10.1002/mds.28195.

P206

Association between cognitive functions and supervised mobility parameters in people with Parkinson's disease: the added value of backward walking assessment

Pierre Pacilio[1], E. Bianchini[1,2], D. Rinaldi[1], M. Alborghetti[1], S. Galli[1], L. De Carolis[1], T. Milane[2,3], C. Hansen[3], F.E. Pontieri[1], N. Vuillerme[2,4,5]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Univ. Grenoble Alpes, AGEIS, Grenoble, France
[3]Department of Neurology, Kiel University, Kiel, Germany
[4]Institut Universitaire de France, Paris, France
[5]LabCom Telecom4Health, Orange Labs & Université Grenoble Alpes, CNRS, Inria, Grenoble INP-UGA, Grenoble, France

Introduction: The co-existence of both cognitive and gait impairments are frequent in people with Parkinson's disease (PwPD) [1-2]. However, while the association between cognitive deficit and impaired forward walking (FW) assessed under supervised condition is well established [3], less is known for more challenging mobility tasks, such as turning and backward walking (BW) [4].

Objectives: To evaluate the association between cognitive functions and supervised FW, turning and BW parameters, measured during standardized mobility tasks in PwPD.

Methods: Seventy-two PwPD in ON condition [females: 22 (31%); age: 68.8±8.5; disease duration: 5.7±3.9; LEDD: 522±266 mg; mHY: 2 (2-2.5; 1-3); MDS-UPDRS-III: 28 (22-33; 11-46)] performed three supervised standardized mobility tests: 1) an instrumented 20-meter FW task (iFW) at self-selected speed and (2) an instrumented Timed-Up-and-Go (iTUG) test at self-selected speed during which they wore a lower-backmounted inertial motion unit (BTS G-WALK), and (3) the 3-meter backward walking test (3MBWT). The main outcome measures were: (1) speed for iFW, (2) mean angular velocity (MAV) of the intermediate 180° turn for iTUG, and (3) speed for BW. Patients further underwent a cognitive evaluation through the Montreal cognitive assessment (MoCA) and Word-Color Stroop Test (WCST). Univariate linear regressions were used to calculate how much variance of each supervised mobility test measure was explained by cognitive functions.

Results: WCST time showed a positive correlation with FW speed (R=0.408; p<0.001) and explained 15.4% of variance, with TUG MAV (R=0.405; p<0.001) and explained 15.2% of variance, and with BW speed (R=0.428; p<0.001) and explained 17.2% of variance. MoCA score showed a positive correlation only with BW speed (R=0.246; p=0.037) and explained 4.7% of variance.

Conclusions: Executive functions explained a larger portion of variance of BW compared with FW and turning in PwPD. Global cognitive functions showed a minimal contribution only to BW. Taken together, these results support for the use of BW assessment considering the stronger association with cognitive functions in PwPD.

References:

[1] Mirelman, A.; Bonato, P.; Camicioli, R.; Ellis, T.D.; Giladi, N.; Hamilton, J.L.; Hass, C.J.; Hausdorff, J.M.; Pelosin, E.; Almeida, Q.J. Gait Impairments in Parkinson's Disease. Lancet Neurol 2019, 18, 697–708, doi:10.1016/S1474-4422(19)30044-4.
[2] Aarsland, D.; Batzu, L.; Halliday, G.M.; Geurtsen, G.J.; Ballard, C.; Ray Chaudhuri, K.; Weintraub, D. Parkinson Disease-Associated Cognitive Impairment. Nat Rev Dis Primers 2021, 7, 47, doi:10.1038/s41572-021-00280-3.

[3] Yogev-Seligmann, G.; Hausdorff, J.M.; Giladi, N. The Role of Executive Function and Attention in Gait. Mov Disord 2008, 23, 329–342; quiz 472, doi:10.1002/mds.21720.
[4] Correno, M.B.; Hansen, C.; Chardon, M.; Milane, T.; Bianchini, E.; Vuillerme, N. Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. Int J Environ Res Public Health 2022, 19, 12810, doi:10.3390/ijerph191912810.

P207

Differences and association in Wearing-Off Questionnaire 19 (WOQ-19) score between people with Parkinson's disease and caregivers: a proof-of-concept study

Silvia Galli[1], E. Bianchini[1,2], D. Rinaldi[1], M. Alborghetti[1], L. De Carolis[1], P. Pacilio[1], F.E. Pontieri[1]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Université Grenoble Alpes, AGEIS, Grenoble, France

Introduction: Wearing-off (WO) is a common motor complication in people with Parkinson's disease (PwPD) [1] and Wearing-Off Questionnaire 19 (WOQ-19) is a well-established and effective patient-reported instrument to assess its presence [2]. Some evidence suggested that caregivers (CG) may notice symptoms of WO even before the patients [3], but the role of CG in the detection of WO has been poorly investigated.

Objectives: To assess differences and associations in WOQ-19 score between PwPD and CG.

Methods: Thirty-nine PwPD [females: 28 (32%); age: 68.7±8.4 years; disease duration: 6.4±3.6 years; mHY: 2 (2-2.5; 1-3); MDS-UPDRS-III: 28 (22-32; 11-50)] and 39 CG were asked to independently complete a WOQ-19 questionnaire during scheduled outpatient visits. The total WOQ-19 score was calculated as well as each sub-item. Mann-Whitney test was used to assess differences in total WOQ-19 score between PwPD and CG. Spearman's correlation coefficient and Intraclass correlation coefficient (ICC) (2,1) were used to evaluate the association and the agreement between the two groups, respectively. Chi-square test was used to assess the differences in individual items between PwPD and CG.

Results: No significant differences were found in WOQ-19 score between PwPD [2(0-4; 0-10)] and CG [2(0-6; 0-13)] (W=690.5; p=0.475). Spearman's test showed a weak-to-moderate correlation between PwPD and CG in WOQ19 score (R=0.476; p=0.002). ICC (2,1) showed a poor agreement between PwPD and CG scores [0.428 (CI95% 0.142-0.650)]. Chi-square test showed no differences in any individual items between the two groups (all $p>0.05$).

Conclusions: PwPD and CG reported similar scores at WOQ-19. However, the association and agreement between the two groups was poor. Our findings suggest that CG-reported WOQ-19 could not be a reliable and valid surrogate of patient-reported score. Since the role of CG is increasingly recognized in PwPD management, future studies are encouraged to further investigate this aspect and confirm our findings.

References:

[1] Stacy, M. The Wearing-off Phenomenon and the Use of Questionnaires to Facilitate Its Recognition in Parkinson's Disease. J Neural Transm (Vienna) 2010, 117 , 837–846, doi:10.1007/s00702-010-0424-5.
[2] Mantese, C.E.; Schumacher-Schuh, A.; Rieder, C.R.M. Clinimetrics of the 9- and 19-Item Wearing-Off Questionnaire: A Systematic Review. Parkinsons Dis 2018, 2018 , 5308491, doi:10.1155/2018/5308491.
[3] Matthews, H.; Stamford, J.; Saha, R.; Martin, A.; Off-Park survey steering group Exploring Issues Around Wearing-off and Quality of Life: The OFF-PARK Survey of People with Parkinson's Disease and Their Care Partners. J Parkinsons Dis 2015, 5, 533–539, doi:10.3233/JPD-150547.

P208

Parkinson's disease and Amyotrophic Lateral Sclerosis coexistence: a case report of Brait-Fahn-Schwartz disease

Valentina Cenacchi, G. Prandin, M. Liccari, T.M.I. Lombardo, G. Iania, M. Catalan, P. Manganotti

Clinical Unit of Neurology, Department of Medicine, Surgery and Health Sciences, University Hospital of Trieste ASUGI, University of Trieste, Trieste, Italy

Case report: An 85-year-old man with unremarkable medical and family history presented to our Movement Disorders Clinic for a 6-month rest tremor in his right hand. He also reported hyposmia, stipsis and REM sleep Behavior Disorder (RBD)-like symptoms for several years. Brain CT and MRI showed mild global atrophy and chronic ischemia, while dopamine transporter SPECT imaging revealed a marked symmetric nigrostriatal degeneration. He received a diagnosis of Parkinson's Disease (PD) and started L-DOPA with a good clinical response.
Interestingly, one year before referral he had noticed unintentional weight loss, anxiety and depression; chest radiograph, colonoscopy and abdominal ultrasound were normal. These clinical signs were therefore considered secondary to PD until, 10 months after starting L-DOPA, he returned to our Clinic lamenting increasing fatigue, exertional dyspnea and hypophonia. On examination, extrapyramidal involvement was accompanied by proximal hyposthenia, atrophy, diffuse fasciculations, and bilateral Hoffmann sign. He did not have autonomic, cerebellar nor cognitive impairment. Diffuse Lower Motor Neuron involvement was confirmed by electroneurogram-electromyogram examination, allowing a diagnosis of Amyotrophic Lateral Sclerosis (ALS) to be made according to the Gold Coast criteria. Riluzole was started.
Lumbar puncture revealed high-titer anti-GM1 antibodies positivity: in the hypothesis of an autoimmune share of pathology he underwent human immunoglobulin infusion, without benefit. His clinical conditions deteriorated rapidly to the point to require respiratory and nutritional support.

Discussion: There are a few syndromes in which parkinsonism and ALS share the same pathogenesis [1]. However, the isolated co-occurrence of the two (i.e., without any additional neurological signs), the temporal course with PD preceding ALS, the dopamine transporter SPECT imaging positivity and the good L-DOPA response – as in our patient - configure the diagnosis of Brait-Fahn-Schwartz disease. This condition's pathology is still unclear and up to date fewer than 50 cases worldwide have been described [1,2,3]. Whole exome sequencing may help identify possible causative mutations.

References:

[1] Gilbert RM, Fahn S, Mitsumoto H, Rowland LP. Parkinsonism and motor neuron diseases: twenty-seven patients with diverse overlap syndromes. Mov Disord. 2010 Sep 15;25(12):1868-75. doi: 10.1002/mds.23200. PMID: 20669307.
[2] Aslam A, Sarmad E, Nawaz A, Numan A, Ahmad A, Hassan MA. Brait-Fahn-Schwartz Disease: A Unique Co-Occurrence of Parkinson's Disease and Amyotrophic Lateral Sclerosis. Case Rep Neurol. 2023 Sep 21;15(1):207-214. doi: 10.1159/000532092. PMID: 37901127; PMCID: PMC10601670.
[3] Calvo A, Chiò A, Pagani M, Cammarosano S, Dematteis F, Moglia C, Solero L, Manera U, Martone T, Brunetti M, Balma M, Castellano G, Barberis M, Cistaro A, Artusi CA, Vasta R, Montanaro E, Romagnolo A, Iazzolino B, Canosa A, Carrara G, Valentini C, Li TQ, Nobili F, Lopiano L, Rizzone MG. Parkinsonian traits in amyotrophic lateral sclerosis (ALS): a prospective population-based study. J Neurol. 2019 Jul;266(7):1633-1642. doi: 10.1007/s00415-019-09305-0. Epub 2019 Apr 4. PMID: 30949819.

P209

Pareidolia in patients with alpha-synucleinopathies and visuo-spatial dysfunction: reports of two cases

Eleonora Bertoncello, M. Tinazzi, S. Tamburin, E. Mantovani

Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Pareidolia, the tendency to perceive a fictional image inside a nonspecific but evocative scenery, is reported to occur more frequently in alpha-synucleinopathies, in particular Lewy Body Dementia (LBD) and Parkinson's disease-dementia (PD-D). Noise Pareidolia Task (NPT) is a neuropsychological test not yet validated in Italy to assess pareidolia.

Objectives: To report two clinical cases where pareidolia was assessed with the NPT.

Methods: Neuropsychological evaluation including NPT was administered in a 60-year-old woman with LBD, hallucinations and delusions, and in a 62-year-old man with PD-D. NPT consists of 20 images, some including a face and others containing only noise patterns. The total score considers the number of correctly identified faces (maximum 7) and negative controls (maximum 13) and the pareidolic errors (maximum 13).

Results: Neuropsychological evaluation showed impairment in executive, visuo-spatial and attentive functions in the LBD patient and in memory, attention, visuo-spatial, executive and semantic functions in the PD-D patient. NPT showed deficit in visual perception (respectively 3/7 and 6/7) and increased pareidolia (respectively 6/13 and 8/13) in both patients.

Conclusions: NPT is a promising test in patients with alpha-synucleinopathies and visuo-spatial abnormalities. Future studies should explore its role in larger populations of patients, including early disease stages.

P210

Short-term effect of CPAP on sleep disordered breathing and sleep architecture in MSA patients

Giulia Lazzeri[1], M. Houot[2,3,4], M. Patout[5,7,8], C. Londner[5,7,8], C. Philippe[5,7,8], J. Ruggeri[5,6], B. Degos[5,6], F. Cormier[5,6], M. Vidailhet[5,6], J.C. Corvol[5,6], I. Arnulf[5,7,8], D. Grabli[5,6], P. Dodet[5,7,8]

[1]Centro Parkinson e Parkinsonismi, ASST G. Pini-CTO, Milano, Italy
[2]Center of Excellence of Neurodegenerative Disease (CoEN), AP-HP, Pitié-Salpêtrière Hospital, Paris, France
[3]Department of Neurology, Institute of Memory and Alzheimer's Disease (IM2A), AP-HP, Pitié-Salpêtrière Hospital, Paris, France
[4]Clinical Investigation Centre (CIC) Neuroscience, Brain Institute, Pitié-Salpêtrière Hospital, Paris, France
[5]Sorbonne Université, Paris Brain Institute, Inserm, CNRS, Paris, France
[6]Department of Neurology, Pitié-Salpêtrière Hospital, APHP, Paris, France
[7]Assistance Publique-Hôpitaux de Paris-Sorbonne (AP-HP-Sorbonne), Hôpital la Pitié-Salpêtrière, Service des Pathologies du Sommeil, Paris, France
[8]Inserm UMRS1158 Neurophysiologie Respiratoire Expérimentale et Clinique, Sorbonne Université, Paris, France

Introduction: SBD are frequent in MSA, mainly represented by inspiratory stridor, obstructive and central sleep apnea/hypopnea syndrome (SAS), impacting the quality of sleep. A treatment with CPAP can be proposed but its short-term effect on sleep architecture and breathing parameters remains unclear.

