Consiglio Direttivo
Accademia LIMPE-DISMOV

Presidente
Mario Zappia

Presidente Eletto
Michele Tinazzi

Past President
Leonardo Lopiano

Segretario
Alessandro Tessitore

Tesoriere
Roberto Ceravolo

Consiglieri
Laura Avanzino
Matteo Bologna
Miryam Carecchio
Roberto Erro
Alessandra Nicoletti
Mario Giorgio Rizzone
Fabrizio Stocchi

Presidente del Congresso e del Comitato Scientifico
Pietro Cortelli

Comitato Scientifico
Giovanni Abbruzzese
Alberto Albanese
Angelo Antonini
Gennarina Arabia
Paolo Barone
Alfredo Berardelli
Ubaldo Bonuccelli
Paolo Calabresi
Giovanna Calandra Buonaura
Maria Gabriella Ceravolo
Carlo Colosimo
Giovanni Cossu
Giovanni Defazio
Alessio Barnaba Di Fonzo
Roberto Eleopra
Marco Guidi
Mariachiara Malaguti
Roberto Marconi
Francesca Morgante
Alessandra Nicoletti
Marco Onofrj
Antonio Pisani
Alberto Priori
Roberto Quatrale
Mario Giorgio Rizzone
Mariachiara Sensi
Alessandro Stefani
Fabrizio Stocchi
Filippo Tamma
Gioacchino Tedeschi
Michele Tinazzi
Franco Valzania

Comunicazioni Libere

C1

Heterogeneity of prodromal Parkinson symptoms in siblings of Parkinson disease patients

Luca Baldelli[1], S. Schade[2,3], S. Jesús[4,5], S.R. Schreglmann[6], L. Sambati[1,7], P. Gómez-Garre[4,5], C. Halsband[2,3], G. Calandra-Buonaura[1,7], A.D. Adarmes-Gómez[4,5], F. Sixel-Döring[8,9], C. Zenesini[7], C. Pirazzini[7], P. Garagnani[10], M.G. Bacalini[7], K.P. Bhatia[6], P. Cortelli[1,7], B. Mollenhauer[8,11], C. Franceschi[7], P. Mir[4,5], C. Trenkwalder[3,8], F. Provini[1,7]

[1]Department of Biomedical and NeuroMotor Sciences (DiBiNeM), University of Bologna, Bologna, Italy
[2]Department of Clinical Neurophysiology, University Medical Center Göttingen, Göttingen, Germany
[3]Department of Neurosurgery, University Medical Center Göttingen, Göttingen, Germany
[4]Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain
[5]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain
[6]University College London (UCL), Institute of Neurology, London, U. K.
[7]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[8]Paracelsus-Elena-Klinik Kassel, Kassel, Germany
[9]Neurologische Klinik, Philipps-University, Marburg, Germany
[10]Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Bologna, Italy
[11]Department of Neurology, University Medical Center Göttingen, Göttingen, Germany

Introduction: A prodromal phase of Parkinson's disease (PD) may precede motor manifestations by decades. PD patients' siblings are at higher risk for PD, but prevalence and distribution of prodromal symptoms are unknown [1].

Objectives: The study objectives were 1) to assess motor and non-motor features estimating prodromal PD probability [2] in PD siblings recruited within European PROPAG-AGEING project; 2) to compare motor and non-motor symptoms to the well-established DeNoPa cohort.

Methods: 340 PD siblings from three sites (Bologna, Seville, Kassel/Goettingen) underwent clinical and neurological evaluations of PD markers. The German part of the cohort was compared with German de-novo PD patients (dnPDs) and healthy controls (CTRs) from DeNoPa.

Results: Fifteen (4.4%) siblings presented with subtle signs of motor impairment, with MDS-UPDRS-III scores not clinically different from CTRs. Symptoms of orthostatic hypotension were present in 47 siblings (13.8%), no different to CTRs (p=0.072). No differences were found for olfaction and overall cognition; German-siblings performed worse than CTRs in visuospatial-executive and language tasks. 3/147 siblings had video-polysomnography-confirmed REM sleep behavior disorder (RBD), none was positive on the RBD Screening Questionnaire. 173/300 siblings had <1% probability of having prodromal PD; 100 between 1-10%, 26 siblings 10-80%, one fulfilled the criteria for prodromal PD.

Conclusions: According to the current analysis we cannot confirm the increased risk of PD siblings for prodromal PD. Siblings showed a heterogeneous distribution of prodromal PD markers and probability. Additional parameters, including strong disease markers, should be investigated to verify if these results depend on validity and sensitivity of prodromal PD criteria [3], or if siblings' risk is not elevated.

References:

[1] A.J. Espay et al. Disease modification and biomarker development in Parkinson disease: Revision or reconstruction? Neurology 94, 481-494.

[2] S. Heinzel et al. Update of the MDS research criteria for prodromal Parkinson's disease. Mov Disord.

[3] N. Giagkou et al. A Prospective Validation of the Updated Movement Disorders Society Research Criteria for Prodromal Parkinson's Disease. Mov Disord 35, 1802-1809.

C2

Plasma Cys-C correlates with plasma NfL levels and predicts disease progression in Parkinson's disease

Alberto Imarisio[1], A. Pilotto[1,2], E. Garrafa[3], F. Conforti[1], S. Masciocchi[1], R. Turrone[1], S. Gipponi[1], E. Cottini[1], M.C. Rizzetti[2], M. Pizzi[4], H. Zetterberg[6,7,8,9], N.J. Ashton[6,10,11,12], A. Hye[11,12], A. Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]FERB Onlus, Ospedale S. Isidoro, Trescore Balneario, Bergamo, Italy
[3]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy
[4]Division of Pharmacology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy
[5]Department of Neuroscience Imaging and Clinical Sciences, University G. d'Annunzio of Chieti-Pescara, Chieti, Italy
[6]Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[7]Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden
[8]Department of Neurodegenerative Disease, UCL Institute of Neurology, London, UK
[9]UK Dementia Research Institute at UCL, London, UK
[10]Wallenberg Centre for Molecular and Translational Medicine, Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[11]King's College London, Institute of Psychiatry, Psychology & Neuroscience, Maurice Wohl Clinical Neuroscience Institute, London, UK
[12]NIHR Biomedical Research Centre for Mental Health & Biomedical Research Unit for Dementia, South London & Maudsley Nhs Foundation, London, UK

Background: Previous studies reported increased plasma levels of Cystatin C (Cys-C) in Parkinson's disease (PD) and claimed for a possible association with disease severity and progression.

Objectives: To evaluate plasma Cys-C in PD and healthy controls (HC) and test its association with markers of peripheral inflammation, neurodegeneration and clinical progression in a longitudinal study.

Methods: Plasma Cys-C, high-sensitive C-reactive protein (hsCRP), interleukin 6 (IL-6) and Neurofilament Light Chain (NfL) were assessed at the baseline in 71 consecutive non-demented PD and 69 HC. PD patients underwent an extensive motor and cognitive assessment at baseline and after 2 years of follow-up. The association of Cys-C with disease severity was evaluated in a multilinear model adjusted for the effect of age, sex, disease duration and peripheral inflammation.

Results: Cys-C levels appeared to be higher in PD compared to controls and correlated with the neuronal marker NfL ($r = 0.204$, $p = 0.046$). In longitudinal analyses, PD patients with higher Cys-C levels exhibited faster motor progression at two years of follow-up independently from the peripheral inflammatory profile.

Conclusions: Cys-C was associated with higher NfL levels and a remarkably faster motor progression in PD independently from peripheral inflammation. Further studies are needed in order to understand the mechanisms underpinning the association of Cys-C with higher neuronal damage markers in neurodegenerative diseases.

C3

Dopaminergic networks reconfigurations in prodromal dementia with Lewy bodies

Andrea Pilotto[4,5], S. Caminiti[1,2,3] E. Premi[4,6], E. Ferrari[4], G. Bonzi[4], S. Gipponi[4], E. Cottini[4], B. Paghera[7], D. Perani[1,2,3], A. Padovani[4,5]

[1]Vita-Salute San Raffaele University, Milan, Italy
[2]In Vivo Human Molecular and Structural Neuroimaging Unit, Division of Neuroscience, San Raffaele Scientific Institute, Milan, Italy
[3]Nuclear Medicine Unit, San Raffaele Hospital, Milan, Italy
[4]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[5]Parkinson's Disease Rehabilitation Centre, FERB ONLUS – S. Isidoro Hospital, Trescore Balneario, Italy
[6]Stroke Unit, Azienda Socio Sanitaria Territoriale Spedali Civili, Spedali Civili Hospital, Brescia, Italy
[7]Nuclear Medicine Unit, University of Brescia, Brescia, Italy

Background: Dopaminergic deficits are a core feature of dementia with Lewy bodies (DLB) but the involvement of nigrostriatal and extranigrostriatal networks is still debated in the prodromal phases of the disease.

Aim: To examine local and long-distance dopaminergic alterations in prodromal DLB patients and compare them with patients with DLB dementia and Parkinson's disease (PD)

Methods: We included 20 prodromal Lewy bodies with mild cognitive impairment (MCI-LB) patients, 29 DLB patients, 79 PD patients without cognitive decline or dementia, and 73 healthy controls (CG) who underwent [123I]FP-CIT-SPECT imaging. The occipital-adjusted specific to nondisplaceable binding ratio (SBR) in cortical and subcortical regions were compared among the groups adjusting for the effects of age, sex, disease duration, and motor impairment. Between-groups differences in ventral and dorsal dopaminergic networks molecular connectivity were evaluated via partial-correlation analysis.

Results: All clinical groups showed lower [123I]FP-CIT-SPECT SBR in the olfactory cortex, putamen, and caudate nuclei than CG. Thalamic SBR appeared to be selectively reduced in DLB and MCI-LB compared to CG and PD. Molecular connectivity assessment revealed a widespread loss of inter-connections among subcortical and cortical targets of DA networks in PD and DLB. The MCI-LB group showed strong and widespread metabolic connectivity reconfigurations in the two networks compared to the CG.

Conclusions: MCI-LB are characterized by early local and system-level alterations, with increased and decreased molecular connectivity suggesting a complex neural compensation mechanisms in the prodromal phase of DLB.

C4

Impact of tracheostomy for stridor on survival in Multiple System Atrophy

Giulia Giannini[1,2], I. Cani[2], F. Provini[1,2], A. Cecere[1], F. Mignani[1], P. Guaraldi[1], P. Cortelli[1,2], G. Calandra-Buonaura[1,2]

[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Clinica Neurologica Rete Metropolitana NEUROMET, Bologna, Italy
[2]Department of Biomedical and NeuroMotor Sciences (DiBiNeM), Alma Mater Studiorum - University of Bologna, Bologna, Italy

Introduction: Prevalence of stridor in Multiple System Atrophy (MSA) ranges from 12% to 42%. Stridor treatment mainly comprised tracheostomy or continuous positive airway pressure (CPAP), but guidelines for the use of these treatments in MSA patients have yet to be established. Few studies on small samples have analysed the role of treatment type as predictor of survival.

Objective: To evaluate the predictive value of stridor treatment in a cohort of patients with MSA comparing tracheostomy and CPAP.

Methods: This is a retrospective and prospective cohort study including 182 MSA patients evaluated at least once a year during the disease course. Stridor was video-polysomnography-confirmed. Time of stridor treatment (CPAP or tracheostomy) and latency from stridor onset were collected. Survival data, from disease onset to time of death, were calculated with Kaplan-Meier curves. Predictors were identified in univariate and multivariable Cox regression analyses.

Results: A total of 182 (107 males, mean disease duration: 7.8 ± 3.9 years) patients with MSA were included in the study, 141 were deceased at the time of study. On the total sample, 75 patients were diagnosed with stridor: 22 patients were treated with tracheostomy and 29 with CPAP, while 24 patients did not receive treatment. Treatment with tracheostomy showed longer survival when compared both with treatment with CPAP or no-treatment (incidence rate of death: 12 vs. 21 vs. 23 per 100 person-years, respectively).
Both patients without treatment and treated with CPAP showed an increased risk of death at univariate Cox regression when compared to those treated with tracheostomy. CPAP remained an independent factor associated with shorter survival (HR=2.63, p=0.029) also after adjustment for other confounders.

Conclusions: This is the largest study comparing survival between tracheostomy and CPAP in MSA patients with stridor. Treatment with tracheostomy showed longer survival when compared both with treatment with CPAP or no-treatment.

C5

Spinal cord excitability and plasticity in hereditary spastic paraparesis: A Neurophysiological Study

Alessandro Zampogna[1], A. Guerra[1], F. Asci[1], A. Funcis[1], C. Celletti[2], F. Camerota[2], A. Berardelli[1], A. Suppa[1,3]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Department of Physical Medicine and Rehabilitation, Sapienza University of Rome, Rome, Italy
[3]IRCCS Neuromed Institute, Pozzilli (IS), Italy

Introduction: Pure hereditary spastic paraparesis (HSP) is a neurodegenerative disorder characterized by slowly progressive lower limb weakness and spasticity due to the impairment of corticospinal fibres [1]. The pathophysiological mechanisms underlying motor disorders in HSP are largely elusive [2]. Also, the possible pathophysiological role of abnormal spinal excitability and plasticity is unknown.

Objective: This study aims to investigate spinal cord excitability and plasticity in pure HSP.

Methods: Fifteen patients with pure HSP (SPG4) and ten age-matched healthy subjects (HS) participated in this study. Patients were clinically assessed through standardized scales including the Spastic Paraparesis Rating Scale, modified Ashworth scale and Barthel scale. To examine spinal excitability, we evaluated the H reflex (HR) and the reciprocal inhibition (RI) curve, at seven different interstimulus intervals (ISIs), in the soleus (SO) muscle of the dominant limb. To investigate spinal plasticity, we assessed long-term changes in the HR amplitude and RI curve, before and after a specific spinal cord plasticity-inducing protocol based on focal muscle vibration (fMV) (i.e., 30-minutes of fMV over the SO muscle) [3].