Objectives: To evaluate the short-term effect of continuous positive airway pressure (CPAP) on sleep architecture and sleep disordered breathing (SDB) in a large retrospective series of patients with multiple system atrophy (MSA) with and without SDB based on two consecutive nights in video-polysomnography (v-PSG).

Methods: Consecutive MSA patients with available data (n = 67) recorded at the Sleep Unit of Pitié Salpêtrière Hospital, Paris, France, between April 2009 and July 2022 were included. SDB was defined by the presence of stridor and/or apnea-hypopnea index (AHI)≥15. We compared the clinical-demographic data between patients with and without SDB and the change in sleep parameters between the 2 nights in three groups: 1) with SDB and CPAP on the 2nd night 2) with SDB without CPAP, 3) without SDB, using linear mixed models. Group 1 patients were classified as responders to CPAP if on the 2nd night AHI was ≤10 and stridor was absent.

Results: SDB was present in 39/67 (58.2%) patients, 8 (20.5%) had isolated stridor, 16 (41.1%) SAS and 15 (38.4%) both. MSA-C patients were more often associated with SDB (64.1% vs 28.6%, p=0.006) compared to MSA-P patients. Patients with SDB had higher AHI (27.3 vs 2.5, p<0.001) and more fragmented sleep (median arousal index (AI) of 14.5 vs 7.5 (p=0.005)). After one night with CPAP, patients in group 1 had a decreased AHI (p<0.001), AI (p 0.024), and N2 stage duration (p=0.024) as well as an increased saturation in oxygen in all sleep stages (p<0.001) and REM sleep duration (p=0.020) compared to the other groups. Among them, 15/25 (60 %) were responders, 3 (20%) with isolated stridor, 4 (26.7%) with SAS, 8 (53.3%) with both.

Conclusions: SDB is more frequent in MSA-C patients. We found a short-term effect of CPAP on the sleep architecture with a better continuity in sleep and a rebound in REM sleep, as well as a good efficiency on SBD. Further studies exploring the value of this short-term response to predict the effect of CPAP over time are necessary.

P211

Impaired mitochondrial respiration in REM-sleep behaviour disorder: a biomarker of Parkinson's disease?

Gerardo Ongari[1], C. Ghezzi[1], D. Di Martino[1], M. Avenali[2,5], M. Terzaghi[3,5], A. Pisani[4,5], F. Blandini[6], S. Cerri[1]

[1]IRCCS Mondino Foundation, Unit of Cellular and Molecular Neurobiology, Pavia, Italy
[2]IRCCS Mondino Foundation, Neurorehabilitation Unit, Pavia, Pavia, Italy
[3]IRCCS Mondino Foundation, Unit of Sleep Medicine and Epilepsy, Pavia, Italy
[4]IRCCS Mondino Foundation, Movement Disorders, Pavia, Italy
[5]University of Pavia, Department of Brain and Behavioural Sciences, Pavia, Italy
[6]IRCCS Policlinico Maggiore Hospital, Milano, Italy

Introduction: Idiopathic REM sleep disorder (iRBD) serves as a crucial early indicator of Parkinson's disease (PD). However, limited research has investigated the mechanisms contributing to PD development in individuals with iRBD.

Objectives: Considering the established link between mitochondrial dysfunctions and sleep disturbances in PD [1-2], our study aimed to assess mitochondrial alterations in fibroblasts obtained from iRBD subjects, with the objective of characterizing a predictive biochemical profile.

Methods: The study involved 28 participants, divided into three groups: 10 individuals diagnosed with iRBD, 8 PD patients who evolved from iRBD (RBD-PD), and 10 healthy controls. We conducted an evaluation of mitochondrial function, including an assessment of mitochondrial morphology, analysis of mitochondrial protein expression levels via western blot, and measurement of mitochondrial respiration using a Seahorse XFe24 analyzer.

Results: Under basal conditions, mitochondrial respiration exhibited no significant differences between iRBD and control fibroblasts. However, when subjected to an increased energy demand, iRBD fibroblasts displayed a significant ($P = 0.006$) decline in maximal and spare respiration compared to controls. Intriguingly, RBD-PD patients demonstrated similar alterations, with an additional significant reduction in oxygen consumption associated with ATP production ($P = 0.032$). Furthermore, RBD-PD patients manifested a significant decrease in protein levels of complexes III ($P = 0.02$) and V ($P = 0.002$) compared to controls, together with fragmentation of the mitochondrial network. iRBD patients exhibited comparable but milder alterations.

Conclusions: All together, these findings suggest that mitochondrial dysfunctions in individuals with iRBD may predispose them to a deterioration in their bioenergetic profile, as we observed in RBD-PD patients, highlighting these alterations as potential predictors of the phenoconversion to PD.

References:

[1] A. M. Smith et al., "Mitochondrial dysfunction and increased glycolysis in prodromal and early Parkinson's blood cells," Mov. Disord., vol. 33, no. 10, pp. 1580–1590, Oct. 2018, doi: 10.1002/mds.104.
[2] C. Milanese et al., "Peripheral mitochondrial function correlates with clinical severity in idiopathic Parkinson's disease," Mov. Disord., vol. 34, no. 8, pp. 1192–1202, 2019, doi: 10.1002/mds.27723.

P212

The role of the COQ2 gene in multiple system atrophy: a case report of a patient with a COQ2 gene variant and atypical clinical course undergoing treatment with high-dose ubiquinol

David De Monte[1,2], G. Ermanis[1,2], E. Belgrado[3], A. Bernardini[1], F. Janes[1], G. Pellitteri[1], E. Betto[4], I. Lonigro[5], G. Carrozzo[6,7], P. Guaraldi[6], P. Cortelli[6,7], G.L. Gigli[1,2], M. Valente[1,2]

[1]Clinical Neurology Unit, Santa Maria della Misericordia University Hospital, Azienda Sanitaria Friuli Centrale (ASUFC), Udine, Italy
[2]Department of Medical Area, University of Udine, Udine, Italy
[3]Neurology Unit, Santa Maria della Misericordia University Hospital, Azienda Sanitaria Friuli Centrale (ASUFC), Udine, Italy
[4]Institute of Medical Genetics, Azienda Sanitaria Friuli Centrale (ASUFC), Udine, Italy
[5]Lab. Genetica Medica, Istituto per le Malattie Rare "Mauro Baschirotto", B.I.R.D. Foundation, Costozza di Longare (VI), Italy
[6]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[7]Department of Biomedical and NeuroMotor Sciences (DIBINEM), Alma Mater Studiorum, University of Bologna, Bologna, Italy

Introduction: Parkinson's disease (PD) and multiple system atrophy (MSA) are neurodegenerative diseases that show similarities in their pathophysiological pathways and in their clinical course [1]. The identification of a specific respiratory chain defect (complex I deficiency) in PD patients 10 years ago stressed the relevance of mitochondrial dysfunction pathogenic role in neurodegenerative diseases, where coenzyme Q10 plays a key role in the transport of electrons from complex I (NADHubiquinone oxidoreductase) and complex II (succinate-ubiquinone oxidoreductase) to complex III (ubiquinol-cytochrome c reductase). [2, 3] Moreover, recent studies in Japan have associated MSA with variants in the COQ2 gene, which encodes para-hydroxybenzoate-polyprenyl transferase and whose mutations appear to be associated with a primary deficiency of coenzyme Q10 [4]. Since not all the available evidence in literature are coherent to link such mutations to a clear MSA phenotype, we have questioned whether variants in the COQ2 gene are associated with a particular form of parkinsonian syndrome (PD or atypical parkinsonisms) [5, 6, 7].

Objectives: Here we report the case of a patient with a homozygous c.683 A>G variant (new nomenclature c.553 A>G) of COQ2 who was initially diagnosed as Clinically Probable PD but in a few years of disease progression met the criteria for Probable MSA.

Methods: Comprehensive genetic, neurological and imaging assessments were conducted to clarify the aetiology of his disorder. Among these, RTQuIC on nasal brushing and MRI spectroscopy provided further information to support the diagnosis while a muscle biopsy highlighted the impairments resulting from the COQ2 mutation.

Conclusions: Mitochondrial oxidative stress plays a key role in pathogenesis of different neurodegenerative disorders acting as an upstream factor, thus explaining why COQ2 mutations could be involved in development of parkinsonian syndromes with an atypical course. Understanding the pathogenetic role of these mutations could suggest new therapeutic approaches in addition to the standard of care.

References:

[1] Halliday GM, Holton JL, Revesz T, Dickson DW. (2011) Neuropathology underlying clinical variability in patients with synucleinopathies. Acta Neuropathol 122:187–204 10.1007/s00401-011-0852-9.

[2] Mizuno Y, Ohta S, Tanaka M, Takamiya S, Suzuki K, Sato T, Oya H, Ozawa T, Kagawa Y. Deficiencies in complex I subunits of the respiratory chain in Parkinson's disease. Biochem Biophys Res Commun. 1989 Sep 29;163(3):1450-5. doi: 10.1016/0006-291x(89)91141-8. PMID: 2551290.
[3] Turunen M, Olsson J, Dallner G (2004) Metabolism and function of coenzyme Q. Biochim Biophys Acta 1660:171–199
[4] Multiple-System Atrophy Research Collaboration. (2013) Mutations in COQ2 in familial and sporadic multiple-system atrophy. N Engl J Med 369:233–44. 10.1056/NEJMoa1212115.
[5] Mitsui J, Matsukawa T, Uemura Y, Kawahara T, Chikada A, Porto KJL, Naruse H, Tanaka M, Ishiura H, Toda T, Kuzuyama H, Hirano M, Wada I, Ga T, Moritoyo T, Takahashi Y, Mizusawa H, Ishikawa K, Yokota T, Kuwabara S, Sawamoto N, Takahashi R, Abe K, Ishihara T, Onodera O, Matsuse D, Yamasaki R, Kira JI, Katsuno M, Hanajima R, Ogata K, Takashima H, Matsushima M, Yabe I, Sasaki H, Tsuji S. High-dose ubiquinol supplementation in multiple-system atrophy: a multicentre, randomised, double-blinded, placebo-controlled phase 2 trial. EClinicalMedicine. 2023 Apr 14;59:101920. doi: 10.1016/j.eclinm.2023.101920. PMID: 37256098.
[6] Mikasa M, Kanai K, Li Y, Yoshino H, Mogushi K, Hayashida A, Ikeda A, Kawajiri S, Okuma Y, Kashihara K, Sato T, Kondo H, Funayama M, Nishioka K, Hattori N. COQ2 variants in Parkinson's disease and multiple system atrophy. J Neural Transm (Vienna). 2018 Jun;125(6):937-944. doi: 10.1007/s00702-018-1885-1. Epub 2018 Apr 11. PMID: 29644397.
[7] Matsukawa T, Porto KJL, Mitsui J, Chikada A, Ishiura H, Takahashi Y, Nakamoto FK, Seki T, Shiio Y, Toda T, Tsuji S. Clinical and Genetic Features of Multiplex Families with Multiple System Atrophy and Parkinson's Disease. Cerebellum. 2022 Sep 13. doi: 10.1007/s12311-022-01426-z. Epub ahead of print. PMID: 36097244.

P213

Deep bran stimulation in Parkinson's Disease: comparison between clinical-based and imaging-based programming in a case series

Ginevra Tecilla[1], S. Sarubbo[3], F. Corsini[3], R. Bacchin[2], B. Giometto[2], M.C. Malaguti[2]

[1]Department of Neurology, Santa Maria del Carmine Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Rovereto, Trento, Italy
[2]Department of Neurology, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[3]Department of Neurosurgery, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy

Introduction: Clinical-based programming (CBP) in deep brain stimulation (DBS) for Parkinson's Disease (PD) is a time consuming process. The imaging-based programming (IBP) reduces programming time and the clinical motor outcomes have been proven to be comparable to CBP [1,2]. However, available studies comparing these two techniques are few at the moment.

Objectives: To compare CBP and IBP in terms of volume of the electrostatic field (VEsF) which overlaps with the DBS anatomical target (subthalamic nucleus-STN) and VEsF external to the STN; To evaluate the level of agreement in parameters of stimulation settings between CBP and IBP (lead selection, current intensity's distribution); To confirm that IBP is a time-saving procedure compared to CBP.

Methods: We selected PD patients with chronic STN-DBS who underwent DBS surgery at the Santa Chiara Hospital. We used GUIDE XT™, a software that generates the patient's anatomy and the leads' position using a preoperative magnetic resonance imaging (MRI) and a postoperative computed tomography (CT) scan. Through GUIDE XT™ we reproduced the CBP (retrieved from the standard-of-care clinical programming) and created the IBP for each patient. The IBP was generated with the purpose to stimulate the STN's dorsolateral area and avoid neighbouring cerebral regions possibly related to side effects. For each stimulation (two per patient) we collected the following data: VEsF (percentage of VEsF overlapping with STN, VEsF not overlapping with STN), stimulation parameters (rings/contacts used, current's splitting between the contacts) and time spent for generating CBP and IBP. In a subgroup of patients, who did not receive complete benefits from CBP, the IBP was set.

Results: VEsF obtained through IBP overlapped more with STN than CBP and the amount of VEsF external to the STN was smaller with IBP than CBP. Concerning the comparison on the stimulation parameters, the highest level of agreement between CBP and IBP was observed for distal rings, whereas most variability was found for central rings. Moreover, our study confirmed that IBP is a time-saving procedure in DBS programming process. The clinical observation in the small cohort of patients who tested the IBP, showed the need to reduce medical treatment to avoid drug-induced hyperkinetic movements.

Conclusions: IBP consists in a time-saving procedure compared to CBP in DBS for PD and our study suggests that this approach is more precise in targeting the VEsF. Therefore, IBP can help clinicians in choosing the most effective contacts for each patient. However, more studies on clinical outcomes of IBP and CBP are needed to clarify this issue.

References:

[1] Waldthaler J, Bopp M, Kühn N, Bacara B, Keuler M, Gjorgjevski M, Carl B, Timmermann L, Nimsky C, Pedrosa DJ. Imaging-based programming of subthalamic nucleus deep brain stimulation in Parkinson's disease. Brain Stimul. 2021 Sep-Oct;14(5):1109-1117. doi: 10.1016/j.brs.2021.07.064.
[2] Lange F, Steigerwald F, Malzacher T, Brandt GA, Odorfer TM, Roothans J, Reich MM, Fricke P, Volkmann J, Matthies C, Capetian PD. Reduced Programming Time and Strong Symptom Control Even in Chronic Course Through Imaging-Based DBS Programming. Front Neurol. 2021 Nov 8;12:785529. doi: 10.3389/fneur.2021.785529.