Results: When considering excitability, HSP patients showed higher HR amplitude and lower HR inhibition at 2, 3 and 20 ISIs of the RI curve than HS. Concerning plasticity, HS showed significant long-term depression of the HR amplitude at 5 and 30 minutes after fMV over the SO muscle. Conversely, in HSP patients, fMV left the HR amplitude and the RI curve unchanged.

Conclusions: HSP patients are characterized by abnormal spinal cord excitability (e.g. increased motoneuron excitability associated with decreased excitability of RI pathways). Also, the reduced modulation of the HR and RI curve following fMV points to abnormal spinal cord plasticity in HSP. Overall, these findings support the hypothesis that abnormal spinal cord excitability and plasticity play a role in the pathophysiological mechanisms underlying motor disorders in HSP.

References:

[1] PVS de Souza, WBV de Rezende Pinto, GN de Rezende Batistella, T Bortholin, ASB Oliveira. Hereditary Spastic Paraplegia: Clinical and Genetic Hallmarks. Cerebellum. (2017), 16, 525-551. doi: 10.1007/s12311-016-0803-z.

[2] C Crone, NT Petersen, JE Nielsen, NL Hansen, JB Nielsen. Reciprocal inhibition and corticospinal transmission in the arm and leg in patients with autosomal dominant pure spastic paraparesis (ADPSP). Brain (2004), 127, 2693–2702. doi: 10.1093/brain/awh319.

[3] L Rocchi, A Suppa, G Leodori, C Celletti, F Camerota, J Rothwell, A Berardelli. Plasticity Induced in the Human Spinal Cord by Focal Muscle Vibration. Front Neurol. (2018), 9, 935. doi: 10.3389/fneur.2018.00935.

C6

Exploring a cohort of 593 European Huntington's disease patients with 41 CAG triplets in expanded allele and mid-adult or tardive disease age of onset

Martina Petracca[1], S. Di Tella[2], P. Zinzi[1,3], M. Solito[1], M.R. Lo Monaco[4], M.C. Silveri[2,6], A.R. Bentivoglio[1,5]

[1]Movement Disorders Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy
[3]Clinical Psychology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS Rome, Italy
[4]Geriatric Day-Hospital, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[5]Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[6]Medicine of the Ageing, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background: Huntington's disease (HD) is a genetic, neurodegenerative disorder characterised by progressive motor and cognitive symptoms and psychobehavioral problems. The expansion in CAG number in HTT gene causes HD and negatively correlates with age of onset accounting for up to 70% of its variability [1-2].

Aims: To investigate clinical, behavioural and cognitive characteristics of HD patients with the same 41 CAG repeats on the expanded allele and common mid-adult ($CoHD_{41CAG}$, 30-59 years) or late onset disease ($LoHD_{41CAG}$, ≥60 years) [3].

Methods: From Enroll-HD Periodic Dataset were selected 593 European HD patients with 41 CAG: 360 $CoHD_{41CAG}$ and 233 $LoHD_{41CAG}$.
The two groups were compared for sex, age, education, disease duration, functional and motor performance, inheritance, symptoms onset, psychiatric anamnesis, neuropsychological profile and psychobehavioural outcomes.

Results: $CoHD_{41CAG}$ (mean onset 52.1±6.0) and $LoHD_{41CAG}$ (mean onset 64.2±3.5) did not differ for gender nor for CAG in normal allele, with mean disease duration shorter in the $LoHD_{41CAG}$ group (8.1±5.8 vs 6.4±3.8 years, p<.001). Phenotypical differences evidenced in body mass index, motor and functional performance with worse scores in $LoHD_{41CAG}$ (p<.001). In psychiatric history, $CoHD_{41CAG}$ more frequently reported depression and suicidality than $LoHD_{41CAG}$ patients (p=.001), whereas $LoHD_{41CAG}$ more often experienced apathy (p=.001). With respect to current psychobehavioural assessment, depression was higher in $CoHD_{41CAG}$, while no differences emerged in apathy, irritability, psychosis, and obsessive/compulsive symptoms. Neuropsychological evaluation revealed a comparable general cognitive status. Significant differences were only found on Stroop Interference Test (p=.023) and Trail Making Test-B (p=.020) with worse performance for $LoHD_{41CAG}$.

Conclusions: $CoHD_{41CAG}$ and $LoHD_{41CAG}$ show similar cognitive deterioration pattern, while motor and functional performance is worse in $LoHD_{41CAG}$. In psychiatric aspects, $LoHD_{41CAG}$ manifested lower current depression scores and less anamnestic suicidality and depression. Further studies are

required to identify possible factors influencing age of onset useful for a differential management of patients with typical or tardive onset.

References:

[1] NS Wexler, J Lorimer, J Porter et al. Venezuelan kindreds reveal that genetic and environmental factors modulate Huntington's disease age of onset. Proc Natl Acad Sci U S A. 2004 Mar 9;101(10):3498-503.

[2] M Oosterloo, EK Bijlsma, SM van Kuijk, F Minkels,CE. de Die-Smulders. Clinical and genetic characteristics of late-onset Huntington's disease. Parkinsonism Relat Disord. 2019;61:101-105. doi:10.1016/j.parkreldis.2018.11.009.

[3] E Capiluppi, L Romano, P Rebora et al. Late-onset Huntington's disease with 40-42 CAG expansion. Neurol Sci. 2020;41(4):869-876.

C7

Longitudinal structural and functional brain alterations in Parkinson's disease patients with freezing of gait

Elisabetta Sarasso[1], F. Agosta[1,2,5], N. Piramide[1,5], T. Stojkovic[6], I. Stankovic[6], S. Basaia[1], A. Tomic[6], V. Markovic[6], E. Stefanova[6], V.S. Kostic[6], M. Filippi[1-5]

[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]Neurorehablitation 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]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: No longitudinal studies have explored the progression of both structural/functional alterations in PD patients with freezing of gait (PD-FoG).

Objectives: To investigate cortical/subcortical and network functional alterations in PD-FoG patients, PD developing FoG (PD-FoG-converters) and PD not developing FoG (PD-non-converters) over one and two years.

Methods: Thirty PD-FoG, 11 PD-FoG-converters and 11 PD-non-converters, age, sex, education, disease duration and severity matched, were followed for two years. Thirty age, sex and education matched healthy controls were included at baseline. Participants underwent clinical/MRI visits to evaluate cortical thickness, basal ganglia volumes and functional graph metrics at baseline and their changes over two years. Correlations between baseline MRIs and clinical worsening in PD groups and a ROC curve to investigate if any MRI measure at baseline could differentiate PD-FoG-converters and non-converters were run.

Results: At baseline, PD-FoG had widespread cortical/subcortical atrophy, while PD-FoG-converters and non-converters showed atrophy in sensorimotor areas and basal ganglia. PD-FoG-converters relative to controls and PD-FoG showed higher global and parietal local efficiency and clustering coefficient. Over time, PD-FoG showed posterior cingulate atrophy but stable functional graph metrics. PD-FoG-converters accumulated occipital atrophy and reduced parietal clustering coefficient, while PD-non-converters showed fronto-parietal and temporal atrophy and increased sensorimotor path length. Both structural and functional baseline MRI alterations correlated with worse executive/attentive functions over time in PD-FoG. Higher parietal clustering coefficient at baseline differentiated PD-FoG–converters from PD-non-converters.

Conclusions: Structural MRI is a useful tool to monitor PD progression, while functional MRI may be helpful to identify FoG conversion early.

Funding
Ministry of Education, Science, and Technological Development of the Republic of Serbia (project #175090), Italian Ministry of Health (Grant #RF-2018-12366746).

C8

Sleep disorders and cognitive dysfunctions in a large cohort of advanced Parkinson's disease patients

Alberto Romagnolo[1], E. Montanaro[1], M. Fabbri[2], C.A. Artusi[1], G. Imbalzano[1], C. Ledda[1], M.G. Rizzone[1], L. Lopiano[1], M. Zibetti[1]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]Department of Neurosciences, Clinical Investigation Center CIC 1436, Parkinson Toulouse Expert Center, NS-Park/FCRIN Network and NeuroToul COEN Center, Toulouse University Hospital; INSERM; University of Toulouse 3, Toulouse, France

Background: Parkinson's disease **(**PD) is increasingly recognized as a multidimensional disorder, characterized by several non-motor symptoms, including sleep and cognition disturbances. Studies on the relationship between sleep problems and neuropsychological functions, mainly conducted in early to moderate PD patients, outline mixed results [1,2]. We analysed the relationship between subjectively reported sleep alterations and cognitive functions in a large cohort of 181 advanced PD patients.

Methods: All consecutive, non-demented, PD candidates for device-aided therapy completed two sleep questionnaires - the PD Sleep Scale (PDSS-2) and the Epworth Sleepiness Scale (ESS) - and underwent a comprehensive battery of neuropsychological tests encompassing five cognitive domains (reasoning, memory, attention, frontal executive functions, language). A linear regression analysis was used to estimate correlations between sleep and cognitive scores, while ANCOVA was used to compare cognitive scores between patients with or without significant sleep alterations. Analyses were adjusted for age, disease duration, LEDD, and years of education.

Results: Patients showed mild-to-moderate sleep problems (PDSS-2=23.4±1.2) and mild daytime sleepiness (ESS=8.6±5.1). Significant correlations ($p<0.05$) were found between PDSS-2 total score and non-verbal reasoning, attentive skills, executive functions and language abilities. Similar results were found also for the "Motor symptoms at night" and "PD symptoms at night" PDSS-2 subscales, while the "Disturbed sleep" subscale did not show significant correlations with cognitive scores. No correlations were found between sleep measures and memory tests scores. The 59 patients (32.6%) with clinically relevant sleep disturbances performed worse on attention, executive functions and language. No significant correlations were found between daytime sleepiness and any neuropsychological test.

Conclusions: In advanced PD patients, sleep disturbances selectively correlate with specific neuropsychological functions and not with short-term memory and consolidation. Pending confirmations by means of longitudinal studies, our observations suggest the potential impact of sleep disturbances treatment on the modulation of cognitive decline in advanced PD patients [3,4].

References

[1] G. Maggi, L. Trojano, P. Barone, G. Santangelo. (2021) Sleep Disorders and Cognitive Dysfunctions in Parkinson's Disease: A Meta-Analytic Study. Neuropsychol Rev (2021) Mar 29. doi: 10.1007/s11065-020-09473-1 (online ahead of print).
[2] A. Pilotto, A. Romagnolo, J.A. Tuazon et al (2019) Orthostatic hypotension and REM sleep behaviour disorder: impact on clinical outcomes in α- synucleinopathies. J Neurol Neurosurg Psychiatry 90:1257-1263. https://doi.org/ 10.1136/jnnp-2019-320846.

[3] M.E. Pushpanathan, A.M. Loftus, M.G. Thomas, N. Gasson, R.S. Bucks. (2016) The relationship between sleep and cognition in Parkinson's disease: A metaanalysis. Sleep Med Rev 26:21-32. https://doi.org/ 10.1016/j.smrv.2015.04.003.
[4] K. Stavitsky, S. Neargarder, Y. Bogdanova, P. McNamara, A. Cronin-Golomb. (2012) The impact of sleep quality on cognitive functioning in Parkinson's disease. J Int Neuropsychol Soc 18:108-117. https://doi.org/ 10.1017/S1355617711001482.

C9

Parkinsonism-like phenotype in carriers of beta-glucocerebrosidase gene mutation with anti-GluR3 and anti-basal ganglia antibodies

Francesca Di Biasio[1], E. Monfrini[2], G. Lazzeri[2], T. Benzi Markushi[3], S. Morbelli[1,3], R. Marchese[1], L. Avanzino[1,5], A. Di Fonzo[2,4]

[1]IRCCS Policlinico San Martino, Genoa, Italy
[2]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[3]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Genoa, Italy
[4]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[5]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy

Introduction: Mutations in the beta-glucocerebrosidase gene (*GBA*) have been well described as risk factor for developing Parkinson's disease [1], while little is known about the connection with atypical parkinsonisms [2,3]. We report two cases of patients with parkinsonism-like phenotype, carrying a *GBA* L444P mutation and positivity to anti-GluR3 and anti-basal ganglia antibodies (ABGAs) [4].
Case 1 The first case is a 51-year-old woman with a one-month history of falls, bradykinesia and rigidity with negative family history. She presented severe akinetic-rigid parkinsonism associated to supranuclear vertical gaze palsy and postural instability. A trial with Levodopa was attempted with poor response. The brain MRI revealed atrophy of the posterior putamen (L>R). Dopamine transporter (DAT)-SPECT demonstrated reduced specific-to-not-displeacable ratio values in bilateral putamen (L>R), while FDG-PET showed markedly reduced uptake in both putamina (L>R).
Case 2 The second patient is a 66-year-old with rigidity and bradykinesia of the left arm, and postural instability developed at 63 years. Her medical history revealed a previous breast cancer and hypertension. The neurological examination disclosed severe rigidity and bradykinesia with dystonia of the left limbs, supranuclear vertical gaze palsy and a marche à petit pas. A trial with Levodopa was attempted with no response. The FDG–PET showing a reduction of the uptake in both putamina (R>L). The brain MRI revealed putaminal hypotrophy, together with mild mesencephalic atrophy with modest Hummingbird Sign. For both patients genetic testing revealed the heterozygous L444P mutation of t h e *GBA* gene. An autoimmune panel showed positivity of anti-GluR3 and ABGA antibodies on both serum and CSF.

Discussion: It is known that PD patients with *GBA* mutations have younger age at onset and may present a higher disease severity score [5], but the clinical phenotype is different from the atypical parkinsonism. Despite no sure evidence, with our cases we may hypothesize a possible role of autoimmunity (anti-GluR3 and ABGAs) combined with *GBA* mutation, in the genesis of a parkinsonism-like phenotype.