P214

The role of the subthalamic nucleus during turning whilst walking in patients with Parkinson's disease

Rita Habib[1,2], C. Palmisano[3], A. Mazzoni[4], A. Pedrocchi[1], M. Muthuraman[3], I.U. Isaias[2,3]

[1]Department of Electronics, Information and Bioengineering, NearLab, Politecnico di Milano, Milan, Italy
[2]Parkinson Institute Milan, ASST G.Pini-CTO, Milan, Italy
[3]Department of Neurology, University Hospital of Würzburg and Julius Maximilian University of Würzburg, Würzburg, Germany
[4]The BioRobotics Institute and Department of Excellence in Robotics and AI, Sant'Anna School of Advanced Studies, Pisa, Italy

Introduction: Turning whilst walking is a challenging component of locomotor ability especially for subjects with Parkinson's disease (PD). Specifically, turnings in PD have been associated with an increased risk of falls which leads to diminished quality of life [1]. Deep brain stimulation of the subthalamic nucleus (STN-DBS) is a mainstay treatment for PD, but with limited efficacy in gait and balance impairments. Unveiling the subthalamic activity related to turnings in PD is an urgent and unmet need to optimize available neuromodulation protocols.

Objectives: To investigate the neural activity of the STN during turning whilst walking in patients with PD.

Methods: We recorded bilateral subthalamic local field potentials (LFPs) in seven patients with idiopathic PD (age 60±5 years; disease duration 11±4 years; UPDRS-III: 40±13; mean±standard deviation) implanted with the Percept PC device (Medtronic, PLC) in meds-off/stim-off condition, i.e., in the morning after overnight withdrawal of all dopaminergic medication and after pausing DBS for at least 30 min. The patients walked back and forth on a 10 m walkway with 180° turns at the end of each walking trial (n. 14-45 turnings, according to the clinical condition of the patient). The start and peak angular velocity of each turn was collected using an inertial measurement unit (Opal, APDM) placed on the sternum. For each turn, we classified the STN as contralateral or ipsilateral to the internal leg with respect to the turning direction. A time-frequency analysis of the LFPs during 600 millisecond windows centred around the initiation of the turns was conducted.

Results: During turning, the power in the beta-low band [13 20]Hz of the contralateral STN correlated positively with the peak angular velocity.

Conclusions: Our findings suggest that subthalamic beta-low power modulation plays a role in the turning whilst walking task in patients with PD. We provide additional evidence of a lateralised contribution of frequency-specific subthalamic beta oscillatory activity in parkinsonian motor control [2][4].

References:

[1] J. E. Visser et al. , 'Quantification of trunk rotations during turning and walking in Parkinson's disease', Clinical Neurophysiology, vol. 118, no. 7, pp. 1602–1606, Jul. 2007, doi: 10.1016/j.clinph.2007.03.010.
[2] A. Canessa, C. Palmisano, I. U. Isaias, and A. Mazzoni, 'Gait-related frequency modulation of beta oscillatory activity in the subthalamic nucleus of parkinsonian patients', Brain Stimulation, vol. 13, no. 6, pp. 1743–1752, Nov. 2020, doi: 10.1016/j.brs.2020.09.006.

[3] G. Arnulfo et al. , ‘Phase matters: A role for the subthalamic network during gait’, PLoS ONE, vol. 13, no. 6, pp. 1–19, 2018, doi: 10.1371/journal.pone.0198691.
[4] F. Avantaggiato et al. , ‘Intelligibility of speech in Parkinson’s disease relies on anatomically segregated subthalamic beta oscillations’, Neurobiology of Disease , vol. 185, p. 106239, Sep. 2023, doi: 10.1016/j.nbd.2023.106239.

P215

Non-invasive brain stimulation for the treatment of cognitive and neuropsychiatric non-motor symptoms in Parkinson's disease: preliminary evidence from a systematic review of randomized controlled trials

Elisa Mantovani, E. Bertoncello, M. Tinazzi, S. Tamburin

Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction: Cognitive and neuropsychiatric symptoms are common non-motor complications of Parkinson's disease (PD), yet their management remains a major unmet need [1]. Non-invasive brain stimulation (NIBS) may represent a viable nonpharmacological therapeutic tool for their treatment [2].

Objectives: To provide a comprehensive overview of studies using NIBS techniques for the treatment of cognitive and neuropsychiatric non-motor symptoms in PD.

Methods: PubMed/MEDLINE, EMBASE and the Cochrane Library were searched from inception to December 19th, 2023 for randomized, sham-controlled trials evaluating the effects of repeated sessions of NIBS on PD-related cognitive (e.g., mild cognitive impairment, dementia) and neuropsychiatric (e.g., depression, apathy) non-motor complications [3]. Open-label trials, reports of single NIBS sessions, and studies with no therapeutic aim but only to assess neurophysiological measures were excluded. Studies were grouped according to the type of NIBS technique and the target nonmotor symptom.

Results: 25 studies with a total of 998 PD patients (sample size: 9–106) fulfilled eligibility criteria and were therefore included; 4/25 studies had a cross-over design. Twenty studies used transcranial magnetic stimulation (TMS, 4 of which applied patterned protocols), while 5 studies used transcranial direct current stimulation (tDCS). Most trials applied NIBS for facilitatory purposes. The most targeted nonmotor symptoms were those related to cognition (15/25, 60%), depression (14/25, 56%), anxiety (2/25, 8%) and apathy (2/25, 8%). General measures of non-motor symptoms were included in 4 studies (16%). Results were consistent only for anxiety (significant improvement after active TMS protocols), and apathy (no significant changes between active and sham). Studies were highly variable in terms of stimulation target and parameters, outcome measures, treatment duration and follow-up.

Conclusions: The methodological heterogeneity of the included studies did not allow firm conclusions on the efficacy of NIBS for treating cognitive and neuropsychiatric non-motor symptoms in PD. Future studies should offer further insight on this topic.

References:

[1] LeWitt PA, Chaudhuri KR. Unmet needs in Parkinson disease: Motor and non-motor. Parkinsonism Relat Disord. 2020 Nov;80 Suppl 1:S7-S12. doi: 10.1016/j.parkreldis.2020.09.024.
[2] Mantovani E, Zucchella C, Argyriou AA, et al. Treatment for cognitive and neuropsychiatric non-motor symptoms in Parkinson's disease: current evidence and future perspectives. Expert Rev Neurother. 2023;23(1):25-43. doi: 10.1080/14737175.2023.2173576.
[3] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. doi: 10.1136/bmj.n71.

P216

A case of Parkinson's disease in a CADASIL patient

Jacopo Spagliardi[1,3], C. Gendarini[1,3], A. Maranzano[3], C. Morelli[3], A. Ciammola[3], N. Ticozzi[2,3], F. Girotti[2,3,4]

[1]Neurology Residency Program, Università degli Studi di Milano, Milan, Italy
[2]Department of Pathophysiology and Transplantation, Dino Ferrari Center, Università degli Studi di Milano, Milan, Italy
[3]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milan, Italy
[4]Parkinson and Movement Disorders Unit, IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Introduction: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an increasingly recognized cause of inherited smallvessel disease. Its clinical presentation is heterogenous, comprising migraine, stroke, and progressive cognitive impairment [1]. In recent years, a growing number of cases of vascular parkinsonism in CADASIL patients has been reported, further expanding its phenotypic spectrum [2]. To date, however, there is only minor evidence of an existing correlation between degenerative movement disorders and CADASIL [3]. Here we describe a case of Parkinson's disease in a CADASIL patient.

Case description: A 66 year-old-woman was admitted to our neurology unit because of a 2-year-long history of progressive right-sided akineto-rigid parkinsonism. Her clinical history was remarkable for an episode of left-sided paresthesias at the age of 44, which had subsequently led to a diagnosis of CADASIL, confirmed through both genetic testing and skin biopsy. A brain MRI, performed to exclude a rightsided basal ganglia infarct, only showed mild vascular involvement of the basal ganglia. Therefore, she underwent a complete neurovascular workup, comprising Doppler ultrasonography of neck arteries, heart telemetry and blood metabolic panel, which was unremarkable. The subsequent 123I-Ioflupane SPECT brain imaging was consistent with bilateral leftpredominant pre-synaptic dopaminergic striatal denervation. Lastly, a L-DOPA challenge test was performed and showed a 60% improvement in the UPDRS III score (OFF score 20, ON score 8). Thus, a diagnosis of Parkinson's disease was made.

Conclusions: Our patient was diagnosed with CADASIL and subsequently developed Parkinson's disease. We believe this to be coincidental. To our knowledge, however, no instances of L-DOPA-responsive parkinsonism in CADASIL have previously been reported. Therefore, we believe that further studies are needed to investigate any existing association between these two entities.

References:

[1] Dichgans, M et al. "The phenotypic spectrum of CADASIL: clinicalfindings in 102 cases." Annals of neurology vol. 44,5 (1998): 731-9.
[2] Ragno, Michele et al. "Parkinsonism is a late, not rare, feature of CADASIL: a study on Italian patients carrying the R1006C mutation." Stroke vol. 44,4 (2013): 1147-9.
[3] Rice, Claire M et al. "Autopsy-confirmed, co-existent CADASIL and multiple system atrophy." Parkinsonism & related disorders vol. 17,5 (2011): 390-2.

P217

The wide spectrum of PSP-like syndromes: a case report

Davide Greco[1,2], A. Iacono[1,2], S. Valente[1,2], F. Piattellini[1,2], G. Grigioni[2], L. Caremani[2], A. Govoni[2], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Department of Neuro-Muscular-Skeletal and Sensorials Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

Introduction: Progressive supranuclear palsy (PSP) is the most common form of atypical parkinsonism, characterized by vertical gaze palsy, akinesia, postural instability and cognitive impairment The syndrome is a neurodegenerative disease, however vascular, autoimmune, paraneoplastic and infectious causes are reported related to this disease.

Objectives: We describe the case of a 79 years old man with atypical presentation of PSP.

Methods: Patient underwent to serial neurological evaluations, brain magnetic resonance imaging (MRI), brain PET-FDG scan, audiological evaluation and blood tests.

Results: We present the case of man who manifested at the age of 78, subacute onset of walking and balance problems with tendency to fall backward with rapid trend. Memory impairment and behavioural changes were also reported, indeed his family described him as more apathetic and irritable. Furthermore he had signs of autonomic dysfunction (urge incontinence and constipation) and sleep talking. The neurological evaluation highlighted vertical gaze palsy, loss of postural reflexes, mild bradykinesia and applause sign. Atrophy of temporo-insular and frontoparietal cortex, mild atrophy of the midbrain and vascular encephalopathy were evidenced at the brain MRI. The Brain PET-FDG scan showed hypometabolism in the midbrain. At the audiological evaluation bilateral hypoacusia and nystagmus in all positions were reported. Further investigations, as autoantibodies dosage (IgLON5) and markers of neurodegeneration are ongoing.

Conclusions: This case displays a clinical feature compatible with a PSP-like syndrome. Atypical presentation of parkinsonism may be the manifestation of systemic pathologies such as autoimmune diseases (e.g. with anti igLON5 antibodies), for whose diagnosis is fundamental for possible timely therapies.

P218

The association between questionnaires-based and smartwatch-based sleep parameters in people with Parkinson's disease

Francesco Garramone[1], E. Bianchini[1,2], T. Milane[2,3], D. Rinaldi[1], M. Alborghetti[1], S. Galli[1], L. De Carolis[1], P. Pacilio[1], P. Lombardo[1], C. Hansen[3], F.E. Pontieri[1], N. Vuillerme[2,4,5]

[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Univ. Grenoble Alpes, AGEIS, Grenoble, France
[3]Department of Neurology, Kiel University, Kiel, Germany
[4]Institut Universitaire de France, Paris, France
[5]LabCom Telecom4Health, Orange Labs & Univ. Grenoble Alpes, CNRS, Inria, Grenoble INP-UGA, Grenoble, France

Introduction: Sleep disturbances, usually assessed with clinical questionnaires, are frequent in people with Parkinson's disease (PwPD) [1]. Meanwhile, digital health technologies, such as smartwatches, are now used as non-invasive tools to monitor sleep and detect changes in sleep patterns [2,3]. However, only few studies investigated the association between questionnaires-based and smartwatch-based sleep parameters in PwPD [4].

Objectives: To evaluate the association between questionnaires-based and smartwatch-based sleep parameters in PwPD.

Methods: Seventy-four PwPD [females: 25 (34%); age: 68.6±8.4 years; disease duration: 6.4±4.7 years; LEDD: 554±312 mg; mHY: 2 (2-2.5; 1-3); MDS-UPDRS-III: 28 (22-32; 11-50)] worn a Garmin Vivosmart 4 smartwatch for 5 consecutive nights on the wrist least affected by the disease. Total sleep time (TST), REM, shallow and deep sleep time as well as wake after sleep onset (WASO) were computed via the smartwatch. Patients further underwent a clinical evaluation by means of the Parkinson's disease sleep scale version 2 (PDDS2) and Epworth sleepiness scale (ESS). Spearman's correlation coefficient was used to evaluate the association between questionnaires-based and smartwatch-based sleep parameters in PwPD. Mann-Whitney test was used to compare sleep parameters between patients with and without sleep problems (PDSS2 ≥15), with and without excessive daytime sleepiness (ESS≥10) and with and without nocturnal hypokinesia (item 2.9 of MDS-UPDRS-II≥1).

Results: ESS score showed a weak negative correlation with TST (R=-0.275; p=0.018) and REM sleep time (R=-0.353; p=0.002). PDSS2 showed a weak positive correlation with WASO (R=0.379; p<0.001). No difference was found for any of the smartwatch-based parameters between PwPD with and without sleep problems [18 (24%) and 56 (76%), respectively], daytime sleepiness [12 (16%) and 62 (84%), respectively] and nocturnal hypokinesia [25 (34%) and 49 (66%), respectively].

Conclusions: Smartwatch-based data collected in real-world conditions in PwPD showed an association with self-reported sleep quality and daytime sleepiness measures.

References:

[1] Schrempf, W.; Brandt, M.D.; Storch, A.; Reichmann, H. Sleep Disorders in Parkinson's Disease. J Parkinsons Dis 2014, 4, 211–221, doi:10.3233/JPD-130301.
[2] Stavitsky, K.; Saurman, J.L.; McNamara, P.; Cronin-Golomb, A.Sleep in Parkinson's Disease: A Comparison of Actigraphy and Subjective Measures. Parkinsonism Relat Disord 2010, 16, 280–283, doi:10.1016/j.parkreldis.2010.02.001.

[3] Li, P.; van Wezel, R.; He, F.; Zhao, Y.; Wang, Y. The Role of Wrist-Worn Technology in the Management of Parkinson's Disease in Daily Life: A Narrative Review. Front Neuroinform 2023, 17, 1135300, doi:10.3389/fninf.2023.1135300.
[4] Ko, Y.-F.; Kuo, P.-H.; Wang, C.-F.; Chen, Y.-J.; Chuang, P.-C.; Li, S.-Z.; Chen, B.-W.; Yang, F.-C.; Lo, Y.-C.; Yang, Y.; et al. Quantification Analysis of Sleep Based on Smartwatch Sensors for Parkinson's Disease. Biosensors (Basel) 2022, 12, 74, doi:10.3390/bios12020074.

P219

Mind and movement in Parkinson's disease: what we learned from yoga practice

Sara Varanese[1], L. Bonanni[2]

[1]Asl 2 Lanciano-Vasto-Chieti, Ospedale Civile San Pio, Vasto Chieti, Italy
[2]G. d'Annunzio University of Chieti-Pescara, Medicine and Aging Department, Chieti, Italy

Introduction: In one of the best-known Indian scripture (The Bhagavad Gita) yoga practice is referred as "skill in action".

Objectives: To report the experience of specifically designed Sivananda hatha yoga in Parkinson's disease (PD) patients from Abruzzo Region, central Italy.

Methods: 24 patients followed by the Movement Disorder Center of Vasto Hospital, Abruzzo, were enrolled in a three months yoga 80 minutes class once a week, structured as: meditation with breathing training (10 minutes), asana practice (60 minutes), deep relaxation through guided meditation (10 minutes). At enrollement (T0) and end of the program (T1) patients were evaluated with Unified Parkinson's Disease Rating Scale (UPDRS) I, II, III, IV, Freezing of Gate (FOG), PDQ39 and subitems. Dopaminergic treatments here reported as levodopa equivalent dose (LED) remained stable, but patients were allowed to take 1 extra L-dopa dose (ELD) per day. Thirteen patients matched for age, disease duration and Hoeh and Yahr stage (HY) not involved in any yoga practice were followed as control group.

Results: The yoga group was composed by 10 males and 14 females, mean ±SD age 65,5±6,78 years (range 52-78 years); mean disease duration 6,8±3,67 (range2-18years); HY I-IV. At T0 the group showed: mean UPDRS I 12±4,59; mean UPDRS II 12,1±4,79; mean UPDRS III 27,5±7,66; mean UPDRS IV 1,8±3,7; mean FOG score 9,4±6,2; mean PDQ39 total score 57±17,6; PDQmobility score 16,5±7.4; PDQ-ADL score 7,8±3,0; PDQ-emotional score 15,9±3,5; PDQ stigma score 10,9±1,02; PDQ-cognition score 0,9±0,99; PDQ-communication score 2±2,7; PDQ-body score 3,8±1,4. At T1 the following scores improved: UPDRS I ($p=0.025$), FOG ($p=0.013$), PDQ39 ($p=0.023$), PDQ-emotional ($p<0.001$) and PDQstigma ($p=0.005$). LED remained unchanged between T0 and T1; in the16 patients used to take ELD these decreased at T1 (mean ELD at T0=7,33±2,8; mean ELD at T1=1,33±0,98; $p=0.043$). All patients reported decreased OFF time at T1 ($p=0.053$). No difference were found in the control group, but 6 patients needed pharmacological adjustment due to worsening of rigidity and OFF time.

Conclusions: Yoga practice trains the mind to be alert, aware and focused on physical sensations and movements and this may be a key strategy for patients to cope with the disease.

P220

NET: A Home-based rehabilitation application for fall risk patients – a pilot feasibility and usability study

Gaia Bonassi [1], L. Iallonardo[1], C. Cosentino[1], E. Ravizzotti[1], S. Mezzarobba[1], A. Botta[2], L. Mori[1,2], C. Trompetto[1,2], L. Avanzino[2,3], E. Pelosin[1,2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, and "RAISE Ecosystem, Genova, Italy
[2]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[3]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy

This research introduces NET, an innovative home-based rehabilitation application developed within the framework of the European Union "RAISE (Robotics and AI for Socio-economic Empowerment)" program. Targeting patients at risk of falls, NET offers a tailored rehabilitation protocol designed to enhance balance and strength through progressively challenging exercises, crafted by physiotherapists.

NET addresses the escalating challenges in managing chronic fall-risk patients within the national healthcare system by providing a personalized rehabilitation approach. The application enables the creation of individualized rehabilitation protocols, allowing physiotherapists to monitor patient adherence to sessions. Moreover, utilizing the PC's camera, NET incorporates motion tracking, yielding an accuracy index for healthcare professionals. Applying the Action Observation concept, exercises are executed by an avatar, with the patient represented, via motion tracking, as a shadow when correctly framed by the camera.

Preliminary data from a pilot feasibility and usability study across diverse target populations, including patients with Parkinson's disease, stroke survivors, and osteoporotic individuals, are presented. Participants underwent evaluations using balance tests (MiniBest test, Short Performance Physical Battery, Four Steps Square Test), fear of falling assessments (FES, ABC scale), endurance tests (2 Minutes Walking Test), and cognitive evaluations (Mini-Mental Examination Test). A simulation of a typical session with varied exercise proposals was offered, followed by participant feedback, via a 10-item questionnaire with ratings from 0 to 10, on the session's pleasantness, tool usability, and any less appreciated aspects.

Preliminary findings indicate a favorable reception of the app and satisfactory ease of use. This study lays the foundation for further investigations, showcasing NET's potential as an effective tool in home-based rehabilitation for diverse patient groups.

Acknowledgments including sources of support: This work was carried out within the framework of the project "RAISE - Robotics and AI for Socio-economic Empowerment" and has been supported by European Union - NextGenerationEU.

P221

Dual-task vs single-task gait training to improve spatiotemporal gait parameters in people with Parkinson's disease: a systematic review and meta-analysis

Elisabetta Sarasso[1,2,7], M. Parente[1], F. Agosta[1,2,3], M. Filippi[1,2,3,4,5], D. Corbetta[6]

[1]Vita-Salute San Raffaele University, Milan, Italy
[2]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[6]Department of Rehabilitation and Functional Recovery, IRCCS San Raffaele Scientific Institute, Milan, Italy
[7]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy

Introduction: People with Parkinson's disease (pwPD) present alterations of spatiotemporal gait parameters that impact on walking ability. Preliminary studies suggested that dual-task gait training improves walking parameters; however, if dual-task training can specifically improve dual-task gait performance when compared to single-task training is still unknown.

Objective: We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) to compare the effect of dual-task training relative to single-task training of gait on specific gait parameters during dual-task tests in pwPD.

Methods: Three electronic databases were searched: two reviewers independently selected RCTs, extracted data, applied the Cochrane risk-of-bias tool for randomized trials (Version 2) and the GRADE framework for assessing certainty of evidence. Primary outcomes were dual-task gait speed, stride length and cadence. Secondary outcomes included dual-task cost on gait speed, balance confidence and quality of life.

Results: We included 14 RCTs (548 patients). Meta-analyses showed effects favoring dual-task training over single-task training in improving dual-task gait speed (standardized mean difference [SMD]= 0.33, 95% confidence interval [CI]=0.16-0.51; 10 studies; low certainty evidence), stride length (mean difference [MD]=0.09 meters, 95% CI=0.04-0.14; 4 studies; moderate-certainty evidence) and cadence (MD=5.62 steps/min, 95% CI=4.08-7.15; 5 studies moderate-certainty evidence). We also found a significant effect of dual-task training over single-task training on dual-task cost, balance confidence and quality of life.

Conclusion: Our results support the use of dual-task training relative to single-task training to improve dual-task spatiotemporal gait parameters in pwPD. Further studies are encouraged to better define features of dual-task training and clinical characteristics of pwPD to identify better responders.

P222

Occupational therapy intervention for handwriting training in people with micrographia and Parkinson's disease: outcome research

Giovanni Galeoto, V. Casaccia, A. Berardi, I. Ruotolo, G. Sellitto, R. Simeon, F. Panuccio, E. Amadio, M. Tofani, G. Fabbrini

Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

Introduction: One of the first aspects of daily life to be compromised due to Parkinson's disease (PD) is writing, often characterized by micrography, an "impairment of the fine motor skills of the hand which mainly occur with a progressive or stable reduction in the writing width" [1-2]. However, the evidence supporting the rehabilitation of this activity is still scarce with few significant results.

Objectives: The study in question aims to investigate the efficacy of handwriting training and occupational therapy in people with PD and micrographia.

Methods: The intervention was composed by ten sessions of handwriting training and occupational therapy for one month period with follow-up after two and three months. The outcome measures used for the assessment were the Parkinson's Disease Questionnaire-39 (PDQ-39), the Disabilities Of The Arm, Shoulder and Hand (DASH) questionnaire, the Jebsen Taylor Hand Function Test (JTHFT) and a handwritten pangram. The results were then subjected to statistical analysis, using the non-parametric Wilcoxon test to calculate statistical significance ($p < 0.05$).

Results: 16 individuals with PD were enrolled in this study. According to the statistical analysis of the collected results between the first and second follow-up, statistically significant results were obtained in all the considered tools. However concerning the pangram, the statistical significance is reduced in subsequent follow-up (3 months without treatment).

Conclusions: The study in question showed important results for the proposed treatment, reporting its effectiveness. However, after 3 months from the end of the treatment, improvements start to fade off; it is therefore imperative that the patient continues the treatment over time in order to maintain a good amplitude in handwriting. This study provides evidence to support the use of this treatment in the occupational therapy clinical practice and can be considered a starting point to improve research in this field.

References:

[1] Wagle Shulka A, Ounpraseuth S, Okun M, Gray V, Schwankhaus J, Metzer W. Micrographia and related deficits in Parkinson's disease: a cross-sectional study. BMJ Open. 2012.

[2] Nackaerts E, Michely J, Heremans E, Swinnen S, Smits-Engelsman B, Vandenberghe W, et al. Training for Micrographia Alters Neural Connectivity in Parkinson's Disease. Front Neurosci. 2018;12(3).

P223

Osteopathic manipulative treatment in Parkinson's disease: double blind sham-controlled cross-over study

Sara Varanese[1], V. Cozzolino[2], M.P. Buongarzone[1], S. Viola[1], L. Cicchitti[3], F. Quaglietta[3], V. De Angelis[1], D. Travaglini[1], L. Bonanni[4]

[1]Asl 2 Lanciano-Vasto-Chieti, Ospedale Civile San Pio, Vasto, Chieti, Italy
[2]Advanced Ostheopaty Institue, Milano, Italy
[3]Accademia Italiana Osteopatia Tradizionale, Pescara, Italy
[4]G. d'Annunzio Univeristy of Chieti-Pescara, Medicine and Aging Department, Chieti, Italy

Introduction: Patients with Parkinson's disease (PD) exhibit a variety of motor and non-motor symptoms such as fatigue, pain, constipation and urinary issues.

Objectives: The primary objective of this study is to evaluate the effect of osteopathic manipulative treatment (OMT) in PD.

Methods: This is a double blind sham-controlled cross-over study. The study involved 140 patients dived in sham group (65) and OMT group (75). The study consisted in the following visits: T0 baseline/randomization, T1 after 4 weeks of omt/sham treatment, T2 after 4 weeks of rest (no treatment), T3 after 4 weeks of cross-over treatment and T4 after 4 weeks of rest (no treatment). Patient were evaluated at T0, T1,T2, T3 and T4 with the following: the revised MDSUnified Parkinson's Disease Rating Scale (MDS-UPDRS), the Hoehn and Yahr staging system (H&Y), the Visual analogue scale for pain (VAS), the Fatigue severity scale (FSS), and a questionnaire for urinary incontinence (ICIQ-FS); all patients were also questioned about the number of bowel movements per week. The dopaminergic treatments here reported as as levodopa equivalent dose (LED) remained stable over the study period, but patients were allowed to take 1 extra L-dopa dose per day if needed.

Results: At baseline mean (standard deviation, SD) age of patients were 66.89 (2.85), H&Y stage ranged between 2 and 4, mean (SD) MDS-UPDRS total score was 60 (17.30), mean (SD) LED was 690,44 (86.52) mean (SD) VAS was 5 (0.7), mean (SD) FFS was 42.44 (3.97[l1]). Compared to baseline OMT group improved at 4 weeks follow up in the following: VAS ($p=0.001$), constipation ($p<0.0001$), fatigue ($p=0.07$), UPDRS I ($p=0.02$), UPDRS III ($p=0.05$), tremor ($p=0.01$), rigidity ($p=0.002$). The sham group did not show any changes compared to baseline.

Conclusions: The data presented suggest that osteopathic manipulation may be an effective physical complementary treatment in the management of several troublesome symptoms of PD which generally show poor response to traditional pharmacological interventions.

P224

Singin training in people with Parkinson's disease: a feasibility study

Assunta Trinchillo[1], E. Marcuzzo[2], F.P. Cucinotta[1,3], F. Morgante[1,3], L. Ricciardi[1]

[1]Neuroscience and Cell Biology Institute, Neuromodulation and Motor Control Section, St George's University of London, London, UK
[2] Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Introduction: Singing training (ST) in Parkinson's Disease (PD) may improve lung capacity, voice's volume, and mood. However, the evidence on the feasibility of ST is poor, and the efficacy on orofacial symptoms, voice quality and trunk posture is unknown [1,2].

Objective: Here, we evaluated the feasibility of ST in PD and tested its effect on voice quality, orofacial symptoms and posture.