References:
[1] E. Sidransky, G. Lopez. The link between the GBA gene and parkinsonism. Lancet Neurol 2012; 11:986–998.

[2] R. Asselta, V. Rimoldi, C. Siri C et al. Glucocerebrosidase mutations in primary parkinsonism. Parkinsonism Relat Disord 2014;20:1215–1220.
[3] M. Picillo, S. Petrucci, E.M. Valente, S. Pappata, F. Squame, M. Ginevrino, L. Pace, P. Barone, M.T. Pellecchia. Progressive Supranuclear Palsy–Like Phenotype in a GBA E326K Mutation Carrier.
[4] R. Dale, V. Merheb, S. Pillai, D. Wang, L. Cantrill, T. Murphy, H. Ben-Pazi, S. Varadkar, T. Aumann, M. Horne, A. Church, T. Fath e F. Brilot, «Antibodies to surface dopamine-2 receptor in autoimmune movement and psychiatric disorders» Brain. 2012 Nov;135(Pt 11):3453-68.
[5] L.M. Chahine, J. Qiang, E. Ashbridge et al. Clinical and biochemical differences in patients having Parkinson disease with vs without GBA mutations. JAMA Neurol 2013;70:852–858.

C10

Longitudinal study of clinical and neurophysiological features in essential tremor

Luca Angelini[1], A. De Biase[1], G. Paparella[2], P. Amisano[1], A. Di Vita[1], M. Panfili[1], A. Maraone[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: Essential Tremor (ET) is a common and heterogeneous disorder characterized by motor and non-motor symptoms. Only a few studies have attempted to estimate symptoms progression in ET.

Objective: This is a longitudinal study aiming to investigate by a clinical and a kinematic evaluation whether and to what extent motor and non-motor manifestations of ET evolve in time.

Methods: We enrolled 24 ET patients who underwent a baseline and a follow-up evaluation (mean follow-up interval: 33.96 months). We assessed tremor through clinical scales and kinematic recordings; patients also underwent neuropsychological tests and structured interviews to investigate cognitive and psychiatric disorders. Correlation analysis was also performed between clinical and kinematic data.

Results: At follow-up evaluation, we observed higher Fahn-Tolosa-Marin Tremor Rating Scale scores than baseline (30.29 ± 13.42 vs. 20.58 ± 11.55, P=0.01), with a higher percentage of patients presenting tremor of more than one body segment (83.33% vs. 41.67%; P<0,01). Kinematic analyses, however, did not reveal amplitude and frequency tremor changes over time (all Ps>0.05). At follow-up, we also observed an increased percentage of ET patients with rest tremor (29.17% vs. 75%, P<0.01). Moreover, the kinematic analysis revealed slowed velocity and reduced movement amplitude during finger tapping. The cognitive assessment showed a trend towards worsening over time, while psychiatric evaluation showed no changes between baseline and follow-up. Correlation analysis did not individuate any relationship between clinical and demographic factors and kinematic data in ET.

Conclusions: ET is a progressive disorder characterized by multiple body segments involvement over time and the occurrence of soft signs, e.g. rest tremor, bradykinesia, and possibly cognitive deficits. Further studies are needed to better delineate features and factors influencing ET progression over time.

C11

Statins in Parkinson's disease: influence on motor progression

Giovanni Palermo[1], S. Giannoni[1], M. Giuntini[2,3], E. Belli[1,3], G. Bellini[1,3], D. Frosini[1,3], G. Siciliano[3], R. Ceravolo[1,3]

[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]Unit of Neurology, S. Stefano Prato Hospital, Azienda Toscana Centro, Prato, Italy
[3]Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Introduction: It has been speculated that statins are neuroprotective and are associated with a reduced risk of Parkinson's disease (PD) [1], but only a few studies have investigated the influence of statins on the progression of PD [2-3].

Objective: To evaluate whether long-term statin use may affect motor progression in a large cohort of *de novo* patients with PD.

Methods: We conducted a 4-year retrospective observational cohort study to assess patients with PD. The patients were consecutively recruited from a single tertiary center between January 2015 and January 2017. Information on motor function was obtained using the MDS-Unified Parkinson disease Rating Scale (UPDRS)-III and all subjects were extensively characterized, including information about lifestyle habits, cardiovascular risk factors and cholesterol blood levels.

Results: Of the 181 participants included in the study, 104 patients were evaluated for eligibility (42 patients were exposed to statin therapies and 62 were not treated with statins). They presented similar scores in UPDRS III at baseline but the statins users had a lower motor impairment at 4 years compared to non-user PD patients. Additionally, statin treatment resulted in slower progression of the rigidity score of UPDRS over 4 years. No other significant differences were observed between PD patients with and without statins.

Conclusions: Early PD patients with long-term statin usage showed lower motor deterioration after 4 years of disease duration compared with patients not taking statins at diagnosis, suggesting a possible influence of statins on disease progression in PD. Further investigation is warranted to understand the potential beneficial effects of statin treatment on clinical symptoms in PD.

References:

[1] Carroll CB, Wyse RKH. Simvastatin as a Potential Disease-Modifying Therapy for Patients with Parkinson's Disease: Rationale for Clinical Trial, and Current Progress. J Parkinsons Dis. 2017, 7:545-568.
[2] Lin CH, Chang CH, Tai CH, et al. A Double-Blind, Randomized, Controlled Trial of Lovastatin in Early-Stage Parkinson's Disease. Mov Disord. 2021, 36:1229-1237.
[3] Carroll CB, Webb D, Stevens KN, et al. Simvastatin as a neuroprotective treatment for Parkinson's disease (PD STAT): protocol for a double-blind, randomised, placebo-controlled futility study. BMJ Open 2019, 9:e029740.

C12

Predictive factors for deep brain stimulation efficacy in Parkinson's disease: presurgical variables and neuroimaging

Carlo Alberto Artusi, S. Della Casa, E. Montanaro, A. Romagnolo, M. Zibetti, M.G. Rizzone, L. Lopiano, M. Bozzali

Department of Neuroscience 'Rita Levi Montalcini', University of Torino, Torino, Italy

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) is an effective treatment for complicated Parkinson's disease (PD). However, unsatisfactory outcomes are not rare.

Objective: To identify and weight clinical/demographic factors predicting STN-DBS outcome, and propose a novel neuroimaging-based approach to guide STN-DBS implantation and parameter setting.

Methods: In 147 PD patients who underwent STN-DBS we analyzed pre- vs. 1-year postsurgical changes in ADL (UPDRS-II), motor symptoms (UPDRS-III), Off-time (UPDRS-item 4.1), and dyskinesia (UPDRS-item 4.3) entering the following presurgical variables: sex, age, disease duration, Levodopa-Equivalent Daily-Dose (LEDD), UPDRS-III response to levodopa, axial symptoms (UPDRS-III axial subscore), and mild-cognitive-impairment. Exploratorily, we estimated the anatomical distribution of the area modulated by DBS (volume of tissue activated -VTA-) on patients' STN and surrounding structures by the fusion of presurgical MRI and postsurgical CT images, and correlated imaging with clinical effects.

Results: STN-DBS yielded an 8.1% improvement of motor symptoms, 68.7% of dyskinesia, and 68.1% of Off-time, while ADL worsened of 21.6%. The model explained 59% of UPDRS-III (R2: 0.59, coeff: 1.69), 33% of dyskinesia (R2: 0.33, coeff: 1.97), 68% of Off-time (R2: 0.68, coeff: 1.67) and 31% of ADL change (R2: 0.31, coeff: 1.63). UPDRS-III response to levodopa was the strongest predictor of motor symptoms and Off-time improvement (p=0.04 and 0.01), along with axial subscore for Off-time improvement (p=0.02). Analyzing four patients, two with good and two with unsatisfactory DBS outcome, improvement in the former was driven by stimulation centered in the dorsolateral part of STN. Muscle contractures were explained by VTA overlapping with the internal capsule and malaise by VTA trespassing medial and anterior boards of STN.

Conclusions: UPDRS-III response to levodopa and axial symptoms are important predictors of DBS outcome, but demographic and clinical features do not fully explain STN-DBS outcome variability. VTA analysis is a promising tool for patients' management.

C13

Nigral iron accumulation in Parkinson's disease motor subtypes: results from an ultra-high field magnetic resonance study

Nicole Campese[1], E. Del Prete[1], D. Frosini[1], G. Donatelli [2,3], M. Lancione[2,4], M. Cencini[2,4], M. Costagli[2,5], G. Lucchi[3], M. Tosetti[2,4], M. Cosottini[2,3], R. Ceravolo[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Fondazione IMAGO7, Pisa, Italy
[3]Neuroradiology Unit, Department of Translational Research on New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
[4]IRCSS Stella Maris, Pisa, Italy
[5]Dipartimento di Neuroscienze, Oftalmologia, Genetica, Riabilitazione e Scienze Materno-infantili (DiNOGMI), Università di Genova, Genova, Italy

Introduction: In Parkinson's disease (PD) an abnormal iron deposition in the substantia nigra (SN), tracked *in vivo* by Quantitative Susceptibility Mapping (QSM) MRI techniques, seems to represent an early crucial event of the underlying neurodegenerative cascade [1]. Growing evidence supports the existence of different clinical PD endophenotypes, showing divergent motor and non-motor trajectories along the disease course [2]. Whether regional differences in nigral iron overload may underly distinctive clinical phenotypes and whether instrumental biomarkers may help better stratify PD subtypes has not been clarified yet.

Objective: Here we aim to assess regional differences in nigral iron overload in tremor-dominant (TD) compared to postural instability gait disorder (PIGD) parkinsonian patients.

Methods: we recruited patients diagnosed with Parkinson's disease [2] within 4 years from symptoms onset, who underwent an ultra-high field MRI (7T) exam of the brain between 2015 and 2020. Motor phenotypes have been classified as TD or PIGD according to published criteria [3]. Regions of interest (ROIs) were manually drawn bilaterally in the *SN pars dorsalis* and *ventralis*, *pars reticulata* and in the nigrosome 1 and applied to QSM-maps for the quantitative analysis.

Results: 43 PD patients (22 males, age=59.64±12.34, disease duration=2.23±1.07 years) were included in the study. Among them 28% (n=12) were classified as PIGD, 67% (n=29) as TD, 5% (n=2) as indeterminate. The PIGD and TD subgroups did not differ for age (p=0.689) and disease duration (p=0.788). The QSM-based quantitative analysis showed no differences between PIGD and TD phenotypes both in the SN *pars ventralis* (p=0.520), *dorsalis* (p=0.674), the *pars reticulata* (p=0.941) and the nigrosome 1 (p=0.603).

Conclusions: in our cohort we found no differences in nigral iron load in TD compared to PIGD patients in none of the explored subregions, suggesting a shared underlying pattern of nigral damage. The assessment of extra-nigral structures may provide further insights into the neuroanatomical substrates of different clinical presentations.

References

[1] E Biondetti et al., The spatiotemporal changes in dopamine, neuromelanin and iron characterizing Parkinson's disease. Brain. 2021.
[2] AJ Hughes et al., Accuracy of clinical diagnosis of idiopathic Parkinson's disease. A clinico-pathological study of 100 cases. JNNP 1992.

[3] GT Stebbins et al., How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: comparison with the unified Parkinson's disease rating scale. Mov Disord. 2013.

C14

Functional gait disorders: demographic and clinical correlations

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

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Italy
[3]FERB Onlus, Ospedale S. Isidoro, Trescore Balneario, Bergamo, Italy
[4]Neurosciences Research Centre, Molecular and Clinical Sciences Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, U.K.
[5]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy
[6]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry - Scuola Medica Salernitana, University of Salerno, Baronissi (SA), Italy
[7]Center for Neurodegenerative Diseases Parkinson and Movement Disorders, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[8]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[9]Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[10]Department of Medical Area, Neurology Unit, ASST Pavia, Pavia, Italy
[11]Botulinum Toxin Center, Neurology Unit A.O.U. Mater Domini, Catanzaro, Italy
[12]Aldo Ravelli Research Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[13]IRCCS Neuromed, Pozzilli, Italy
[14]Department of Neuroscience, Imaging and Clinical Sciences, University G. D'Annunzio, Chieti-Pescara, Italy
[15]Unit of Epidemiology and Medical Statistics, Department of Diagnostics and Public Health, University of Verona, Verona, Italy
[16]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano (Milan), Italy
[17]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[18]Department of Advanced Medical and Surgery Sciences, University of Campania - Luigi Vanvitelli, Naples, Italy
[19]Department of Neuroscience - Rita Levi Montalcini, University of Turin, Turin, Italy
[20]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[21]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[22]Movement Disorder Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, 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, 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 Dept., Central Country Hospital, Bolzano, Italy

[28]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy

[29]University and Institute of Research and Medical Care San Raffaele Roma, Rome, Italy

Objective: We aimed to describe the clinical and demographical features of patients with functional gait disorders (FGDs) and to compare them to patients with functional motor disorders (FMDs) without FGDs (No-FGDs).

Methods: In this multicenter observational study, we enrolled patients with a clinically definite diagnosis of FMDs in 25 tertiary movement disorders centers in Italy. Each subject with FMDs underwent a comprehensive clinical assessment, including screening for different subtypes of functional gait disorders. Multivariate regression models were implemented in order to estimate the adjusted odds ratio (OR; 95% confidence interval) of having FGDs in relation to sociodemographic and clinical characteristics.

Results: Out of 410 FMDs, 26.6% (n=109) of patients exhibited FGDs. The most frequent FGDs were slow gait (n=43, 39.4%), astasia-abasia (n=26, 23.8%), and knee buckling (n=24, 22%). They exhibited single FGDs in 51.4% (n=56) or complex FGDs (more than one type of FGDs) in 48.6% (n=53) of cases. On multivariate regression analysis, the presence of FGDs was more likely associated with older age (OR 1.03, 95% CI 1.01-1.04), functional visual symptoms (OR 2.19, 95% CI 1.08-4.45), and the diagnosis of somatoform disorders (OR 2.97, 95% CI 1.08-8.17). FGDs were also more likely to undergo physiotherapy (OR 1.81, 95% CI 1.08-3.03).