Methods: Eight people with PD (PwP) were enrolled in a 3-months ST, one lesson per week for two hours. The following variables were collected before (T0) and at the end of 3-months ST (T1): 1) vocal characteristics obtained from voice recordings of subjects holding the vowel sound /a/ as long as possible (analysed with PRAAT software) [4-6]; 2) angles of anterior trunk flexion and lateral trunk flexion quantified using the NeuroPostureApp [7]; 3) neuropsychiatric symptoms and quality of life by means of specific validated questionnaires [8-9]; 4) orofacial symptoms measured with the MDS-UPDRS item for hypomimia, the Radboud Oral Motor Inventory for Parkinson's Disease (ROMP) and the bedside swallowing test. Measures of feasibility (percentage of attendance and patients' feedback) were collected. The Wilxocon test was employed for paired comparisons before and after the intervention.

Results: All subjects (3 females, age 64.25 ± 4.43 years, disease duration 10.25 ± 4.50 years) completed the training. The attendance rate was 75% of the total number of lessons. All subjects would recommend ST to other PwP. The following voice characteristics improved at T1 compared to T0: volume ($p=0.02$), formant number 1 ($p=0.03$) and HNR ($p=0.006$), these last two items being metrics of speech and voice quality. Apathy ($p=0.04$); depression ($p=0.02$) and anxiety ($p=0.01$) also improved. Angles of the anterior and lateral trunk flexion were significantly reduced (respectively $p=0.03$; $p=0.04$).

Conclusions: The ST intervention resulted feasible and impacted positively on patients' voice and speech quality, mood, and posture [9-15].

References:

[1] Di Benedetto P, Cavazzon M, Mondolo F, Rugiu G, Peratoner A, Biasutti E. Voice and choral singing treatment: a new approach for speech and voice disorders in Parkinson's disease. Eur J Phys Rehabil Med. 2009 Mar;45(1):13-9. PMID: 18987565.
[2] Elizabeth L. Stegemöller, Hollie Radig, Paul Hibbing, Judith Wingate & Christine Sapienza (2017) Effects of singing on voice, respiratory control and quality of life in persons with Parkinson's disease, Disability and Rehabilitation, 39:6, 594-600, DOI:10.3109/09638288.2016.1152610
[3] Shih LC, Piel J, Warren A, Kraics L, Silver A, Vanderhorst V, Simon DK, Tarsy D. Singing in groups for Parkinson's disease (SING-PD): a pilot study of group singing therapy for PD-related voice/speech disorders. Parkinsonism Relat Disord. 2012 Jun;18(5):548-52. doi: 10.1016/j.parkreldis.2012.02.009. Epub 2012 Mar 19. PMID: 22436653.

[4] Tamplin J, Morris ME, Marigliani C, Baker FA, Noffs G, Vogel AP. ParkinSong: Outcomes of a 12-Month Controlled Trial of Therapeutic Singing Groups in Parkinson's Disease. J Parkinsons Dis. 2020;10(3):1217-1230. doi: 10.3233/JPD-191838. PMID: 32538865.
[5] Butala A, Li K, Swaminathan A, Dunlop S, Salnikova Y, Ficek B, Portnoff B, Harper M, Vernon B, Turk B, Mari Z, Pantelyat A. Parkinsonics: A Randomized, Blinded, Cross-Over Trial of Group Singing for Motor and Nonmotor Symptoms in Idiopathic Parkinson Disease. Parkinsons Dis. 2022 Sep 20;2022:4233203. doi: 10.1155/2022/4233203. PMID: 36247106; PMCID: PMC9553721.
[6] Azadi H, Akbarzadeh-T MR, Shoeibi A, Kobravi HR. Evaluating the Effect of Parkinson's Disease on Jitter and Shimmer Speech Features. Adv Biomed Res. 2021 Dec 25;10:54. doi: 10.4103/abr.abr_254_21.
[7] Tinazzi M, Geroin C, Bhidayasiri R, Bloem BR, Capato T, Djaldetti R, Doherty K, Fasano A, Tibar H, Lopiano L, Margraf NG, Merello M, Moreau C, Ugawa Y, Artusi CA; International Parkinson and Movement Disorders Society Task Force on Postural Abnormalities. Task Force Consensus on Nosology and Cut-Off Values for Axial Postural Abnormalities in Parkinsonism. Mov Disord Clin Pract. 2022 May 9;9(5):594-603. doi: 10.1002/mdc3.13460. PMID: 35844289; PMCID: PMC9274349.
[8] García-Batista ZE, Guerra-Peña K, Cano-Vindel A, Herrera-Martínez SX, Medrano LA. Validity and reliability of the Beck Depression Inventory (BDI-II) in general and hospital population of Dominican Republic. PLoS One. 2018 Jun 29;13(6):e0199750. doi: 10.1371/journal.pone.0199750. PMID: 29958268; PMCID: PMC6025862.
[9] Leentjens AF, Dujardin K, Pontone GM, Starkstein SE, Weintraub D, Martinez-Martin P. The Parkinson Anxiety Scale (PAS): development and validation of a new anxiety scale. Mov Disord. 2014 Jul;29(8):1035-43. doi: 10.1002/mds.25919. Epub 2014 May 23. PMID: 24862344..
[10] Jiménez-Jiménez FJ, Gamboa J, Nieto A, Guerrero J, Orti-Pareja M, Molina JA, García-Albea E, Cobeta I. Acoustic voice analysis in untreated patients with Parkinson's disease. Parkinsonism Relat Disord. 1997 Apr;3(2):111-6. doi: 10.1016/s1353-8020(97)00007-2. PMID: 18591065.
[11] Ramig LA, Scherer RC, Titze IR, Ringel SP. Acoustic analysis of voices of patients with neurologic disease: rationale and preliminary data. Ann Otol Rhinol Laryngol. 1988;97:164–172. 6. Hertrich I, Ackerman H.
[12] Abur D, Lester-Smith RA, Daliri A, Lupiani AA, Guenther FH, Stepp CE. Sensorimotor adaptation of voice fundamental frequency in Parkinson's disease. PLoS One. 2018 Jan 26;13(1):e0191839. doi: 10.1371/journal.pone.0191839. PMID: 29373589; PMCID: PMC5786318.
[13] Mollaei F, Shiller DM, Baum SR, Gracco VL. Sensorimotor control of vocal pitch and formant frequencies in Parkinson's disease. Brain Res. 2016 Sep 1;1646:269-277. doi: 10.1016/j.brainres.2016.06.013. Epub 2016 Jun 8. PMID: 27288701; PMCID: PMC4975987.
[14] Ikui Y, Nakamura H, Sano D, Hyakusoku H, Kishida H, Kudo Y, Joki H, Koyano S, Yamauchi A, Takano S, Tayama N, Hirose H, Oridate N, Tanaka F. An Aerodynamic Study of Phonations in Patients With Parkinson Disease (PD). J Voice. 2015 May;29(3):273-80. doi: 10.1016/j.jvoice.2014.08.012. Epub 2015 Mar 17. PMID: 25795370.
[15] Motta S, Cesari U, Paternoster M, Motta G, Orefice G. Aerodynamic findings and Voice Handicap Index in Parkinson's disease. Eur Arch Otorhinolaryngol. 2018 Jun;275(6):1569-1577. doi: 10.1007/s00405-018-4967-7. Epub 2018 Apr 23. PMID: 29687184.

P225

"Head as light as if I were always in your hands": proposal of cognitive multisensory rehabilitation in patients with cervical dystonia

G. Sgubin[1,2,3,4], E. Cella[4], M. Sossi[4], A. Zanette[4], M. Deodato[2,3,4], P. Manganotti[2,3]

[1]Department of Life Science, University of Trieste, Trieste, Italy
[2]Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy
[3]Azienda Sanitaria Universitaria Giuliano Isontina, Trieste, Italy
[4]School of Physiotherapy, University of Trieste, Trieste, Italy

Introduction: Cervical dystonia is a movement disorder characterized by motor symptoms and pain. The role of somatosensory inputs in its pathophysiology is supported by clinical signs and by the literature [1].
Rehabilitation is usually an adjunct therapy to botulinum neurotoxin injections and most patients never receive targeted treatment [2]. Patients tend to reduce social participation and to over-control the affected part.
Cognitive multisensory rehabilitation [3], focus on somatosensory reorganization and subsequent motor improvement in the dystonic body part, incorporating somatosensory perception and motor imagery-guided exercise.

Methods: Two patients with cervical dystonia received CMR for 20 total sessions. Rehabilitative intervention was based on exercise in supine and seated position. To solve perceptual tasks, patients had to achieve relaxation of the neck and the whole body. Subsequently, the physiotherapist guided the patients' movement to response to perceptual demands. Motor imagery was used to program the movement.
Patients provided detailed information about symptoms in pain map before the treatments and after. Qualitative data were also collected regarding language used by patients to describe the way they program the movement to perform.

Results: After treatment, patients reported higher level of autonomy, with a return to activities as walking, driving and socializing. Pain maps show a reduction in affected areas and greater precision in pain locations. Additionally, there is a change in the language used to describe movements.
Patients report performing exercises at home daily and not needing manual therapy. Furthermore, the time between BoNT injections has increased.

Conclusions: Studies available in literature suggest that treatment cannot disregard the perceptual aspect of movement. The strategies reported by patients who 'fight' dystonia are not effective and increase their disability level.
A rehabilitation treatment aiming at recovering attention and perception to the affected area seems to allow patients to gain awareness and to manage dystonia more autonomously.

References:

[1] Avanzino, L. et al., 2014. Frontiers in human neuroscience, 8, 1000.
[2] Prudente, C. et al., 2018. Movement disorders clinical practice, 5(3), 237-245.
[3] Van de Winckel, A. et al., 2020. Scientific Reports, 10(1).1

P226

Constant and Intensive Rehabilitation Treatment (TRIC) in patients with Parkinson's disease: a pilot study

Christian Gelao[1], F. Angeloro[1], C. Palmirotta[2], S. Tagliente[2], G. Lagravinese[2], S. Aresta[1,2], P. Battista[2,3], P. Fiore[1,4], B. Minafra[1]

[1]Istituti Clinici Scientifici Maugeri IRCCS, Neurorehabilitation Unit of Bari Institute, Bari, Italy
[2]Istituti Clinici Scientifici Maugeri IRCCS, Laboratory of Neuropsychology, Bari Institute, Bari, Italy
[3]Global Brain Health Institute (GBHI), University of California San Francisco, CA, USA
[4]Department of Physical and Rehabilitation Medicine, University of Foggia, Foggia, Italy

Introduction: Scientific literature largely supports the importance of physical activity as a lifestyle component for patients with Parkinson's disease (PD). Performing exercises promotes a neuroprotective effect in patients with PD, enriches motor skills, and consequently improves the quality of life. Several studies showed that a structured approach based on therapeutic exercise improved patients' motor performance. Still, this improvement was retained only for a limited period (e.g., after discharge from the hospital).

Objectives: This pilot study aimed to investigate the effects of a tailored intensive exercises program, dedicated to patients with PD, at post-treatment and 3 months follow-up.

Methods: We developed a new therapeutic program, namely TRIC (Constant and Intensive Rehabilitation Treatment) which focuses on therapeutic exercises and aerobic activities. N=20 patients with idiopathic PD (age 75.55±8.99 years, H&Y 1.87±0.74; MDS-UPDRS-III 25.8±9.88) underwent n=36 training sessions, each lasting 60 minutes, according to a personalized and progression modulated program, for 12 consecutive weeks. Outcome measures on standardized test scores were collected. In particular, we measured the degree of motor impairment, mobility, balance, and gait. Comparison pre-post measures were calculated by paired samples t-test.

Results: All patients completed all phases of this study. We found significant differences pre-post treatment in balance, as measured by the BERG BALANCE SCALE ($p<.001$), and in gait, as measured by the 6 MINUTE WALKING TEST ($p<.001$). These differences were still significant at the 3-month follow-up.

Conclusions: Findings indicate that physical activity may result in a lasting improvement of impaired motor function in individuals with a neurodegenerative disease such as PD.

P227

Muscle-targeted nutritional support and rehabilitation (MIRT) to treat Parkinsonian patients with risk of fall: a multicentric, randomized, single-blind study

Giampietro Gabrielli[1], A. Perfetti[2], P. Marcanti[2], A. Accardo[1], C. Iarlori[3], O. Santilli[4], A. Quaroni[5], M. Girmegna[5], A. Molino[6], C. Bosio[7], K. Molatore[8], M. Grancagnolo[8], M. Ferrario[9], R. Frappoli[9], T. Sogoian[10], J. Mantini[11], G. Frazzitta[12]

[1]Fisioterapista, Studio Cure Integrate, Centro MIRT, Livorno, Italy
[2]Fisioterapista, Studioerre, Centro MIRT, Brescia, Italy
[3]Neurologo, Fondazione Papa Paolo Sesto, Centro MIRT, Pescara, Italy
[4]Fisiatra, Fondazione Papa Paolo Sesto, Centro MIRT, Pescara, Italy
[5]Fisioterapista, PV Care, Centro MIRT, Stradella (PV), Italy
[6]Fisiatra, Istituto Riabilitazione RIBA, Centro MIRT, Torino, Italy
[7]Fisioterapista, Istituto Riabilitazione RIBA, Centro MIRT, Torino, Italy
[8]Fisioterapista, Centro Ri-abilita, Centro MIRT, Traona (SO), Italy
[9]Fisioterapista, Centro Sim-patia, Centro MIRT, Valmorea (CO), Italy
[10]Fisiatra, Fisiosport Terraglio, Centro MIRT, Venezia- Mestre, Italy
[11]Fisioterapista, Fisiosport Terraglio, Centro MIRT, Venezia-Mestre, Italy
[12]Neurologo, Presidente MIRTparkproject, Italy

Introduction: Previous studies have shown how muscle-targeted nutritional support associated with intensive multidisciplinary treatment (MIRT) is able to improve the effects of rehabilitation [1].

Objectives: Evaluate whether MIRT associated to a muscle-targeted nutritional support in patients with Parkinson's disease and balance disorder (stage 2-4 Hoehn-Yahr) reduces the risk of falling.