Conclusions: People with FMDs may present with different and overlapping types of FGDs, which may occur in older age. The association of FGDs with functional visual symptoms and somatoform disorders opens up to new avenues to the understanding of the neural mechanisms of these disorders.

Data were extracted from the Italian Registry of Functional Motor Disorders, supported by the Fondazione LIMPE and the Accademia LIMPE-DISMOV RADAC Project.

References:

M. Tinazzi, F. Morgante, E. Marcuzzo, R. Erro, P. Barone, R. Ceravolo, S. Mazzucchi, A. Pilotto, A. Padovani, L.M. Romito, R. Eleopra, M. Zappia, A. Nicoletti, C. Dallocchio, C. Arbasino, F. Bono, A. Pascarella, B. Demartini, O. Gambini, N. Modugno, E. Olivola, V. Di Stefano, A. Albanese, G. Ferrazzano, A. Tessitore, M. Zibetti, G. Calandra-Buonaura, M. Petracca, M. Esposito, A. Pisani, P. Manganotti, F. Stocchi, M. Coletti Moja, A. Antonini, G. Defazio, C. Geroin. Clinical Correlates of Functional Motor Disorders: An Italian Multicenter Study. Mov Disord Clin Pract. 2020 Sep 22;7(8):920-929.

C15

Gender-related predictors of development of dyskinesias and motor/non-motor fluctuations in Parkinson's disease: baseline results of the Italian multicentric, 2-year observational, longitudinal prospective study

Maria Claudia Russillo[1], M. Picillo[1], M. Amboni[2], G. Arabia[3], L. Avanzino[4], M. Canesi[5], R. Ceravolo[6], C.E. Cicero[7], R. Cilia[8], A. De Rosa[9], A.B. Di Fonzo[10], R. Di Micco[11], R. Eleopra[8], V. Fetoni[12], B. Garavaglia[13], M. Giuntini[6], G. Lazzeri[10], R. Marchese[4], A. Nicoletti[7], C. Pacchetti[14], M. Pilleri[15], C.L. Scaglione[16], F. Stocchi[17], A. Tessitore[11], L. Vacca[17], M.A. Volontè[18], G. Volpe[12], R. Zangaglia[14], V. Conti[19], V. Izzo[19], 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]Movement Disorders Centre, Hermitage-Capodimonte, Naples, Italy
[3]Centro Disordini del Movimento, University "Magna Graecia" of Catanzaro, Catanzaro, Italy
[4]Centro per la Malattia di Parkinson e i Disordini del Movimento, Ospedale Policlinico "San Martino", Dipartimento Universitario di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili, University of Genova, Genova, Italy
[5]Struttura Complessa Medicina Fisica e Riabilitazione, Asl 4 Chiavarese, Chiavari, Italy
[6]UO Neurologia, Azienda Ospedaliero-Universitaria Pisana, University of Pisa, Pisa, Italy
[7]Dipartimento "G.F. Ingrassia", Sezione di Neuroscienze, University of Catania, Catania, Italy
[8]Istituto Neurologico "Carlo Besta", Unità di Neurologia, University of Milan, Milan, Italy
[9]Parkinson's Disease Center, University "Federico II" of Naples, Naples, Italy
[10]Foundation I.R.C.C.S. "Ca' Granda" Ospedale Maggiore Policlinico, University of Milan, Milan, Italy
[11]UOS Malattia di Parkinson e Altri Disordini del Movimento, AOU "L. Vanvitelli", University of Naples, Naples, Italy
[12]"Fatebenefratelli e Oftalmico Hospital", University of Milan, Milan, Italy
[13]Molecular Neurogenetics Unit - "Center for Advanced Diagnostics and Research on Neurological Mitochondrial Disorders of Infancy and Childhood" Department of Experimental Research and Diagnostics, Foundation I.R.C.C.S. Istituto Neurologico "Carlo Besta", University of Milan, Milan, Italy
[14]SC Parkinson e Disordini del Movimento, Istituto Neurologico Nazionale Fondazione "C. Mondino", I.R.C.C.S., University of Pavia, Pavia, Italy
[15]Casa di Cura Privata Villa Margherita, Neurology Service, Arcugnano (Vicenza), Italy
[16]I.R.C.C.S.- Istituto di Scienze neurologiche and DIBINEM- "Alma Mater Studiorum" - University of Bologna, Bologna, Italy
[17]I.R.C.C.S. "San Raffaele Pisana", University of Rome, Rome, Italy
[18]Department of Neurology and Clinical Neurophysiology, INSPE, "San Raffaele" Hospital Scientific Institute, University of Milan, Milan, Italy
[19]Operative Unit of Clinical Pharmacology and Pharmacogenetics at University Hospital "San Giovanni di Dio e Ruggi d'Aragona", University of Salerno, Salerno, Italy

Introduction: Evidence suggests that female gender represents a risk factor for development of dyskinesias and motor/non-motor fluctuations (MNMF) in Parkinson's disease (PD) patients treated with levodopa [1]. However, this matter has never been explored longitudinally in relation to the start of levodopa therapy.

Objective: To assess whether gender affects development of dyskinesias and MNMF in PD patients starting treatment with levodopa and followed-up for two years.

Methods: We recruited 287 PD patients (173 males, 114 females) either drug-naïve or on monoamine oxidase inhibitors and/or dopamine agonists and requiring the prescription of levodopa according to their clinical needs. MDS-UPDRS, WOQ-19, QUIP-RS, NMSS, HAMD, HAM-A, AES, MoCA, SEADL, PDQ-39, SCOPA-AUT and Morisky scales were administered at baseline and will be repeated at 1-year and 2-year follow-ups. The protocol also includes pharmacokinetic, pharmacogenetic and metabolic assessments. Paired t-Test was used to evaluate differences between men and women at baseline.

Results: At baseline, men and women did not for age, age at onset, disease duration, Hoehn and Yahr stage, MDS-UPDRS, NMSS, SCOPA-AUT, and apathy. The HAM-A and HAM-D score were significantly higher in women compared to men ($p=0.030$; $p=0.037$); the MoCA score was higher in men compared to women ($p=0.023$). In a sub-group of patients, pharmacokinetic analysis of levodopa showed higher AUC and Cmax in women compared to men ($p=0.0043$; $p=0.0155$) after normalizing for patient weight. Moreover, metabolism at rest, fat free mass and total water were higher in men as compared to women ($p=0.027$; $p>0.001$; $p=0.002$).

Conclusions: We found gender differences in depression, anxiety and global cognition at baseline. Pharmacokinetic, independent of body weight, and metabolic differences are possibly implicated in the development of motor complications, which will be investigated later in the study.

References

[1] S Hassin-Baer, I Molchadski, OS Cohen, Z Nitzan, L Efrati, O Tunkel, AD Korczyn. (2011). Gender effect on time to levodopa-induced dyskinesias. Journal of Neurology, 258(11), 2048–2053.

C16

Primary familial brain calcification: a cohort of study e and review of literature

Michele Mainardi[1], G. Bonato[1], A. Perfetto[1], R. Biundo[2], F. Pistonesi[2], L. Salviati[3], A. Antonini[1], M. Carecchio[1]

[1]Movement Disorders Unit, Department of Neuroscience, University of Padua, Padua, Italy
[2]Department of General Psychology, University of Padua, Padua, Italy
[3]Clinical Genetics Unit, Department of Women's and Children's Health, University of Padua, Padua, Italy

Introduction: Primary familial brain calcification (PFBC) is a neurodegenerative disorder characterized by a combination of neurological, psychiatric, and cognitive symptoms due to calcium deposition in basal ganglia and other cerebral areas. Six causative genes have been discovered so far (SLC20A2, PDGFRB, PDGFB, XPR1, MYORG, JAM2), but up to 50% of cases carry no mutations in known genes.

Objective and Methods: 1) to describe a cohort of 23 PFBC patients who underwent genetic testing of all known PFBC-related genes and a complete neuropsychological evaluation; a detailed definition of calcium deposits localization was also achieved by reviewing patients' brain CT scans; 2) to review all genetically defined PFBC cases published from 2012 to 2021.

Results: Out of 23 patients included. Mean age of onset of symptoms was 53.7 years. Parkinsonism was the most frequent clinical feature over disease course (65%) often associated with other movement disorders. 12 patients (52%) had genetic test, 21.7% carried pathogenic mutations in *SLC20A2*, 9% in PDGFRB and in JAM2 while, 36.3% had biallelic mutations in *MYORG* gene. Twenty patients underwent a full neuropsychological assessment; 50% fulfilled the diagnostic criteria for Mild Cognitive Impairment, 5% had dementia and 45% patients were cognitively normal.

Literature review: We performed a systematic literature review (from 2012 to July 2021), reporting at least one genetically determined PFBC case. We selected only the articles reporting clinical, radiological and molecular findings, with 75 articles including 200 probands. Of these, 47.6% carried mutations in SCL20A2, 14.3% in PDGFB, 4.1% in PDGFRB, 6.6% in XPR1, 25.5% in MYORG and 2% JAM2.

Conclusions: PFBC is genetically, phenotypically and radiologically heterogeneous. Our study confirms the higher frequency of SLC20A2 and MYORG mutations in affected subjects and the clinical variability over disease course. Deeper genotyping is needed in negative PFBC patients to discover new PFBC related genes.

C17

Effect of levodopa on γ tACS-iTBS-induced plasticity of the primary motor cortex in Parkinson's disease

Valentina D'Onofrio[1], A. Guerra[2], F. Asci[2], A. Zampogna[1], G. Fabbrini[1,2], A. Berardelli[1,2], A. Suppa[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli (IS), Italy

Introduction: Boosting γ oscillations through transcranial alternating current stimulation (tACS) restores the impaired intermittent theta-burst stimulation (iTBS)-induced plasticity of the primary motor cortex (M1) in Parkinson's disease (PD) [1]. However, it is unknown whether this beneficial effect can be modulated by levodopa.

Objective: To test whether levodopa modulates the effects of combined γtACS-iTBS stimulation on M1 plasticity in PD.

Methods: Fourteen patients underwent four separate, randomized sessions: real or sham γtACS-iTBS both tested in patients OFF (>12 hours of levodopa withdrawal) and ON therapy (1 hour after levodopa). Motor-evoked potentials (MEPs) evoked by single-pulse TMS and short-interval intracortical inhibition (SICI) were recorded before and after sham or real γtACS-iTBS. All patients underwent clinical evaluation, including UPDRS-III.

Results: UPDRS-III scores were higher in OFF than in ON sessions. MEP amplitude was comparable before and after sham tACS-iTBS, regardless of the patients' dopaminergic state. Similarly, SICI did not change after tACS-iTBS, both in the OFF and ON sessions. Conversely, MEP amplitude significantly increased and SICI induced greater inhibition after real than sham γtACS-iTBS. The amount of MEP facilitation and SICI modulation induced by real γtACS-iTBS was similar in patients OFF and ON therapy.

Conclusions: Our data confirm that levodopa does not ameliorate the impaired iTBS-induced M1 plasticity in PD [2,3]. Conversely, boosting cortical γ oscillations during iTBS application improved M1 plasticity in PD. Real γtACS-iTBS also enhanced GABA-A-ergic transmission, as tested by SICI. The lack of levodopa influence on neurophysiological measures suggests that the γtACS-related effects would imply non-dopaminergic mechanisms [4].

References:

[1] Guerra et al., 2020. J Neurosci; 40:4788-4796.
[2] Suppa et al., 2011. Exp Neurol; 227:296-301.
[3] Suppa et al., 2016. Brain Stimul; 9:323–335.
[4] Kühn et al., 2017. Exp Neurol; 298:122-133.

C18

Combined GCASE/alpha-synuclein pattern may identify specific prodomal parkinsonian profile in GBA carriers

Micol Avenali[1,2], S. Cerri[3], C. Cerami[4,5], C. Crespi[2,4], M. Gegg[6], M. Toffoli[6], S. Mullin[6], D. Hughes[7], E.M. Valente[8,9], C. Tassorelli[1,2], A.H. Schapira[6], F. Blandini[2,3]

[1]Neurorehabilitation Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[3]Cellular and Molecular Neurobiology Unit, IRCCS Mondino Foundation, Pavia, Italy
[4]Cognitive Computational Neuroscience Research Unit, IRCCS Mondino Foundation, Pavia, Italy
[5]Scuola Universitaria Superiore IUSS Pavia, Pavia, Italy
[6]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK
[7]Lysosomal Storage Disorders Unit, Royal Free Hospital and Department of Haematology, UCL, London, UK
[8]Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia, Italy
[9]Department of Molecular Medicine, University of Pavia, Pavia, Italy

Background and aims: Glucocerebrosidase (GBA) gene mutations are the most frequent genetic risk factor for Parkinson disease (PD). Relationship between GBA status and increased risk for GBA-PD is still unclear. We investigated whether glucocerebrosidase activity (GCase) and α-synuclein levels
in blood cells in asymptomatic subjects carrying GBA mutations (GBA carriers) are associated with a more severe prodromal PD profile.

Methods: 31 GBA carriers, 28 GBA-PD and 38 healthy controls (HC) were enrolled in this study. A two-step cluster analysis was performed to split the subjects into different clusters based on their biochemical profile analysing GCase and α-synuclein separately and in combination. Motor and non-motor features (UPDRS-III, BDI, SCOPA-AUT, MoCA, RBDsq, PDSS, UPSIT) for prodromal PD were merged in a 7-item cumulative clinical index (CI). One-way ANOVA assessed the effect of cluster analysis groupings on the CI.