Methods: A multicentre, randomized (1:1), single blind study, where 40 patients with Parkinson's disease and a history of fear of falling are randomized in two groups: a group that will undergo MIRT for a month treated with a muscle-targeted nutritional support and a control group which will instead undergo only MIRT for a month. The study duration is 12 months. Patients will be assessed with the UPDRS, Berg Balance Scale, FES-I (Falls Efficacy Scale International) and will keep a Falls Diary. Each centre will enrol 6 patients: in each centre there will be a responsible for the randomisation, while the operators who will treat the patients will not be aware whether they are patients belonging to the experimental group or the control group. A blind operator will carry out the rating scales at the time of enrolment (T0), after 1 month (T1) and at the 3-month follow-up (T2).
Inclusion criteria: Parkinson's disease stage 2-4, subjective fear of falling or history of falls, BERG Balance Scale ≤ 50.
Exclusion criteria: Parkinsonism, Cognitive disorders, Polyneuropathies, Strokes, head trauma, cerebellar disorders, Myasthenia, Alcoholism

Conclusions: All patients, at the end of the one-month intensive treatment, will continue, until the end of the study, to perform exercises, suggested by the physiotherapist, at home and which will be the same for the patients of both groups.

References:

[1] Muscle-targeted nutritional support for rehabilitation in patients with parkinsonian syndrome. Barrichella M et al. Neurology 2019 Jul 30;93(5):e485-e496.

P228

Multidisciplinar Intensive Rehabilitation Treatment (MIRT) for outpatient Parkinsonian patients: a multicentric Italian study

Giampietro Gabrielli[1], A. Perfetti[2], A. Magri[2], A. Accardo[1], C. Iarlori[3], E. Di Tillio[4], A. Quaroni[5], M. Girmegna[5], A. Molino[6], C. Bosio[7], K. Molatore[8], M. Grancagnolo[8], M. Ferrario[9], R. Frappoli[9], T. Sogoian[10], J. Mantini[11], G. Frazzitta[12]

[1]Fisioterapista, Studio cure integrate, centro MIRT, Livorno, Italy
[2]Fisioterapista, Studioerre, Centro MIRT, Brescia, Italy
[3]Neurologo, Fondazione Papa Paolo Sesto, Centro MIRT, Pescara, Italy
[4]Referente MIRT Project, Fondazione Papa Paolo Sesto, Centro MIRT, Pescara, Italy
[5]Fisioterapista, PV Care, Centro MIRT, Stradella (PV), Italy
[6]Fisiatra, Istituto Riabilitazione RIBA, Centro MIRT, Torino, Italy
[7]Fisioterapista, Istituto Riabilitazione RIBA, Centro MIRT, Torino, Italy
[8]Fisioterapista, Centro Ri-abilita, Centro MIRT, Traona(SO), Italy
[9]Fisioterapista, Centro Sim-patia, Centro MIRT, Valmorea (CO), Italy
[10]Fisiatra, Fisiosport Terraglio, Centro MIRT, Venezia-Mestre, Italy
[11]Fisioterapista, Fisiosport Terraglio, Centro MIRT, Venezia-Mestre, Italy
[12]Neurologo, Presidente MIRTparkproject, Italy

Introduction: Previous studies have shown how an intensive multidisciplinary treatment (MIRT) for hospitalized patients is able to reduce symptoms progression and improve the quality of life in Parkinsonian patients [1-2].

Objectives: To evaluate whether treatment of MIRT outpatient Parkinsonian patients (stage 2-4 Hoehn-Yahr) may reduce symptoms progression and improve the quality of life.

Methods: 400 patients with Parkinson's disease will be evaluated in a multicentre open-study for one year. All of them will undergo the same intensive rehabilitation treatment for a month and a maintening treatment with specific exercise for the following 11 months.
The study duration will be 18 months. Patients will be assessed with the UPDRS, Berg Balance Scale, FES-I (Falls Efficacy Scale International, Timed up and go test, PDQ-39. Each centre will enrol 50 patients. Inclusion criteria: Parkinson's disease stage 2-4. Exclusion criteria: Parkinsonism, cognitive and cerebellar disorders, polyneuropathies, strokes, head trauma.

References:

[1] Intensive rehabilitation treatment in early Parkinson's disease: a randomized pilot study with a 2-year follow-up. Frazzitta G. et al Neurorehabil Neural Repair. 2015 Feb;29(2):123-31.
[2] Efficacy of intensive multidisciplinary rehabilitation in Parkinson's disease: a randomised controlled study. Frazzitta G. et al J Neurol Neurosurg Psychiatry. 2018 Aug;89(8):828-835.

P229

Immersive virtual reality and gait control: unveiling dual-task influences in functional gait disorders

Francesca Salaorni[1], M. Gandolfi[1], G. Bonardi[1], C. Perin[1], A. Sandri[1], L. Malgarise[1], F. Schena[1], L. Avanzino[2,3], E. Pelosin[2,4], C. Geroin[1], D. Vidale[5], M. Pirini[5], M. Fiorio[1], M. Tinazzi[1]

[1]University of Verona, Verona, Italy
[2]Ospedale Policlinico San Martino, IRCCS, Genoa, Genoa, Italy
[3]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy
[4]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[5]Khymeia SRL, Padua, Italy

Introduction: Functional Motor Disorders (FMDs) are part of the broader scope of Functional Neurological Disorders, including tremors, paresis, dystonia, and gait disorders. Functional gait disorders (FGDs) are among the most disabling symptoms affecting patients with FMDs [1], for which management and rehabilitation are crucial for functional recovery. Literature suggests how some technological tools, such as virtual reality (VR), could improve their management [2] and their walking disorders [3]. However, studies still need to be conducted to explore VR effects on FMDs. Moreover, clinical evidence observed an improvement in symptoms when patients are distracted, proving that a dual-task paradigm is a practical approach to investigating the mechanisms of high-level gait control in these conditions [3].

Objectives: This study aimed to explore how an immersive VR protocol might impact spatiotemporal gait parameters in people with FMDs from healthy controls and Parkinson's patients (PDs) used as a neurological disease comparison group. We also investigated the relationship between dual-task effect gait measures and disease severity.

Methods: A total of 109 subjects, including 43 HC, 46 FMDs, and 20 PDs, underwent spatiotemporal gait analysis during the free walk (ST), cognitive (cDT), and visualfixation (vDT) dual-task in both a real environment (RE) and two virtual environments (a city-like one, VRC, and a reproduction of RE), using Feetme wearables insoles for a total of eight tasks. Immersive virtual reality environments were specifically developed (Khymeia SRL, Italy). Gait speed, swing and stride time variability were assessed as spatiotemporal gait parameters sensitive to the effects of dual tasking in quantifying changes in low and high-level gait control markers.

Results: A parametric statistic such as repeated measure ANOVA was employed with the application of Tukey test correction for post hoc analyses. Broadly, motor performance and automaticity were lower in PDs and FMDs than in HCs in almost all tasks. In all groups, compared to ST and vDT in the RE, gait speed decreased in all tasks ($p<.001$); instead, swing and stride time variability worsened mainly in the cDT in VRC and RE ($p<.001$). In particular, the gait speed of PDs worsened significantly during the cDT in RE and VRC.

Conclusions: Even if still in the exploratory phase, our findings shed light on higher-level gait control mechanisms in FMDs and represent preliminary evidence for measures of dual-task effects for discriminating FMDs from HCs. FMDs showed behavior similar to HCs, suggesting that measures of gait automaticity might be a diagnostic and prognostic gait biomarker in FMDs.

References:

[1] Tinazzi M et al. Parkinsonism Relat Disord 2021; 91:32-36.
[2] Schiza E et al. Front Robot AI. 2019; 6:100.
[3] Gandolfi M et al. Parkinsonism Relat Disord. 2023; 105-291.

P230

A pilot study to psychoeducational interventions for caregivers of individuals with progressive supranuclear palsy

Luca Tommasini[1], M. Cerri[2], E. Del Prete[1], S. Cintoli[1], E. Benevento[2], D. Frosini[1], G. Tognoni[1], R. Ceravolo[1,2]

[1]Department of Medical Specialities, Neurology Unit, AOUP, Pisa, Italy
[2]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy

Introduction: Diagnosis of Progressive Supranuclear Palsy (PSP) greatly affects the lives of both patients and caregivers. Family caregivers of individuals with neurodegenerative diseases face a higher risk of developing psycho-physical difficulties compared to the general population. Psychoeducational interventions are strongly recommended as non-pharmacological treatment to manage patient's cognitive impairment, behavioral disturbances and caregiver burden for both dementia and PSP caregivers [1].

Objectives: This pilot-study explores the effectiveness of psychoeducational interventions for caregivers of patients with cognitive disorders.

Methods: Psychoeducational interventions consist of a structured program of five sessions (2h each) every two weeks, aimed at providing information on motor and cognitive disorders, managing psycho-behavioral symptoms, effective communication (e.g., improving communication and involving others), and the caregiver's experience (e.g., reducing stress, learning to take time for self). The program was delivered in small groups of caregivers by psychologists and neurologists, and it included time for didactics and practice. For all participants we used visual-analogue scale (VAS; ranging from 0 to 100) evaluating: capacity to manage psycho-behavioral symptoms, disease knowledge, social support, leisure time, harmony with the patient and perceived stress. PSP caregivers also completed Parkinsonism Carers Quality of Life (PQoL-Carer). All measures were collected at the beginning and end of the program.

Results: 39 caregivers of dementia patients (AD and FTD) and 18 PSP caregivers were enrolled at the Neurologic Unit of Santa Chiara Hospital, Pisa. Statistical analyses showed a significant improvement in all VAS measures for dementia caregivers. PSP caregivers showed an improvement on all variables except for "harmony with patients", "perceived stress" and PQoL-carer total score ($p<0.05$).

Conclusions: The findings of this pilot-study showed that psychoeducational interventions enhanced specific aspects of caregiving for both groups, highlighting the effectiveness also for PSP caregivers. In the future, expanding participant numbers and including a follow-up session for long-term efficacy assessment will be essential.

References:

[1] Bluett B et al., Best Practices in the Clinical Management of Progressive Supranuclear Palsy and Corticobasal Syndrome: A Consensus Statement of the CurePSP Centers of Care. Front Neurol. 2021 Jul 1;12:694872. doi: 10.3389/fneur.2021.694872. PMID: 34276544; PMCID: PMC8284317.

P231

Adrenergic blocker-mediated reversal of sympathetic overactivity in subjects at risk for Parkinson's disease: a multimodal biomarker study

Michele Tagliati, M. Lima Gregorio, H. Maghzi, E. Hogg, C. Malatt, E. Tan, M.C. Kelly, R. Artal, M. Shehata, B. Renner, P. Sati, G. Pagano

Department of Neurology, Cedars-Sinai Medical Center, Los Angeles, USA

Introduction: Autonomic impairment plays a key role in idiopathic REM Behavior Disorder (iRBD) pathophysiology, associated with a high risk of synucleinopathy. We previously found that iRBD subjects, without clinical or imaging evidence of nigrostriatal degeneration, show signs of sympathetic nervous system (SNS) overactivity as a marker of early PD and predictor of phenoconversion. Carvedilol, an adrenergic blocker, can reduce abnormal SNS activity.

Objectives: To investigate the effects of treatment with carvedilol on markers of sympathetic dysfunction in iRBD subjects at risk for Parkinson`s disease (PD).

Methods: Four male iRBD subjects (age 65.5±6.7) with pre-motor PD symptoms and abnormal Iodine-123 meta-iodobenzylguanidine (123I-MIBG) were assessed for markers of sympathetic activity at baseline, 6 and 12 months after treatment with carvedilol (12.5mg or 25mg twice daily). Study variables included 123I-MIBG late H/M ratio and WR; Heart Rate Variability (HRV) low/high frequency ratio (LF/HF); Neuromelanin sensitive MRI (NM-MRI) contrast-to-noise ratio (CNR) between locus coeruleus (LC) and pons. MDSUPDRS part III and dopamine transporter scan (Ioflupane I^{123}injection) quantitative analysis were used to exclude existing PD.

Results: All subjects had baseline abnormalities consistent with SNS overactivity, resulting in reduced average late H/M (1.51±0.35), high WR (33.7±11.3), elevated LF/HF (4.9±1.7) and LC NM-MRI hyperintensity (3.6±1.4). At baseline, average MDS-UPDRS III scores were 2.8±11.3 and average Ioflupane I^{123}injection putamen/caudate ratio was 0.91±0.05. After treatment with carvedilol, MIBG WR was reduced on average both at 6 (18.1±6.7) and 12 months (18.5±14.4); LF/HF ratio was reduced on average at 6 (3.9±1.3) and 12 months (2.7±1.5); NM-MRI intensity showed reduced intensity after 6 (2.8±0.6) and 12 months of treatment (2.9±0.5). MDS-UPDRS III scores and Ioflupane I^{123} injection measures did not significantly change throughout the study.

Conclusions: Treatment with carvedilol can reverse markers of SNS overactivity in iRBD subjects at risk for PD, suggesting that accepted markers of neurodegeneration may be reversible in the pre-motor stages.

P232

Deep brain stimulation of globus pallidus internus (GPI) in Parkinson's disease (PD): short and long-term outcome

Simone Malaspina[1,2], G. Belluscio[1,2], F. Valentino[1], M. Avenali[1,2], C. Pacchetti[1], R. Zangaglia[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS C. Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy

Introduction: Deep brain stimulation (DBS) is a well-established surgical procedure for treatment of motor complications in PD. Both the subthalamic nucleus (STN) and internal globus pallidus (GPi) are considered nearly equivalent targets for improving PD motor symptoms. However, GPi-DBS has been reported to determine a greater reduction of dyskinesias despite a minor postoperative reduction of dopaminergic therapy than STN-DBS. To date, few studies with small sample size investigated the long-term motor outcomes of GPI-DBS in PD patients.

Objectives: To evaluate short- and long-term GPi-DBS efficacy on motor symptoms in PD.

Methods: We evaluated a cohort of 30 PD patients who underwent GPi-DBS surgery with directional leads from 2018 to 2023 at our center. Patients were assessed before DBS (T0) and 1 (T1) and 5 years (T5) after surgery. Demographic, clinical and treatment data were collected at each timepoint. Motor performances were measured using the Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III) in OFF medication at T0 and in OFF med/ON Stim at T1 and T5.