Results: Cluster analysis based on combined GCase activity/a-synuclein levels provided the best performance splitting the sample into a benign (high GCase/mid-low α-synuclein) and malignant (low GCase/high α-synuclein) profile, discriminating HC from both GBA carriers and GBA-PD. Therefore we found a significant effect of combined GCase/α-synuclein clusters ($F(1.95)=15.495$, $p<0.001$) on clinical profile, revealing a significant difference between the malignant and the benign profiles, with the first showing significantly higher values in the CI with dysautonomia, mood and sleep disorders as the most relevant features.

Conclusions: Our study provides novel information about the relationship between biochemical and phenotypic prodromal PD signatures of GBA carriers.

C19

Evaluation of iron overload in Nigrosome 1 via Quantitative Susceptibility Mapping as a preclinical biomarker of Parkinson's disease in patients with rapid eye movement sleep behavior disorder

Eleonora Del Prete[1], N. Campese[1], D. Frosini[1], G. Donatelli[2,3], M. Lancione[2,4], M. Cencini[2,4], M. Costagli[2,5], G. Lucchi[3], M. Tosetti[2,4], M. Godani[6], D. Arnaldi[5], C. Pacchetti[7], P. Cortelli[8,9], E. Bonanni[1], M. Cosottini[2,3], R. Ceravolo[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]IMAGO7 Foundation, Pisa, Italy
[3]Neuroradiology Unit, Department of Translational Research on New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
[4]IRCCS Fondazione Stella Maris, Pisa, Italy
[5]Dipartimento di Neuroscienze, Oftalmologia, Genetica, Riabilitazione e Scienze Materno-Infantili (DiNOGMI), Università di Genova, Genova, Italy
[6]Neurology Unit, Sant'Andrea Hospital, La Spezia, Italy
[7]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[8]IRCCS Istituto Scienze Neurologiche Bologna, Clinica Neurologica Rete Metropolitana, Bologna, Italy
[9]Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy

Introduction: A major field of research in neurodegenerative disorders is the identification of preclinical biomarkers in subjects with prodromal symptoms. Idiopathic rapid eye movement sleep behavior disorder (iRBD) is considered a prodromal stage of α-synucleinopathies, as Parkinson's disease (PD), dementia with Lewy bodies, and multiple system atrophy [1]. The conversion rate of iRBD to neurodegenerative disorders is 73.4% within 10 years [2]. Brain iron deposition has been suggested to contribute to the damage of dopaminergic neurons. Quantitative Susceptibility Mapping (QSM) MRI technique is able to quantify in vivo iron deposition in the substantia nigra (SN).

Objective: The aim of our study was to investigate differences in iron content in Nigrosome 1 (N1) of the SN between PD patients, iRBD and healthy controls (HC).

Methods: Our study population was composed of PD patients in early stages, iRBD patients and HC. All subjects underwent an ultra-high field MRI (7T) exam of the brain. To quantify iron deposition in N1 T2*-weighted sequences and magnetic susceptibility maps were obtained. N1 ROIs were manually drawn on control subjects and warped onto a study-specific template to obtain probabilistic
N1 ROIs.

Results: In our study 43 PD patients with a disease duration < 4 years, 36 iRBD patients and 14 HC were included. PD patients showed increased N1 susceptibility with respect to both HC ($p<0.0001$) and iRBD ($p<0.01$). In iRBD patients, a significant positive correlation ($r = 0.475$; $p < 0.01$) emerged between N1 susceptibility and disease duration. No significant correlation was found between N1 χ and disease duration in PD patients.

Conclusions: A temporal change in N1 iron content in iRBD patients was identified. We suggest a possible roof effect of the iron deposition in N1 in α-synucleinopathies, although further investigations are needed to better assess the prodromal stages of PD.

References

[1] A Iranzo, E Tolosa, E Gelpi et al. Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study. Lancet Neurol 2013;12(5):443–453.

[2] H An, X Zeng, T Niu, G Li, J Yang, L Zheng, W Zhou, H Liu, M Zhang, D Huang, J Li Quantifying iron deposition within the substantia nigra of Parkinson's disease by quantitative susceptibility mapping. J Neurol Sci. 2018 Mar 15;386:46-52.

C20

A longitudinal evaluation of the peripheral immune phenotype in a cohort of Parkinson's disease patients

Luca Magistrelli[1,2], A. Furgiuele[1,3], E. Contaldi[1,4], M. Legnaro[3], E. Rasini[3], C. Comi[2,3], F. Marino[3,5], M. Cosentino[3,5]

[1]PhD Program in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy
[2]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[3]Centre of Research in Medical Pharmacology, University of Insubria, Varese, Italy
[4]PhD Program in Medical Sciences and Biotechnology, University of Piemonte Orientale, Novara, Italy
[5]Centre of Research in Neuroscience, University of Insubria, Varese, Italy

Background: Pathophysiology of Parkinson's disease (PD) is complex and multifactorial. Recently, the role of immune system has been identified as crucial. Indeed, PD patients display a pro-inflammatory peripheral immune phenotype but less is known about the trend of immunological parameters during disease decourse.

Aim: To evaluate the suitable modifications of immunological parameters in a through characterized population of Italian PD patients.

Subjects and Methods: From 2014, drug naïve PD patients underwent a peripheral blood withdrawal annually, evaluating lymphocytes sub-populations and transcription factors (TF). Patients were excluded in presence of immune disease or immunomodulant/depressant treatment. Clinical and demographic parameters were monitored.

Results: 49 PD patients (33 male, mean age 68±8.4) with at least one follow-up visit were included. Th1 lymphocytes (as % of CD4+ cells) were higher after 2 and 4 years (V0: 15.91±6.61; V2:17.93±9.4; V4:20.88±11.6; p=0.03 and p=0.0006) while Th2 (as total count) were persistently reduced (V0:$0.06*10^3$±0.02; V3: $0.04*10^3$±0.01; p=0.003). Th17 lymphocytes were reduced as percentage (V0: 8.13±4; V1:7.43±3.75; V4:7.84±0.84; p=0.04 and p=0.02) and total count (V0:$0.07*10^3$±0.02; V1: $0.05*10^3$±0.03; V4: $0.05*10^3$±0.0; p=0.01 and p=0.01). Dealing with TF, STAT1 presented constantly increased levels (V0: $1.61*10^{-4}$±0.0001; V1 $2.39*10^{-4}$±0.0001; V2: $2.38*10^{-4}$±$5*10^{-5}$; V3: $2.86*10^{-4}$±0.0001; respectively p=0.01; p=0.006; p<0.0001) while STAT6 levels were reduced (V0:$6.96*10^{-6}$±$9.6*10^{-6}$; V1: $9.01*10^{-7}$±$8.72*10^{-8}$; V2: $1.51*10^{-6}$±$2.8*10^{-6;}$ p<0.0001 and p=0.0001). Total number of Treg was reduced in V3 and V4 ($0.06*10^3$±0.02; V1: $0.05*10^3$±0.01; V4: $0.05*10^3$±0.01, p=0.008 and p=0.0004) and both activated and resting subsets. Accordingly, FOXP3 levels were significantly reduced at V4 compared to baseline (V0: $7.55*10^{-5}$±$6.4*10^{-5}$; V4: $4.55*10^{-5}$±$5.01*10^{-5}$).

Conclusions: This is the first longitudinal study evaluating peripheral immune system in PD. Our data, though preliminary, indicate that the pro-inflammatory phenotype represents and early phenomenon in the disease decourse. Accordingly, immunotherapy in PD, which is under investigation, should be started soon in order to act as disease modifier.

C21

The analysis of voice tremor in spasmodic dysphonia and essential tremor with machine learning

Francesco Asci[1], P. Di Leo[2], G. Saggio[2], G. Costantini[2], A. Berardelli[1,3], A. Suppa [1,3]

[1]IRCCS Neuromed Institute, Pozzilli (IS), Italy
[2]Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

Introduction: Patients with essential tremor and adductor-type spasmodic dysphonia may manifest a prominent voice tremor. The diagnosis of voice tremor is currently based on perceptual and qualitative analysis. We have recently demonstrated in independent studies that advanced voice analysis with machine learning objectively discriminates normal voices from those recorded from patients with essential tremor and dysphonia [1-5].

Objectives: The aim of this study is to achieve a direct and objective discrimination of voice samples recorded from patients with essential tremor and adductor-type spasmodic dysphonia both manifesting voice tremor, in order to disclose the pathophysiological mechanisms of voice tremor.

Methods: We investigated 33 patients with ASD manifesting voice tremor (7 males, 65.6±11.7y), 36 patients with ET with a clinical overt voice tremor (9 males, 72.4±8.6y), and 74 age-matched controls (20 males, 71.0±12.4y). We recorded voice samples from HS, ET and ASD patients, by means of a high definition audio recorder, during the sustained vowel emission. The classification of voice samples was achieved by means of a dedicated machine learning algorithm based on Support Vector Machine (SVM).

Results: Receiver Operating Characteristic (ROC) curves showed that machine learning analysis with SVM and selected features, objectively discriminated between HS and ET (Accuracy: 94.3%; AUC: 0.98), HS and ASD (Accuracy: 95.3%; AUC: 0.98) and finally ET and ASD (Accuracy: 89.6%; AUC: 0.94).

Conclusions: Advanced voice analysis using machine learning algorithm SVM objectively recognizes voice tremor in patients with ET and ASD, thus discriminating the two forms of voice tremor with high accuracy. Our findings suggest that voice tremor differs in patients with ET and ASD. This finding points to different pathophysiological mechanisms underlying voice tremor in the two conditions.

References

[1] A Suppa, F Asci, G Saggio, L Marsili, D Casali, Z Zarezadeh, G Ruoppolo, A Berardelli, G Costantini. Voice analysis in adductor spasmodic dysphonia: Objective diagnosis and response to botulinum toxin. Parkinsonism Relat Disord. 2020 Apr;73:23-30. doi: 10.1016/j.parkreldis.2020.03.012. Epub 2020 Mar 19. PMID: 32222482.
[2] F Asci, G Costantini, P Di Leo, A Zampogna, G Ruoppolo, A Berardelli, G Saggio, A Suppa. Machine-Learning Analysis of Voice Samples Recorded through Smartphones: The Combined Effect of Ageing and Gender. Sensors (Basel). 2020 Sep 4;20(18):5022. doi: 10.3390/s20185022. PMID: 32899755; PMCID:PMC7570582.
[3] A Suppa, F Asci, G Saggio, P Di Leo, Z Zarezadeh, G Ferrazzano, G Ruoppolo, A Berardelli, G

Costantini. Voice Analysis with Machine Learning: One Step Closer to an Objective Diagnosis of Essential Tremor. Mov Disord. 2021 Feb 2. doi: 10.1002/mds.28508. Epub ahead of print. PMID: 33528037.
[4] F Asci, G Costantini, G Saggio, A Suppa. Fostering Voice Objective Analysis in Patients with Movement Disorders. Mov Disord. 2021 Apr;36(4):1041. doi: 10.1002/mds.28537. PMID: 33851751.
[5] F Asci, G Costantini, P Di Leo, G Saggio, A Suppa. Reply to: "Reproducibility of Voice Analysis with Machine Learning". Mov Disord. 2021 May;36(5):1283-1284.doi: 10.1002/mds.28601. PMID: 33991448.

C22

Dopamine transporter imaging and rest tremor pattern in the diagnosis of tremulous disorders

Andrea Quattrone[1], R. Nisticò[2], M. Morelli[1], G. Arabia[1], M. Crasà[3], B. Vescio[4], A. Mechelli[1], G.L. Cascini[5], A. Quattrone[2,3]

[1]Institute of Neurology, University "Magna Graecia", Catanzaro, Italy
[2]Institute of Molecular Bioimaging and Physiology, National Research Council (IBFM-CNR), Catanzaro, Italy
[3]Neuroscience Research Center, University "Magna Graecia", Catanzaro, Italy
[4]Biotecnomed S.C.aR.L. Catanzaro, Italy
[5]Institute of Nuclear Medicine, University "Magna Graecia", Catanzaro, Italy

Background: Differentiating rest tremor (RT) disorders is challenging, and often requires single photon emission computed tomography with^{123}I-ioflupane (123I-FP-CIT SPECT) [1-3].

Objective: To investigate the performance of several tremor electrophysiological features in distinguishing RT patients with and without striatal dopaminergic deficit.

Methods: Two-hundred and five consecutive patients presenting with RT were enrolled. All patients underwent neurological examination, electrophysiological assessment of RT (frequency, phase, amplitude, burst duration, coherence), and 123I-FP-CIT SPECT. The performance of RT electrophysiological features in differentiating between patients with abnormal and normal 123I-FP-CIT SPECT (DaT+ and DaT-, respectively) was analyzed using the receiver operating curve. The association between RT features and 123I-FP-CIT SPECT was evaluated using logistic regression models.

Results: The phase was the RT feature which performed the best (AUC=0.85, 95% CI: 0.80-0.91) in distinguishing DaT+ and DaT- patients. The higher the phase values, the greater the probability of having striatal dopaminergic deficit ($p<0.001$). High tremor phase values (>62°) corresponded to an alternating tremor pattern while low phase values (<62°) were reflected by a synchronous pattern on EMG recordings. In our cohort, 104/115 (90.4%) alternating patients were DaT+, and 85/104 had parkinsonian tremor, while 71/90 (78.9%) synchronous patients were DaT-, and essential tremor plus was the most frequent non-parkinsonian tremulous disorder.

*Conclusions***:** The alternating pattern of RT is a powerful, low-cost and widely available biomarker of striatal dopaminergic deficit in tremulous patients. The evaluation of tremor pattern could help clinicians distinguish parkinsonian RT associated with dopaminergic deficit from non-parkinsonian RT with intact dopaminergic neurons, and guide the decision-making in clinical practice.

References:

[1] KP Bhatia, P Bain, N Bajaj et al. Tremor Task Force of the International Parkinson and Movement Disorder Society. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018; 33(1): 75-87. doi: 10.1002/mds.27121.
[2] J Van de Wardt, AMM van der Stouwe, M Dirkx et al. Systematic clinical approach for diagnosing upper limb tremor. J Neurol Neurosurg Psychiatry. 2020; 91(8): 822-830. doi: 10.1136/jnnp-2019-322676.
[3] F Sixel-Döring, K Liepe, B Mollenhauer, E Trautmann, C Trenkwalder. The role of 123I-FP-CIT-SPECT in the differential diagnosis of Parkinson and tremor syndromes: a critical assessment of 125 cases. J Neurol 2011; 258(12):2147-54. doi: 10.1007/s00415-011-6076-z.

C23

Dysbiosis of gut microbiota in Parkinson's disease patients: early feature and biomarker of disease progression?

Rocco Cerroni[1], D. Pietrucci[2], M. Conti[1], V. Unida[2], A. Farcomeni[3], M. Pierantozzi[1], N.B. Mercuri[1], S. Biocca[2], A. Desideri[2], A. Stefani[1]

[1]Parkinson Centre, Department of System Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]Department of Biology, University of Rome "Tor Vergata", Rome, Italy
[3]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Introduction: Dysbiosis of gut microbiota is considered an hallmark in Parkinson's disease (PD) [1]. However, it is still unclear whether microbiota alterations, in PD, represent a pathogenetic starting point or also a consequence of disease [2].

Objective: Our aim was to investigate microbiota alterations in PD patients at the time of diagnosis and in later stages of the disease, in order to identify dysbiosis not only as an early non-motor feature but also a biomarker of disease progression.

Methods: 98 faecal samples were collected from 30 PD patients at the time of diagnosis (*de novo* PD), 38 PD patients in advanced stages (defined by H&Y stage≥3 and/or LEED>850mg) and 40 healthy controls (HC), represented almost exclusively by cohabitants. Microbiota compositions was studied through 16rRNA amplicon sequencing and classified to taxonomic rank through bioinformatic analysis. A multivaristatistical analysis was performed to identify differential abundant taxa between the three groups (*de novo* PD, advanced PD, HC) considering the effect of potential confounding factors, like lifestyle and eating habits.

Results: The three groups showed differences both in alfa-diversity and in beta-diversity comparisons. We found a progressive reduction in Lachnospiraceae, Bacteroidaceae, Prevotellaceae and Clostridiaceae families moving from HC to *de novo* PD and finally to advanced PD and a reverse trend in Enterobacteriaceae and Lactobacillaceae families.

Conclusions: Our study confirms the presence of microbiota alterations from the earliest stages of PD. Furthermore, a greater and more severe alteration in microbiota composition seems to characterize PD advanced stages, highlighting how this non-motor feature progresses with the severity of disease.

References

[1] JM Boertien, PAB Pereira, VTE 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.

Poster

P1

Bradykinesia in patients with valproate-induced tremor

Alessandro De Biase[1], G. Paparella[1,2], L. Angelini[1], A. Cannavacciuolo[1], D. Colella[1], C. Di Bonaventura[1], A.T. Giallonardo[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

Background: Valproate is one of the most effective treatments for epilepsy. Among its side effects, tremor and parkinsonism have been reported. Earlier neurophysiological observations showed bradykinesia (movement slowness) during upper limb movement in patients with valproate-induced tremor. However, the pathophysiological mechanisms of this movement abnormality are unclear.

Objective: To investigate the possible occurrence of bradykinesia in patients with valproate-induced tremor during finger movements and possible distinguishing features with bradykinesia in Parkinson's disease.

Methods: 22 patients with valproate-induced tremor, 22 patients with Parkinson's disease, and 22 healthy controls were enrolled. All participants underwent a standardized neurological examination, video recordings, and kinematic assessment of the finger tapping. Rest, postural and kinetic tremor of the upper limbs was also objectively recorded in patients using a motion analysis system. One-way analysis of variance was used for between-group comparisons. Correlations analysis was used to test possible correlations between clinical data and kinematic features in patients.

Results: Clinical evaluation and kinematic analysis showed that patients with valproate-induced tremor were slightly bradykinetic, i.e. slower, than healthy controls (both $p<0.05$). Unlike Parkinson's disease patients, however, patients with valproate-induced tremor did not present a decrement in amplitude (sequence effect) during finger tapping. Finally, there was no correlation between bradykinesia and tremor severity in patients.

Conclusions: Bradykinesia (movement slowness) without decrement is a common motor feature in patients with valproate-induced tremor which may suggest distinctive pathophysiological mechanisms.

References

[1] M Alonso-Juarez, JF Baizabal-Carvallo. Distinguishing features between valproate-induced tremor and essential tremor. Acta Neurol Scand 2018; 138: 177–81.
[2] JF Baizabal-Carvallo, M Alonso-Juarez. Valproate-induced rest tremor and parkinsonism. Acta Neurol Belg 2021; 121: 515–9.
[3] M Bologna, A Berardelli, G Paparella, G Ferrazzano, L Angelini, P Giustini et al. Tremor Distribution and the Variable Clinical Presentation of Essential Tremor. Cerebellum 2019; 18: 866–72.
[4] M Bologna, G Paparella, A Fasano, M Hallett, A Berardelli. Evolving concepts on bradykinesia. Brain 2019

[5] SL Main, RJ Kulesza. Repeated prenatal exposure to valproic acid results in cerebellar hypoplasia and ataxia. Neuroscience 2017; 340: 34–47.

[6] JC Morgan, JA Kurek, JL Davis, KD Sethi. Insights into Pathophysiology from Medicationinduced Tremor [Internet]. 1 2017[cited 2019 Dec 2] Available from: https://tremorjournal.org/index.php/tremor/article/view/442.
[7] G Paparella, L Angelini, A De Biase, A Cannavacciuolo, D Colella, C Di Bonaventura et al. Clinical and Kinematic Features of Valproate-Induced Tremor and Differences with Essential Tremor. Cerebellum 2020.
[8] E Perucca. Pharmacological and therapeutic properties of valproate: a summary after 35 years of clinical experience. CNS Drugs 2002; 16: 695–714.
[9] ME Sobaniec-Łotowska, JM Lotowska. Ultrastructural study of cerebellar dentate nucleus astrocytes in chronic experimental model with valproate. Folia Neuropathologica 2005; 43: 166–71.
[10] T Spisák, V Román, E Papp, R Kedves, K Sághy, CK Csölle et al. Purkinje cell numbercorrelated
cerebrocerebellar circuit anomaly in the valproate model of autism. Sci Rep 2019; 9: 9225.
[11] E Vamos, A.Csati, L Vecsei, P Klivenyi. Effects of valproate on the dopaminergic system in mice. Neurol Res 2009; 31: 217–9.
[12] C Zadikoff, RP Munhoz, AN Asante, N Politzer, R Wennberg, P Carlen et al. Movement disorders in patients taking anticonvulsants. Journal of Neurology, Neurosurgery, and Psychiatry 2007; 78: 147–51.
[13] F Brugger, KP Bhatia, FMC Besag. Valproate-Associated Parkinsonism: A Critical Review of the Literature. CNS Drugs. 2016;30(6):527-540

P2

Technology use in Parkinson's disease and parkinsonism: a multicenter survey in real-life Healthy East Lombardy Parkinson (HELP) network

Andrea Pilotto[1,2], S. Nocivelli[1], F. Pepe[3], D. Alimonti[4], J.M. Melgari[5], M. Bianchi[6], V. De Giuli[7], A. Magherini[8], M.C. Rizzetti[2], F. Pisano[9], T. Di Monda[10], M. Gennuso[11], S. Gipponi[1], E. Cottini[1], A. Imarisio[1], S. Masciocchi[1], B. Bigni[3], E. Magni[3], M. Sessa[4], M. Turla[5], B. Ferrero[7], P. Crippa[10], A. Prelle[11], A. Ciccone[8], A. Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Parkinson's Disease Rehabilitation Centre, FERB ONLUS – S. Isidoro Hospital, Trescore Balneario, Italy
[3]Neurology Unit, Poliambulanza Hospital, Brescia, Brescia, Italy
[4]Neurology Unit, Papa San Giovanni Hospital, Bergamo, Italy
[5]Neurology Unit, ASST Esine Hospital, Esine, Italy
[6]Neurology Unit, ASST Cremona Hospital, Cremona, Italy
[7]Neurology Unit, ASST Treviglio Hospital, Treviglio, Italy
[8]Neurology Units, ASST Mantova Hospital, Mantova, Italy
[9]Neurology Rehabilitation Unit, San Marco Clinic, Zingonia-Osio Sotto, Italy
[10]Neurology Rehabilitation Unit, Domus Salutis Rehabilitation Centre, Brescia, Italy
[11]Neurology Unit, ASST Crema Hospital, Crema, Italy

Introduction: Technology use is increasing in the ageing population but no large studies evaluated the access to internet and digital technology in parkinsonian patients.

Objective: To evaluate the real-life use of internet and technological devices in parkinsonian patients.

Methods: A real-life survey in a network of movement disorder outpatient clinics in Lombardy Region, Italy was conducted. Consecutive Parkinson's disease (PD) or atypical parkinsonism patients were asked to complete a standardized questionnaire evaluating the use of technology, internet and devices; the severity of the disease and milestones of disability were evaluated in the cohort.

Results: Four hundred-fifty-four patients in 11 centres were included (mean age 70.5 $\pm$ 9.7 years, mean dis duration 7.1 $\pm$ 5.2 years), namely 411 PD (16.3% with dementia and 44% with motor fluctuations) and 43 atypical parkinsonism. 43% PD and 23.7% of atypical parkinsonism had access to email with a mean use of 6.4 hours per week. 75% of patients had smartphone 12% tablet and 14% computer with no difference between patients with and without motor fluctuations. OFF-line patients were older and exhibited worse motor and non-motor symptoms compared to patients with internet access.

Conclusions: The survey highlighted an heterogeneous use of digital technology and internet in the population. The wide global internet access, prominent via smartphone highlight its potential for monitoring symptoms in clinical routine or in clinical trials. OFF-line patients have an increased risk of disability thus requiring specific interventions from clinicians and health care systems.

P3

Gait disorder, parkinsonism, and striatal dopaminergic function in patients with idiopathic normal pressure hydrocephalus: a prospective longitudinal study

Massimilino Todisco[1,2], R. Zangaglia[1], B. Minafra[1], P. Pisano[3], G. Trifirò[4], I. Bossert[4], N.G. Pozzi[1,5], J. Brumberg[6], R. Ceravolo[7], I.U. Isaias[5], A. Fasano[8,9,10,11], C. Pacchetti[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Neurosurgery Unit, IRCCS San Matteo Foundation, Pavia, Italy
[4]Nuclear Medicine Unit, Istituti Clinici Scientifici Maugeri SpA SB IRCCS, Pavia, Italy
[5]Neurology Department, University Hospital and Julius Maximilian University of Würzburg, Würzburg, Germany
[6]Nuclear Medicine Department, University Hospital Würzburg, Würzburg, Germany
[7]Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[8]Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, University Health Network, Toronto, Ontario, Canada
[9]Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[10]Krembil Brain Institute, Toronto, Ontario, Canada
[11]CenteR for Advancing Neurotechnological Innovation to Application (CRANIA), Toronto, Ontario, Canada

Introduction: Motor phenomenology in idiopathic normal pressure hydrocephalus (iNPH) can include parkinsonism. Striatal dopamine reuptake transporter (DAT) density was found to be reduced and to correlate with the severity of parkinsonism in several iNPH patients. However, pathophysiology of gait disturbances and parkinsonism is still controversial, and large longitudinal evaluations are lacking.

Objective: We aimed to longitudinally assess higher-level gait disorder (HLGD), parkinsonism, and striatal DAT binding in iNPH patients who did or did not undergo shunt surgery.

Methods: At baseline, we evaluated iNPH patients through clinical rating scales, response to levodopa treatment, brain MRI, and [^{123}I]-FP-CIT SPECT. We followed up patients who did or did not undergo lumboperitoneal shunt surgery, and [^{123}I]-FP-CIT SPECT was repeated after two years.

Results: Among 115 iNPH patients, 102 subjects did not show either a significant improvement with levodopa or signs supporting an atypical parkinsonism. In this subgroup, 59 patients underwent shunt surgery. In particular, [^{123}I]-FP-CIT SPECT was performed by 92 subjects at baseline and by 58 subjects also at follow-up. DAT density of caudate nucleus correlated with gait impairment both in patients with a disequilibrium subtype of HLGD and in patients with a locomotor subtype of HLGD. In this latter group, DAT density of putamen and caudate nucleus also correlated with parkinsonism. In patients with a disequilibrium subtype of HLGD, gait and DAT density of caudate nucleus improved after surgery, while worsened without surgery. In patients with a locomotor subtype of HLGD, gait, parkinsonism, and DAT binding of putamen and caudate nucleus improved after surgery, while worsened without surgery.
Conclusions: Parkinsonism in iNPH is featured by lack of levodopa response, but is shunt-responsive in several patients. Gait disturbances and parkinsonism in iNPH could be due to striatal dopaminergic dysfunction, which can be reversible after shunt treatment, while worsens in patients who decline surgery.

P4

Abnormal movement perception in functional limb weakness

Angela Marotta[1], M.Tinazzi[1], M. Zenorini[2], A. Antonini[2], M. Fiorio[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of Neuroscience, University of Padua, Padua, Italy

Introduction: Functional motor disorders (FMD) are characterized by motor symptoms which resemble voluntary movements but are perceived as involuntary by the patients. The mismatch between the apparently voluntary nature of motor symptoms and the sense of involuntariness reported by patients may result to abnormal sense of agency, that is the feeling of control over actions and their consequences [1]. Despite proprioception plays an important role in the sense of agency [2], impairment of the proprioceptive system in FMD has never been previously investigated.

Objective: We tested the hypothesis that functional limb weakness - one of the most frequent phenotypes among FMD is associated with dysfunction of proprioception, by evaluating the amount of tonic vibration reflex (TVR) and the perception of the TVR movement [3].