Results: 30 PD patients (23 Male and 7 Female, mean age 61.3 ±9.6 years) were included, 12 subjects completed the 5-year follow-up assessment. At T1, all subjects showed a significant improvement in MDS-UPDRS-III (T0 OFF med: 34.6±13.8 and T1 20.5±8.5; p 0.0005) and dyskinesias, while there were no significant changes in dopaminergic therapy intake (LEDD; T0: 878.6±352.8; T1: 823.8±441.5). At T5, the benefit on dyskinesias was confirmed (p 0,001) while both LEDD and MDS-UPDRS III scores slightly increased, however not significantly, compared to T1 (LEDD: T0: 878.6±352.8 and T5: 908±416).

Conclusions: GPi-DBS in PD patients in this single-center cohort showed a sustained long-term reduction of dyskinesias as well as motor benefits, without the need for a significant increase in dopaminergic therapy even 5 years after surgery.

P233

Efficacy and safety of Opicapone in Parkinson's disease and motor fluctuations. The Open-Park multicentre study

Roberto Cilia[1], F. Colucci[1], M. Pierantozzi[2], R. Cerroni[2], S. Bonvegna[3], F. Valentino[4], E. Caputo[5], L. Caremani[6], A. Govoni[6], S. Ramat[6], F. Tamma[5], C. Pacchetti[4], A. Zecchinelli[3], I.U. Isaias[3], A. Stefani[2], R. Eleopra[1]

[1]Parkinson and Movement Disorders Unit, Department of Clinical Neurosciences, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Parkinson's Disease Unit, University Hospital of Rome "Tor Vergata", Rome, Italy
[3]Parkinson Institute, ASST G. Pini-CTO, Milan, Italy
[4]IRCCS Mondino Foundation, Pavia, Italy
[5]Department of Neurology, "F. Miulli" General Hospital, Acquaviva delle Fonti, Italy
[6]Parkinson Unit, Neuromuscular-Skeletal and Sensory Organs Department, AOU Careggi, Florence, Italy

Introduction: Opicapone (OPC) proved to be safe and effective in reducing off-time in Parkinson's disease (PD) in clinical trials. [1-5]

Objectives: To provide the preliminary results of the ongoing realworld study Open-Park assessing the safety and the efficacy of OPC.

Methods: This multicentre, observational study enrolled 191 PD patients (mean age 64.9 years) with motor fluctuations, who required OPC as adjunctive therapy. At baseline, PD duration was 9.7±5.1 years, daily levodopa dose 588±253 mg. Data before (V1) and after the initiation of OPC (V2) was collected for 92 patients and assessed for the primary endpoint: change in total MDS-UPDRS I-II-III at V2 versus V1 with paired t-test. Secondary endpoint included adverse events (AEs).

Results: Mean follow-up was 10,5±3,2 months (n=92). MDS-UPDRS parts I-III scores were significantly lower at V2 than V1 (Mean±SD Part I: 8.2±5.6 vs. 9.7±5.9, p=0.007; Part II: 11.2±7.0 vs. 14.5±7.1, p<0.0001; Part III 24.8±13.7 vs. 29.4±14.8; p<0.001). Primary endpoint was reached: MDS-UPDRS I+II+III score was significant reduced at follow-up (44.2±23.4 vs. 53.5±24.2, p<0.0001).

Motor fluctuations significantly improved at V2 (Part IV score 4.75±3.38 vs. 7.10±3.41; p<0.00001). MDS-UPDRS-IV OFF-state subscores were all significantly improved at V2 (item 4.3 time spent in off-state, p<0.0001; item 4.4 functional impact of fluctuations, p<0.0001; item 4.5 complexity of motor fluctuations, p<0.0001; item 4.6 painful off-state dystonia, p=0.03). The MDS-UPDRS-IV dyskinesias subscores and the Hoehn&Yahr stage didn't change. Concerning safety, only 13 out of 191 (7%) of patients experienced any AE, of whom 10/13 dropped-out. Total AEs recorded were 23. Psychiatric disorders (hallucinations, anxiety, agitation, insomnia) accounted for 35% of total AEs, followed by gastrointestinal disorders (30%), whereas motor-related issues (dyskinesias and dystonia) accounted for 22% of AEs.

Conclusions: In a real-world setting, OPC was safe and effective in reducing off-state without increasing dyskinesia in PD with motor fluctuations.

References:

[1] Almeida et. al ., 2013. Clin Pharmacokinet ; 52: 139−151.
[2] Kiss et al., 2010. J Med Chem ; 53: 3396−3411.

[3] Ferreira et al., 2016. Lancet Neurol; 15: 154–65.
[4] Lees et al ., 2017. JAMA Neurol; 74: 197–206.5.
[5] Ferreira et al., 2022. Mov Disord; 37:2272−2283.

P234

The influence of muscle spindle afferent input on subthalamic Local Field Potentials (LFPs) in Parkinson's disease

Tommaso Bocci[1,2], S. Coelli[3], V. Levi[4], R. Eleopra[4], M. Egidi[5], A.M.M. Bianchi[3], A. Priori[1,2]

[1]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[2]Clinical Neurology Unit, "Azienda Socio-Sanitaria Territoriale Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy
[3]Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy
[4]Neurosurgery Department, Functional Neurosurgery, Fondazione Istituto Neurologico Carlo Besta, Milan, Italy
[5]Neurosurgery Unit San Carlo Borromeo Hospital ASST Santi Paolo e Carlo Milan, Italy

Introduction: Subthalamic local field potentials (STN-LFPs) arise from spontaneous and presynaptic input-dependent changes of electrical activity of large ensembles of neurons. Although motor and non-motor symptoms in patients with Parkinson's disease (PD) correlate with STN-LFP, whether they are modulated by peripheral inputs from muscle spindles is unknown. Because adaptive Deep Brain Stimulation (DBS) is controlled by STN-LFPs signals, understanding their origin is crucial.

Objectives: To assess the STN-LFP changes in PD following the muscle afferent spindle input block induced by curarization in patients undergoing surgery for Deep Brain Stimulation (DBS).

Methods: The experimental protocol included STN-LFP recordings in three phases during: awake state (A), propofol sedation (P), curarization (C). Signals (8-80Hz) were analyzed by linear and nonlinear
approaches.

Results: Linear approaches showed that the absolute log signal power for the total spectrum (8-80Hz), the beta band (15-30Hz), the low gamma (31-55Hz) and the high gamma (56-80Hz) bands decreased during P and again eventually increased during C. Nonlinear approaches revealed that the power law 1/f exponent for the 1- 45Hz band increased during C in comparison with A and P.

Conclusions: Linear and non-linear computational analysis of STNLFP suggest that muscle spindle block induced by curarization may shape the STN-LFP pattern in PD, therefore supporting the hypothesis that reafference from muscle input can provide a deterministic contribution to electrical activity in the human subthalamic area.

P235

Gender differences in patients with Parkinson's disease treated with subthalamic or globus pallidus internus deep brain stimulation: results from a single center

Giorgio Belluscio[1,2], S. Malaspina[1,2], M. Avenali[1,2], G. Cosentino[2,3], C. Pacchetti[1], R. Zangaglia[1], F. Valentino[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[3]Translational Neurophysiology Research Unit, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Gender differences exist in Parkinson's disease (PD). It is therefore important to evaluate gender-specific outcomes of DBS in PD in order to improve therapeutic counselling.

Objectives: We investigated gender-differences in response to DBS of the STN or GPi in a group of patients with advanced PD.

Methods: 123 patients with PD (30% F, 70% M) that underwent DBS targeting the STN or GPi were enrolled. Motor outcomes were compared at baseline and 1-year after DBS. In baseline, MDS-UPDRS part III was collected in both OFF and ON state. Dopaminergic drug therapy was converted in Levodopa Equivalent Daily Dose (LEDD). At 1-year follow-up, MDS-UPDRS-III score was assessed in the ON state with the stimulator turned on.

Results: 93 patients were treated with STN-DBS (32,2 % females) while the remaining 30 patients were treated with GPi-DBS (23.3% females). At baseline, there were no gender differences as regards disease duration, LEDD and MDS-UPDRS part III score. At 1-year follow-up, we found better MDS-UPDRS III score for both GPi- and STNDBS and a significant LEDD reduction compared to baseline only after STN-DBS (p=.0001), with no gender-specific differences. The percentage of patients with dyskinesias decreased from 86% to 20% in females and from 91% to 50% in males after GPi-DBS. After STNDBS the decrease was from 93.3% to 66% in females, and from 73% to 34% in males. The percentage of patients with clinical fluctuations decreased from 86% to 14% in females and from 39% to 13% in males after GPi-DBS, while after STN-DBS the decrease was from 56.6% to 27% in females, and from 44% to 28% in males. Overall, the effect of sex was not statistically significant.

Conclusions: Bilateral STN- and GPi-DBS are equally effective in males and females as a treatment for motor complications of PD.

P236

Acknowledging the responses of diverse motor phenotypes to levodopa-carbidopa intestinal gel in advanced Parkinson's disease. A prospective observational study

Kristi Meksi, A. Stefani, M. Pierantozzi, E. Garasto, M. Conti, R. Bovenzi, C. Liguori, T. Schirinzi, N.B. Mercuri, R. Cerroni

Parkinson Centre, Department of System Medicine, University of Rome "Tor Vergata", Rome, Italy.

Introduction: In the advanced stages of Parkinson's disease (PD), the diminishing efficacy of levodopa [1] necessitates the exploration of alternatives, such as levodopa-carbidopa intestinal gel (LCIG) which ensures a controlled delivery mechanism, overcoming oral levodopa's limitations [2]. Acknowledging the diverse motor phenotypes responses to standard oral levodopa, an essential question emerges: does LCIG infusion exhibit a similar spectrum of heterogeneity in motor responses? Resolving this query is crucial for the formulation of individualized therapeutic strategies to optimize efficacy within the complex landscape of advanced PD.

Objectives: This prospective observational study aims to examine, evaluate, and compare the motor responses at the 12-month postimplantation period following LCIG, considering the different motor phenotypes of PD.

Methods: The study enrolled 20 patients in advanced stages of PD who underwent LCIG infusion. Stratification based on motor phenotypes (tremor-dominant, akinetic-rigid, mixed) allowed for a detailed analysis. Motor responses were evaluated at the 12-month follow-up using UPDRS-III scores in both ON and OFF phases. Statistical analyses were employed to identify patterns and variances within and across motor phenotype groups, ensuring a comprehensive investigation into the treatment's effectiveness.

Results: Our analysis revealed a statistically significant motor response at the 12-month interval within each subgroup ($p<0.05$). The improvements in UPDRS-III scores emphasized the sustained therapeutic efficacy of LCIG across various motor phenotypes. Interestingly, despite distinct improvements within each subgroup, no noticeable differences in motor response were observed among the three groups, suggesting an uniform therapeutic impact.

Conclusions: In conclusion, our study aligns with current literature, confirming the efficacy of LCIG in mitigating motor symptoms across diverse phenotypes in advanced PD [2,3]. The absence of noticeable differences in motor response among the three groups, while intriguing, warrants careful interpretation due to the small patient cohort and relatively short follow-up duration. Ongoing investigations with larger cohorts and extended follow-up periods are crucial to substantiate and refine our observations, advancing our comprehension of LCIG infusion's long-term impact in advanced PD.

References:

[1] Tambasco N, Romoli M, Calabresi P. Levodopa in Parkinson's Disease: Current Status and Future Developments. Curr Neuropharmacol. 2018;16(8):1239-1252. doi: 10.2174/1570159X15666170510143821. PMID: 28494719; PMCID: PMC6187751.

[2] Wirdefeldt K, Odin P, Nyholm D. Levodopa-Carbidopa Intestinal Gel in Patients with Parkinson's Disease: A Systematic Review. CNS Drugs. 2016 May;30(5):381-404. doi: 10.1007/s40263-016-0336-5. PMID: 27138916.

[3] Fasano A, García-Ramos R, Gurevich T, Jech R, Bergmann L, Sanchez-Soliño O, Parra JC, Simu M. Levodopa-carbidopa intestinal gel in advanced Parkinson's disease: long-term results from COSMOS. J Neurol. 2023 May;270(5):2765-2775. doi: 10.1007/s00415-023- 11615-3. Epub 2023 Feb 18. PMID: 36802031; PMCID: PMC10130122.

P237

Weight gain in Parkinson's disease after subthalamic nucleus deep brain stimulation: semaglutide as a possible treatment

Gabriele Vadi[1], E. Del Prete[2], L. Becattini[1], G. Bellini[1], R. Ceravolo[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Department of Medical Specialties, Neurology Unit, AOUP, Pisa, Italy

Introduction: Deep Brain Stimulation (DBS) is a surgical therapy now commonly used to treat motor complication in Parkinson's disease (PD). Subthalamic nucleus (STN) DBS can be associated with adverse effects, including a wide range of mood and behavioural changes. Weight gain is extremely frequent in PD patients after STN-DBS, however the mechanism underpinning this side effect is still unknown. GLP-1 agonists, a class of oral antidiabetic drugs, have garnered increasing interest in neurodegenerative diseases, including Parkinson's disease, due to their promising effects observed in both clinical and preclinical trials.

Objectives: To investigate the effect of GLP-1 agonist in controlling weight gain after STN-DBS in Parkinson's disease.

Results: We describe the case of a 59-years-old man with PD and type 2 diabetes who developed weight gain (from 110 to 120kg) after STNDBS within 12 months from surgery, at least in partly due to a binge eating behaviour. The patients achieved an excellent response to semaglutide therapy (0,5 mg), with loss of 7 kg within 3 months.

Discussion: Weight gain after STN-DBS is common and could be related to several factors, varying from hyperdopaminergic drive and binge eating to the reduction in energy expenditure due to DBS effects on dyskinesias and tremor. Semaglutide, a GLP-1 agonist, carries out multiple actions, particularly in reducing blood glucose in a glucose-dependent manner and causing a slight delay in gastric emptying. Interestingly, it can lead to weight loss by reducing calorie intake due to a general decrease in appetite, particularly decreasing the preference for high-fat foods.

Conclusion: To our knowledge, this is the first case of the use of a GLP-1 agonist in a PD patient which contrasts the weight gain after STN-DBS. We hypothesize that GLP-1 agonists could represent a possible therapeutic treatment in these patients, however further evidence are needed to confirm our data.