Methods: 20 patients with functional weakness of the lower and/or the upper limbs and 25 healthy controls were recruited for the study; delivery of 92-Hz transcutaneous vibration of the biceps brachii tendon of the arm elicited elbow flexion (TVR). Participants matched the final position of the vibrated arm with their contralateral tracking arm. The TVR and the perception of the TVR movement were measured as angle movements of the vibrated arm and the tracking arm, respectively.

Results: The TVR and the perception of the TVR movement were significantly reduced in the patients compared to the controls. These abnormalities did not differ between patients with unilateral or bilateral upper limb involvement, or between unaffected and affected side in patients with unilateral impairment, suggesting that the observed deficits were independent of motor impairment.

Conclusions: Proprioceptive disfunction may underlie alterations in body movement and sense of agency in patients with functional limb weakness and may play a role in the pathophysiology of these disorders.

References

[1] Edwards et al., 2013. Curr Opin Neurol; 26: 442–447.
[2] Farrer et al., 2003. Conscious Cognit; 12: 609–619.
[3] Yoneda et al., 2000. Eur J Neurol; 7: 529–533.

P5

Asymmetry in saccadic eye velocity and latency may distinguish corticobasal degeneration from other atypical parkinsonisms

Clara Grazia Chisari[1], G. Mostile[1,2], C. Terravecchia[1], A. Luca[1], G. Sciacca[1], G. Donzuso[1], C.E. Cicero[1], C. Rascunà[1], R. Terranova[1], A. Nicoletti[1], M. Zappia[1]

[1]Department "G.F. Ingrassia", Section of Neuroscience, University of Catania, Catania, Italy
[2]Department of Neurology IC, Oasi Research Institute-IRCCS, Troina, Italy

Background and Aims: Corticobasal degeneration (CBD) is a neurodegenerative condition exhibiting a notable overlap in clinical and pathological characteristics with other atypical parkinsonisms. Several eye movement abnormalities have been described in patients with CBD; however, oculomotor signs are variable and often resemble those of other parkinsonian disorders. This study aimed to define the distinguishing patterns of eye motility dysfunctions in CBD patients compared to other atypical parkinsonisms

Methods: This study screened patients having diagnosis of atypical parkinsonisms including CBD, according to the diagnostic criteria. All patients underwent a complete neuro-ophthalmological examination and the video-oculography (Eyelink®1000 Plus), consisting of three eye motility tasks in order to evaluate fixation, smooth pursuit and saccades.

Results: A total of 11 patients with CBD (4 males [36.4%], age 67.3±7.2 years) and 33 parkinsonian syndromes, including 23 (69.7%) progressive supranuclear palsy (PSP) and 10 (30.3%) multiple system atrophy (MSA), were enrolled. The inter-eye differences (ID) for saccadic velocity and latency were higher in CBD patients compared to PSP and MSA (91.1±63.1 versus 17.1±23.5 and versus 8.4±9.0, $p<0.001$; 65.9±64.1 versus 16.3±21.6 and versus 18.4±24.6, $p<0.001$, respectively). Receiver-operating characteristics (ROC) analysis showed that an ID for velocities measurement >20°ang/s distinguishes CBD from other parkinsonisms with a sensitivity of 90.9% and a specificity of 90.6%, and the area under the ROC curve was calculated as 0.98 (95% CI 0.95-0.99, $P < 0.001$).

Conclusions: CBD exhibit distinct oculomotor features. The asymmetrical involvement of saccadic abnormalities may help to distinguish CBD from PSP and MSA.

P6

Subtle changes in central dopaminergic tone underlies bradykinesia in essential tremor

Donato Colella[1], V. Frantellizzi[2], L. Angelini[1], G. Paparella[3], A. Cannavacciuolo[1], A. De Biase[1], A. Guerra[3], G. De Vincentis[2], A. Berardelli[1,3], M. Bologna[1,3]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Department of Radiological Sciences, Oncology and Anatomical Pathology, Sapienza University of Rome, Rome, Italy
[3]IRCCS Neuromed, Pozzilli (IS), Italy

Introduction: Previous neurophysiological observations indicated that movement slowness (here specifically referred to as bradykinesia) is a common movement abnormality in patients with essential tremor (ET).

Aims: In this study, we further investigate the pathophysiology of bradykinesia in ET patients by evaluating possible correlations between basal ganglia dopaminergic neurotransmission, as assessed by 123I-FP-CIT (DAT-SPECT), and kinematic parameters during finger tapping.

Methods: We enrolled 14 patients with a clinical diagnosis of ET (mean age ± standard deviation-SD: 72 ± 10.7 years). The patients underwent clinical examination, kinematic assessment of finger tapping using an optoelectronic motion system analysis, and DAT-SPECT.

Results: Confirming previous findings, we observed that ET patients had a considerable variability of kinematic measures during finger tapping, with low movement velocity being observed in a subgroup of about the half of patients. In the whole group of ET patients, radiotracer uptake in both striata, as assessed with DAT-SPECT, was normal. However, the degree of uptake in the striatum was significantly lower in patients with lower movement velocity than in those with normal velocity ($P<0.05$). Moreover, we found a correlation between the amount of radiotracer uptake in the striatum and movement velocity during finger tapping, i.e., the lower the radioligand uptake, the lower the movement velocity ($r=0.59$, $P<0.05$).

Conclusion: Despite the evidence of normal radiotracer uptake with DATSPECT examination, the study findings indicate a possible relationship between subtle changes in the central dopaminergic tone and bradykinesia in ET. These data provide further insight into ET pathophysiology. Longitudinal studies are needed to clarify whether subtle dopaminergic tone reduction in ET patients with kinematic evidence of bradykinesia represents a disease subtype or may predict the clinical progression in Parkinson's disease.

P7

Direct costs associated with diagnosing functional neurological disorders

Sofia Cuoco, S. Scannapieco, M. Picillo, M.T. Pellecchia, P. Barone, R. Erro

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

Introduction: Functional neurological disorders (FND) are among the commonest conditions encountered in clinical practice [1]. Nonetheless, they are frequently mis- or undiagnosed which results in a significant diagnostic delay. Besides the negative impact on prognosis [2], it is unclear whether this diagnostic delay is also associated with higher direct costs for the regional health system (RHS) [3].

Objectives: We here aimed to: I) evaluate the percentage of FND in a sample of consecutive patients attending an outpatient neurologic clinic; II) analyze the direct costs associated with the diagnosis of FND as compared to other neurological disorders (OND); and III) analyze possible economical trends associated with clinic-demographic features of FND.

Method: Consecutive patients attending the general neurology outpatient clinic were recruited and underwent a structured assessment to gather demographic and clinical data as well as data regarding their prior diagnostic process (number of consulted specialists, number and type of investigations, ambulance call out, A&E visit, etc.). The costs were hence calculated based on the RHS tariff. Data were analyzed by means of $\chi 2$- test and Mann-Whitney test.

Results: One-hundred-fifty-five consecutive patients were recruited, of whom 28 (18%) had FND, 85 (55%) OND and 42 (27%) presented with comorbid FND and OND (CND). FND performed more specialistic visits (p=.04) and more investigations (p=.02) than OND, which resulted in significantly higher direct total costs [203.34 (384.75) vs 44.1 (216.34); p=.04]. In FND, higher directs costs were associated with younger age, presence of trigger and multiple symptoms. CND did not impact on the direct costs as compared to OND.

Conclusions: The diagnosis of FND significantly impacts on the health systems costs, being two-fold higher than those associated with OND. Public policies should be implemented to raise awareness among general practitioners and other medical disciplines to improve diagnostic process in FND.

References

[1] J Stone, A Carson, R Duncan et al. Who is referred to neurology clinics? The diagnoses made in 3781 new patients. Clin Neurol Neurosurg 2010; 112: 747-51.
[2] J Gelauff, J Stone, M Edwards, A Carson (2014) The prognosis of functional (psychogenic) motor symptoms: a systematic review.J Neurol Neurosurg Psychiatry 85:220–226.
[3] HR Cock, MJ Edwards. Functional neurological disorders: acute presentations and management. Clin Med (Lond). 2018 Oct;18(5):414- 417. doi: 10.7861/clinmedicine.18-5-414. PMID: 30287439; PMCID: PMC6334101.

P8

Attachment styles, identification of feelings and psychiatric symptoms in functional neurological disorders

Sofia Cuoco[1], V. Nisticò[2,3], A. Cappiello[1], S. Scannapieco[1], O. Gambini[2,3,4], P. Barone[1], R. Erro[1], B. Demartini[2,3,4]

[1]Neuroscience Section, Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Dipartimento di Scienze della Salute, University of Milan, Milan, Italy
[3]"Aldo Ravelli" Research Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[4]Unità di Psichiatria II, Presidio San Paolo, ASST Santi Paolo e Carlo, Milan, Italy

Objective: The contribution of psychological and psychiatric symptoms in the development of Functional Neurological Disorders (FND) is unclear [1]. We therefore aimed to investigate the role of different attachment styles (AS) and their relationship with psychiatric symptoms in FND patients as compared with both subjects with neurological disorders (ND) and healthy controls (HC); and the possible differences between patients with functional movement disorders (FMD) and with functional seizures.

Methods: In this case-control study, forty-six patients with FND were compared to 34 with ND and 30 HC, by means of an extensive battery to investigate the presence of alexithymia, depression, anxiety, dissociation and to explore their AS using the Revised Experiences in Close Relationships instrument (ECR-R).

Results: Patients with FND had higher depression and alexithymia as well as an avoidant pattern on the ECR-R than patients with ND. In the FND group, ECR-R avoidance was an independent predictor of psychiatric symptoms and, altogether, ECR-R avoidance, the somatic-affective component of depression and difficulty identifying feelings were independent predictors of FND. Gender, anxiety and difficulty identifying feelings predicted the presence of functional seizures.

Conclusion: The avoidant AS may be an important psychological factor influencing the presence of mood disorders and alexithymia. Their co-occurence might drive maladaptive responses underlying the presence of FND [2]. Although we demonstrated a large overlap between FND phenotypes [3], patients with functional seizures might have higher alexithymia, which in turn could explain a defensive response less anchored to body reactions and physical symptoms.

References:

[1] R. Jalilianhasanpour, B. Williams, I. Gilman, M.J. Burke, S. Glass, G.L. Fricchione, M.S. Keshavan, W.C. Jr LaFrance, D.L. Perez, Resilience linked to personality dimensions, alexithymia and affective symptoms in motor functional neurological disorders. J Psychosom Res., 107 (2018) 55-61.
[2] S. Pick, L.H. Goldstein, D.L. Perez, T.R. Nicholson, Emotional processing in functional neurological disorder: a review, biopsychosocial model and research agenda. J Neurol Neurosurg Psychiatry. 90(6) (2019) 704-711.
[3] R. Erro, F. Brigo, E. Trinka, G. Turri, M.J. Edwards, M. Tinazzi, Psychogenic nonepileptic seizures and movement disorders: A comparative review. NeurolClinPract. 6(2) (2016) 138-149. Review. PubMed PMID: 27104066; PubMed Central PMCID: PMC4828676.

P9

Role of clinical assessment and kinematic analysis for bradykinesia detection in essential tremor

Giulia Paparella[1], A. De Biase[2], L. Angelini[2], A. Cannavacciuolo[2], D. Colella[2], A. Guerra[1], A. Berardelli[1,2], M. Bologna[1,2]

[1]IRCCS Neuromed, Pozzilli (IS), Italy
[2]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy

Introduction: Movement slowness (here specifically referred to as bradykinesia) is a common, yet still unrecognized movement abnormality in patients with essential tremor (ET) [1-3].

Aims: to investigate whether reduced movement velocity in ET patients, as demonstrated by kinematic analysis of finger tapping, is also clinically detectable.

Methods: We retrospectively analyzed the video recordings of finger tapping performed by 58 patients with ET (further divided in two sub-groups: 30 'slow-ET' and 28 'non-slow-ET' according to kinematic analysis[1]), 30 patients with Parkinson's disease (PD) and 30 healthy subjects (HCs). The video assessment was carried out by 4 blinded neurologists, according to the item 3.4 (finger tapping) of the Movement Disorders Society-Unified Parkinson's Disease Rating Scale. We compared the mean scores obtained in the three groups by a Kruskal-Wallis ANOVA. The inter-raters' agreement was calculated by the Fleiss' K.

Results: As expected, Kruskal-Wallis ANOVA showed a significant difference in the blinded finger tapping evaluation between ET, PD and HCs ($p < 0.001$). Namely, the highest scores were observed in PD as compared to the other groups (mean ± standard deviation in PD: 2.21±0.7). In addition, ET had higher video scores than HCs (1.5±0.59 vs. 0.69±0.49, $p < 0.001$). The analysis of the ET subgroups showed higher finger tapping scores in those kinematically categorized as 'slow-ET' compared to the 'non-slow ET' (1.78±0.57 vs 1.2±0.47, $p<0.001$). Finally, we found a moderate to substantial agreement between raters in the three groups (Fleiss K=0.41 for ET, 0.62 for PD and 0.42 for HCs). Among the 'slow-ET' patients, however, 8/30 patients (26.6%) had been considered normal or only slightly impaired at the blinded video evaluation.

Conclusions: The present results may be relevant when considering patients categorization into ET –plus[3], thus emphasizing the need of a careful clinical and kinematic assessment of bradykinesia in ET.

References

[1] M. Bologna, G. Paparella, D. Colella, A. Cannavacciuolo, L. Angelini, D. Alunni-Fegatelli, A. Guerra, A. Berardelli. Is there evidence of bradykinesia in essential tremor? Eur J Neurol. 2020 Aug;27(8):1501-1509.
[2] G. Paparella, A. Fasano, M. Hallett, A. Berardelli, M. Bologna. Emerging concepts on bradykinesia in non-parkinsonian conditions. Eur J Neurol. 2021 Jul;28(7):2403-2422.
[3] K.P. Bhatia, P. Bain, N. Bajaj, R.J. Elble, M. Hallett, E.D. Louis, J. Raethjen, M. Stamelou, C.M. Testa, G. Deuschl. Tremor Task Force of the International Parkinson and Movement Disorder

Society. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018 Jan;33(1):75-87.