P238

A case report of successful bilateral Gamma-Knife Thalamotomy in Essential Tremor resistant to medications

Giovanni Napoli[2,5], M. Malcangi[2,3,5], A. De Simone[2,5], S. Galantucci[2], L.R. Barzaghi[5,6], P. Mortini[5,6], M. Filippi[1,2,3,4,5], M.A. Volonté[2]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]Department of Neurosurgery and Gamma Knife Radiosurgery, IRCCS San Raffaele Scientific Institute, Milan, Italy

Introduction: Some patients with essential tremor (ET) experience severe, disabling and drug-esistant symptoms. In such cases, invasive treatments should be considered. Deep brain stimulation (DBS) and MR-guided focused ultrasound (MRgFUS) thalamotomy are state-of-the-art surgical procedures approved by FDA [1,2,3], but evidence suggests that gamma knife radiosurgery (GKS) is a viable option with a good functional outcome and favorable tolerability [4] despite not having FDA approval.

Objective: We describe the case of a 76-year-old man affected by ET with disabling tremor, who experienced significant improvement following bilateral GKS thalamotomy.

Methods: Our patient, with a 19-year history of ET, displayed a moderate-severe bilateral, left-prevailing kinetic tremor of the upper limbs, with rest and postural components, and also head, jaw, tongue, and voice tremors. At the time of diagnosis, brain MRI revealed a cavernous angioma at the left temporal pole. Over the years, the tremor became disabling, causing dependency in several daily activities. Various drugs were discontinued due to ineffectiveness or adverse events. Thus, bilateral GKS thalamotomy was attempted. In February 2022, the left ventral intermediate nucleus (VIM) was targeted with a 130 Gy dose, followed by the right VIM treated in May 2023 with a 65 Gy dose.

Results: Approximately 9 months after the left thalamotomy, the patient exhibited a significant reduction in right upper limb tremor amplitude, with a remarkable improvement in his autonomy. No adverse events were observed. Following the second treatment, a similar improvement occurred on the opposite side, with no reported adverse events as well.

Conclusions: GKS is a second-line option for medical-resistant tremor syndromes. Bilateral GKS has the potential to safely improve ET patients with severe bilateral limb or axial involvement, if done in a staged manner after a unilateral procedure. Our case suggests the possibility to broaden its application in the symptomatic treatment of ET.

References:

[1] Marin G et al. Deep brain stimulation in neurological diseases and other pathologies . Neurol. Perspect. 2022; 2 (3): 151-159.
[2] Elias WJ et al. A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor. N Engl J Med. 2016 Aug 25; 375 (8): 730-9.

[3] Fishman PS et al. Neurological adverse event profile of magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor. Mov Disord. 2018 May; 33 (5): 843-847.
[4] Kondapavulur S et al. A Systematic Review Comparing Focused Ultrasound Surgery With Radiosurgery for Essential Tremor. Neurosurgery. 2023 Sep 1; 93 (3): 524-538.

P239

Patients' satisfaction in subthalamic nucleus deep brain stimulation for parkinson disease: 5-year follow-up

Eleonora Zirone[1], F. Ruggiero[1], M.T. Molisso[1], A. Tomaselli[1], F. Cogiamanian[1], L. Borellini[1], E. Mailland[1], E. Pirola[1], A. Ampollini[1], A.B. Di Fonzo[1], R. Ferrucci[1,2], D. Mellace[2], A. De Sandi[1], A. Marfoli[2], M. Locatelli[1,2], S. Barbieri[2], F. Mameli[1]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2]University of Milan, Milan, Italy

Introduction: Deep brain stimulation of the subthalamic nucleus (STN-DBS) is an effective treatment for Parkinson's disease (PD). However, despite motor improvement following STN-DBS may be maintained for over 5 years [1,2], it may not be necessarily related to long-term patient satisfaction [3].

Objectives: To evaluate the patients' satisfaction undergoing STNDBS 5 years after surgery.

Methods: Sixteen PD patients were enrolled in this study (8 female, mean [±SD]: age 57.5±8.1 years; disease duration: 11.2±3.8 years). To quantify the patients' satisfaction in DBS treatment we administered a Visual Analogue Scale (VAS) 1 year (T1), and 5 years (T2) after surgery. Cognitive function, QoL, and mood were assessed respectively through the Montreal Cognitive Assessment (MoCA), the Parkinson's Disease Questionnaire-8 (PDQ-8), and the Beck Depression Inventory-II (BDI-II) before (T0) and after surgery (T1; T2). In addition, motor profile (MDS-UPDRS-III) and levodopa equivalent daily dose (LEDD) were acquired from each participant.

Results: We found that patients' satisfaction did not change significantly over time (VAS score: T1 vs T2:7.7±0.9 vs 7.2±0.9, p=0.14). Nevertheless, QoL and mood improved from T0 to T1 (mean [±SD] PDQ-8: 37.1±17.9 vs 24.3±13.4, p=0.02; BDI-II: 10.9±7.1 vs 5.6±2.9, p=0.01), but their scores did not show differences between T0 and T2 ($p>0.05$). Cognitive function did not differ over time ($p>0.05$) while LEDD reduced from T0 to T2 (1106.7±329.8 mg vs 572.9±312 mg, $p<0.001$).

Conclusions: Patients reported a great satisfaction at 5 years after surgical treatment, despite the QoL return almost to pre-DBS levels. This suggest that real changes that follow DBS may not be reflected in changes in the PDQ-8 score. More systematic studies are needed to explore the long-term benefits subjectively perceived by PD patients undergoing STN-DBS.

References:

[1] Krack P. et al. N. Engl. J. Med. 349 (2003) 1925–1934.
[2] Castrioto A. et al. Arch. Neurol. 68 (2011) 1550–1556.
[3] Yamamoto T. et al. J Neurol Sci. 15 (2017) 379-18-21.

P240

Assessing improvement after deep brain stimulation: Do Parkinson's disease patients, their caregivers and neurologists agree?

Denise Mellace[1], F. Mameli[2], F. Ruggiero[2], F. Cogiamanian[2], L. Borellini[2], A. De Sandi[2], A. Marfoli[1], A. Tomaselli[2], E. Zirone[2], A. Priori[3,4], S. Barbieri[2], R. Ferrucci[1,2]

[1]Dipartimento di Oncologia ed Emato-Oncologia, Università degli Studi di Milano, Milan, Italy
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan, Italy
[4]ASST-Santi Paolo e Carlo, S.C. di Neurologia

Introduction: The subjectively perceived outcome of deep brain stimulation (DBS) of the subthalamic nucleus (STN) in patients with Parkinson's disease (PD) is usually reported as positive, particularly about motor symptoms and quality of life [1]. However, individual opinion may vary from patient to patient, and from the perception of their caregivers and neurologists.

Objectives: The purpose of the present study was to evaluate how PD patients, caregivers, and neurologists perceived both psychological and physical improvements six months after STN-DBS.

Methods: 25 patients [(mean ± SD) age 58.9 ± 8.0 years; 9 women] with PD who underwent bilateral STN-DBS, their caregivers and neurologists rated the degree of improvement in physical and psychological domains 6 months after surgery, using two visual analogue scales (VAS) ranging from 0 to 10. Intraclass correlation coefficients (ICC [95% confidence interval]) were calculated to determine reliability between the three raters.

Results: Six months after DBS, patients, caregivers, and neurologists reported an improvement of approximately 60% in the psychological domain and over 75% in the physical domain ($p<0.001$). No significant differences were found between raters in two domains ($p>0.05$). Concordance between the three raters was moderate to good (0.74 [0.41-0.90], $p<0.001$) for psychological improvement and moderate (0.69 [0.27–0.88], $p=0.04$) regarding physical improvement.

Conclusions: PD patients generally report positive benefit six months after DBS, which is also confirmed by caregivers and neurologists. The use of patients and caregivers self-administered questionnaires as well as traditional physician assessments may provide a more comprehensive assessment of DBS outcomes.

References:

[1] Maier et al., 2016. Parkinsonism & related disorders; 24: 41-47.

P241

Validation of Italian QoL Questionnaire for Device-Aided Therapy in Parkinson's patients: impact of DBS on QoL

Elena Pramaggiore[1], M. Sacchetti[1], F. Garini[1], G. Nada[1], D. Sartini[1], R. Fornaro[2], L. Magistrelli[3]

[1]SCDO Psicologia Clinica, Azienda, Ospedaliero Universitaria Maggiore della Carità, Novara, Italy
[2]Neurochirurgo, SCDO Neurochirurgia, Azienda Ospedaliero Universitaria Maggiore della Carità, Novara, Italy
[3]Neurologo, ASST Gaetano Pini-CTO, Milan, Italy

Introduction: This study validates the Italian version of a questionnaire gauging the quality of life in Parkinson's disease patients undergoing therapeutic device implantation [3]. Addressing a literature gap, patients from AOU Maggiore della Carità in Novara, including 10 with Deep Brain Stimulation (DBS) and 3 with an apomorphine infusion pump, were selected for testing.

Objectives: The objective is to assess the Italian-translated questionnaire's validity and explore the impact of DBS and infusion pump treatments on the quality of life of advanced-stage Parkinson's patients, with a focus on motor symptom improvement [2].

Methods: DBS involves inserting two electrodes into the brain, usually targeting the subthalamic nucleus or globus pallidus internus, connected to a subclavicular generator. The infusion pump entails placing a catheter into the small intestine for continuous apomorphine administration [1]. Patients received the Italian version of the Parkinson's Disease QoL for Device-Aided Therapy (PDQ-DAT) questionnaire at T1 (one month) and T2 (three months) postimplantation. Results were compared with the original PDQ-DAT questionnaire, and inter-patient scores at T1 and T2 were analyzed.

Results: Scores from the first 13 patients align with the original version, confirming translation validity. A significant improvement in quality of life across all areas was observed in the comparison of patient scores at T1 and T2.

Conclusions: Preliminary findings suggest the Italian version's validity and highlight improved quality of life with DBS and infusion pump treatments. Further administrations will enrich these results, emphasizing potential benefits for Parkinson's patients undergoing these therapeutic interventions.

References:

[1] Armstrong MJ, Okun MS. Diagnosis and Treatment of Parkinson Disease: A Review. JAMA. 2020 Feb 11;323(6):548-560. doi: 10.1001/jama.2019.22360. PMID: 32044947.
[2] Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021 Jun 12;397(10291):2284-2303. doi: 10.1016/S0140-6736(21)00218-X. Epub 2021 Apr 10. PMID: 33848468.
[3] Kawaguchi M, Miyagi Y, Kishimoto J, Samura K, Tokunaga Y, Watari M, Eguchi H, Ueda S, Iihara K. Development of Quality of Life Questionnaire for Patients with Parkinson's Disease Undergoing STN-DBS. Neurol Med Chir (Tokyo). 2021 Aug 15;61(8):475-483. doi: 10.2176/nmc.oa.2020-0388. Epub 2021 Jun 21. PMID: 34148942; PMCID: PMC8365237.

P242

Apomorphine-induced acute thrombocytopenia in a Parkinson's disease patient with motor fluctuations: a case report

Maria Magdalena Pocora[1,2], M. Avenali[1,3], M.G. Croce[1,4], F. Valentino[3], B. Rugginini[1,4], F. Ferrari[1,4], G. della Porta[1,4], C. Tassorelli[1,2], C. Pacchetti[3], R. Zangaglia[3]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]Headache Science and Rehabilitation Center, IRCCS C. Mondino Foundation, Pavia, Italy
[3]Parkinson's Disease and Movement Disorders Unit, IRCCS C. Mondino Foundation, Pavia, Italy
[4]IRCCS C. Mondino Foundation, Pavia, Italy

Introduction: Apomorphine is a short-acting D1- and D2-like receptor agonist used in the treatment of advanced Parkinson's Disease (PD) with fluctuations. Apomorphine pump infusion is generally well tolerated, however rare side effects have been also reported [1]. Hemolytic anemia is the only hematological complications to be described so far [2,3].

Objectives: To report a rare acute complication during apomorphine pump infusion in a PD patient.

Methods: Data were collected from medical records. Literature was reviewed for relevant content.

Results: A 74 years-old man with PD and severe motor fluctuations started apomorphine infusion pump at 1 mg/h rate and gradually increased to 3,5 mg/h. Three days after the first drug administration the patient developed millimetric petechiae on the lower limbs, which extended to the trunk and arms. Moreover, he showed tongue hematoma and oral petechiae, followed by spontaneous gingival bleeding. His blood tests revealed severe thrombocytopenia (platelet count 12.000/ul). No major bleeding occurred. In the suspicion of a possible Apomorphine adverse event, the drug was immediately withdrawn and steroids were started after Hematology consult. Platelet count gradually increased within normal range and lesions were fully resolved. Diagnostic workup for other causes of thrombocytopenia was negative.

Discussion: Drug-induced immune hemolytic anemia is a rare complication of numerous drugs, including levodopa and dopamine agonists, such as apomorphine. Our patient showed a rapid platelet decrease with normal hemoglobin values, after few days of continuous apomorphine infusion, which completely reversed with steroid therapy. To our knowledge, this is the first case reporting thrombocytopenia as side effect during apomorphine treatment.

Conclusions: Apomorphine infusion pump is an effective and well tolerated treatment in patients with PD and motor fluctuations. Nevertheless, rare acute hematological side effects can also occur, and patients should be monitored with blood tests, especially in the first days of administration.

References:

[1] Carbone F, Djamshidian A, Seppi K, Poewe W. Apomorphine for Parkinson's Disease: Efficacy and Safety of Current and New Formulations. CNS Drugs. 2019;33(9):905-918. doi:10.1007/s40263-019-00661-z.
[2] Pot C, Oppliger R, Castillo V, Coeytaux A, Hauser C, Burkhard PR. Apomorphine-induced eosinophilic panniculitis and hypereosinophilia in Parkinson disease. Neurology. 2005;64(2):392-393. doi:10.1212/01.WNL.0000149757.47854.6F.
[3] Venegas Pérez B, Arquero Portero T, Sánchez Fernández MS, Feliz Feliz C, del Val Fernández J, García-Ruiz PJ. Apomorphine-Induced Immune Hemolytic Anemia. Mov Disord Clin Pract. 2017;4(1):145-147. doi:10.1002/mdc3.12373.

Indice Autori

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z