P10

Functional movement disorders in Italy: frequency, phenotypes and outcomes in an italian cohort

Giulia Di Lazzaro[1,2], R. Lo Monaco[3], M. Petracca[2], F. Bove[2], C. Piano[2], P. Calabresi[2,4], A.R. Bentivoglio[2,4]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Rome, Italy
[3]Geriatric Department, Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Rome
[4]Catholic University of Sacred Heart, Rome, Italy

Objectives and background: Functional movement disorders (FMD) are a relatively new clinical entity characterized by a broad range of symptoms not explained by a classical neurological disease [1]. The exact prevalence of these disorders is not known, but studies estimate that it varies between 2 and 4% [1–3], although it can reach 20% in some centres [4]. Only a few reports focused on FMD epidemiology and no reports from European countries are available. The purpose of this study is to provide additional data from our Movement Disorder Outpatient Clinic on the epidemiology and clinical profile of this type of movement disorder.

Methods: To assess the prevalence and clinical patterns of movement disorders, we reviewed all the available medical records of a large cohort of patients who consecutively attended the Movement Disorders Outpatient Clinic at Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS from December 2014 to May 2016. We recorded the following data for all study participants: age, sex, symptoms and clinical characteristics, specifically age at onset, comorbid conditions with focus on psychiatric disorders, concomitant neurological medications and movement disorders phenotype. All diagnoses have been reviewed in 2021. Patients were clustered in two groups, FMD patients and organic movement disorder (OMD) patients. A statistical analysis using SPSS25 for Mac was conducted. Differences between the two groups in clinical-demographic features were assessed using Chi-squared test and Mann-Whitney test. A $p<0.05$ have been considered statistically significant.

Results: 999 records from patients diagnosed with a movement disorder were analysed. 17 patients (1.7%) had a diagnosis of FMD and 982 (98.3%) a diagnosis of OMD.
Functional patients were younger at diagnosis (mean age at diagnosis 46±20y) than OMD patients (mean age at diagnosis 64±17y) ($p=0.003$). Sex was equally distributed between the two groups, with 497 men and 495 women.
A family history of movement disorders was found in 22% of patients, with no substantial differences between the two groups. The most common movement disorder in both groups was upper limb tremor (51% of neurological and 53% of functional, $p=0.91$), followed by akinesia and dystonia in OMD patients and by dystonia and hemifacial spasm in FMD patients. In particular, hemifacial spasm was significantly more frequent in the FMD than in OMD patients (17% vs 3%, $p=0.00066$). With respect to comorbidities, a history of orthopaedic disorders was present in 34% of patients, neoplastic diseases in 33%, and hypertension in 38% of patients; hypotension, on the other hand, was rare (only 3% of the total). There were no differences between the groups. In both groups, depression was the most common psychiatric comorbidity (59% of FMD and 33% of OMD, $p=0.08$), followed by anxiety (59% in FMD, 23% in OMD, $p=0.004$).
Past traumatic events were more frequently reported in the FMD group (29% of FMD and 3% of

OMD patients, *p*=0.00001).

Discussion and conclusions: Our data is globally in agreement with findings from other studies in different populations. Indeed, the percentage of 1.7% FMD in our population is similar to that reported in the literature [1–3], even though some report higher numbers [4]. This is probably related to the characteristics of the recruiting sites, which can be more specialised in these disorders and can therefore report higher rates of FMD. Interestingly, we found no prevalence differences between males and females with FMD. Probably, this is due to the fact that being FMD a rare movement disorders, the sample size was too small. However, from records of functional patients who attended our centre in the following two years, we found a female prevalence (out of 67 subjects, 44 (66%) were females, and 23 (34%) were males).
Other clinical-demographic features were similar to those previously reported [2–4]. Indeed, the age at diagnosis in FMD patients is lower than in patients OMD. Furthermore, psychiatric comorbidities, and especially anxiety, are more frequent in patients with FMD.
Among the movement disorder phenotype, we confirmed that hyperkinetic movement disorders are more frequent, and especially tremor, followed by dystonia and hemifacial spasm.
In conclusion, our study confirms the previously reported clinic-demographic characteristics of FMD patients also in an Italian cohort.

References

[1] S Kranick *et al.* Psychopathology and Psychogenic Movement Disorders. *Mov. Disord.* 26, 1844–1850 (2011).
[2] M Hallett. Psychogenic movement disorders: A crisis for Neurology. *Curr. Neurol. Neurosci. Rep.* 6, 269–271 (2006).
[3] SA Factor, GD Podskalny &ES Molho. Psychogenic movement disorders: Frequency, clinical profile, and characteristics. *J. Neurol. Neurosurg. Psychiatry* 59, 406–412 (1995).
[4] J Stone *et al.* Who is referred to neurology clinics? - The diagnoses made in 3781 new patients. *Clin. Neurol. Neurosurg.* 112, 747–751 (2010).

P11

Effects of cognitive, motor, and visual dual-task on spatio-temporal gait parameters in patients with functional motor disorders

Marialuisa Gandolfi[1], M. Fiorio[1], P. Torneri[1], E. Pelosin[2], L. Avanzino[3], N. Smania[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[3]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy

Background: Functional motor disorders (FMD) are highly disabling neurological conditions grounded on abnormal attentional focus, beliefs/expectations, and sense of agency [1-2]. Gait disorders increase disability in daily living activities [3]. Understanding their pathophysiology is key to improve rehabilitation management. Our recent posturographic study showed that motor dual-task (m-DT) with eyes closed improves postural control in patients with FMD. No studies have been performed on the effects of different dual-task on gait in FMD [4].

Objective: To assess spatio-temporal gait parameter changes in a sample of FMD and healthy controls (HC) using a dual-task protocol under different attentional conditions.

Material and Methods: 31 patients with FMD (age, 43.37 ± 15.16 years) and 53 healthy controls (age, 43.67 ± 15.12 years) were enrolled. We calculated the dual-task effect (DTE, %) on spatio-temporal gait parameters (i.e., gait speed, step and stride length, the width of the base of support) measured during the single task, m-DT, cognitive dual-task (c-DT), visual dual-task (v-DT)(IBM® SPSS® Statistics version 26.0 for Macintosh).

Results: There was a significant between-group mean change in gait speed DTE ($p=0.038$), step length ($p=0.003$), and stride length ($p=0.005$) (higher DTE values for FMD than HC), and significant Task x Group interaction on gait speed ($p=0.024$), stride length ($p=0.013$), and base of support width ($p=0.008$). In the FMD group, the mean gait speed and stride length DTE were increased by 10.87% and 24.40% on the m-DT and c-DT, respectively. In the HC group, they were raised by 3.41% and 15.46%. Interestingly, similar DTE effects were found for the v-DT ($p=1$) in both groups denoting an enhancement in gait performance.

Conclusions: This study provides novel preliminary evidence to benefit from a visual dual-task to improve spatio-temporal gait parameters in patients with FMD. These findings are relevant for the management of gait disorders in patients with FMD.

References

[1] A Marotta et al., The moving rubber hand illusion reveals that explicit sense of agency for tapping movements is preserved in functional movement disorders, Front. Hum. Neurosci., vol. 11, Jun. 2017, doi: 10.3389/fnhum.2017.00291.
[2] A J Espay et al., Current concepts in diagnosis and treatment of functional neurological disorders, JAMA Neurol., vol. 75, no. 9, pp. 1132–1141, 2018, doi: 10.1001/jamaneurol.2018.1264.

[3] J Nonnekes, E Růžička, T Serranová, S G Reich, B R Bloem, and M Hallett, Functional gait disorders: A sign-based approach, Neurology, vol. 94, no. 24, pp. 1093–1099, 2020, doi: 10.1212/WNL.0000000000009649.
[4] M. Gandolfi et al., Motor dual task with eyes closed improves postural control in patients with functional motor disorders: A posturographic study, Gait Posture, vol. 88, pp. 286–291, Jul. 2021, doi: 10.1016/j.gaitpost.2021.06.011.

P12

Prevalence of sleep disorders in idiopathic normal pressure hydrocephalus

Simone Regalbuto[1,2], M. Terzaghi[1,3], M. Todisco[1,2], R. Zangaglia[2], B. Minafra[2], C. Pacchetti[2]

[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]Unit of Sleep Medicine and Epilepsy, IRCCS Mondino Foundation, Pavia, Italy

Introduction: Idiopathic normal-pressure hydrocephalus (iNPH) is a common condition in the elderly population and is clinically and radiologically defined by distinctive hallmarks: ventriculomegaly, cognitive decline, urinary disfunction, gait impairment with or without parkinsonism [1-2]. The glymphatic system, that is turned on mainly during sleep allowing the clearance of neurotoxic products, could play a crucial role in the pathogenesis of iNPH and neurodegeneration [3].

Objective: The association between sleep disorders and iNPH has been only slightly investigated. The few data available focuses mainly on the frequent link between Obstructive Sleep Apnea (OSA) and iNPH [4]. The aim of our study is to evaluate in patients with iNPH the prevalence and the role of OSA and other sleep disturbances, in particularly Rem Behavior Disorder (RBD), universally known as sleep markers of synucleinopathies.

Methods: We administered specific sleep questionnaires such as Hong-Kong Scale (HKS) for RBD, Berlin Questionnaire (BQ) for OSA and Epworth Sleepiness Scale (ESS) in a retrospective cohort of 60 unselected patients (mean age 72,3, 22 female and 38 male) all diagnosed according to the iNPH International Guidelines, at the Parkinson's Disease and Movement Disorders Unit of the Mondino Foundation in Pavia.

Results: We found that one third of our patients (20/60) has HKS total score suggestive for the presence of RBD (≥ 18; mean: 12,8, sd: 15,6); 24/60 (40%) are at high risk for OSA (BQ-total score = 2), meanwhile 14/60 (23,3%) have low risk (BQ-total score = 1). The majority of our cohort (61,7%) has a significative day time sleepiness evaluated with EES (mean 9,13, ds 5.8).

Conclusions: Clinical interviews found that sleep disorders are quite prevalent in iNPH patients. These findings with that ongoing video polysomnography study could clarify the meaning of sleep disorders in iNPH's phenotypes.

References:

[1] Pozzi et al., 2021. Movement Disorders 36.1 : 124-132.
[2] Todisco, et al., 2021. Neurology 96.23: e2861-e2873.
[3] Reeves et al., Trends in molecular medicine 26.3 (2020): 285-295.
[4] Román et al., Current neurology and neuroscience reports 19.7 (2019): 1-9.

P13

Paroxysmal dyskinesias: clinical features and management throughout pregnancy

Roberta Bovenzi[1], M. Pierantozzi[1], N.B. Mercuri[1,3], A. Pisani[1,3], A. Stefani[1], T. Schirinzi[1]

[1]Department of System Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]IRCCS Fondazione Santa Lucia, European Centre for Brain Research, Rome, Italy
[3]University of Pavia, Pavia, Italy

Introduction: Paroxysmal dyskinesias (PxDs) are a group of rare hyperkinetic movement disorders that mostly occur in young individuals. Treatment mostly relies on antiepileptic drugs; however, because of the teratogenicity of these drugs, the management of pregnancy in PxD patients represents an emerging issue. As well, PxD clinical course during pregnancy is almost unknown.

Objective: To highlight relevant features of PxD throughout pregnancy and provide helpful insights for its management.

Methods: We reported the course and the management of a pregnant 22-old woman (Case 1), followed-up at our centre from the age of 15, when she was diagnosed with PxD due to *PRRT2* variant. Then, an in-depth literature search was performed to collect all pregnant patients suffering with PxD [1-4]. Significant data were extracted and pooled with those from Case 1, running descriptive statistical analysis.

Results: Together with our Case 1, a total cohort of 19 PxD pregnant patients has been collected. The majority (13/19; 68.4%) of patients, including Case 1, presented amelioration of symptoms during pregnancy. Only one patient with non-genetically defined PxD complained with symptoms worsening [1-4]. In our case, antidyskinetic therapy withdrawal (lamotrigine) led to a safe pregnancy outcome.

Conclusions: This study addressed the emerging issue of pregnancy in PxD patients, showing that attacks tend to ameliorate during pregnancy in almost 70% of cases so far reported. This finding may support a safe drug withdrawal, which can prevent risks due to teratogenicity. On the other hand, clinical fluctuations of PxD with pregnancy may suggest a role for hormones in pathophysiology of movement disorders, which needs adequate studies.

References

[1] MK Bruno, M Hallett, K Gwinn-Hardy, B Sorensen, E Considine, S Tucker et al. Clinical evaluation of idiopathic paroxysmal kinesigenic dyskinesia: New diagnostic criteria. Neurology. 2004.
[2] M Fabbri, C Marini, F Bisulli, L Di Vito, A Elia, R Guerrini et al. Clinical and polygraphic study of familial paroxysmal kinesigenic dyskinesia with PRRT2 mutation. Epileptic Disord. 2013.
[3] M Madeja, G Kurlemann. Ceasing of movement-disorder attacks immediately after the onset of pregnancy: Possible effect of human chorionic gonadotropin. Lancet. 1999.
[4] A Friedman, B Zakrzewska-Pniewska, I Domitrz, HY Lee, L Ptacek, H Kwiecinski. Paroxysmal non-kinesigenic dyskinesia caused by the mutation of MR-1 in a large polish kindred. Eur Neurol. 2008.

P14

The odyssey of functional movement disorders patients before diagnosis: experience at a specialized tertiary FMD clinic in Italy

Marialuisa Gandolfi[1], S. Landi[2], M. Tinazzi[1], C. Leardini[3]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona,Verona, Italy
[2]Department of Management, University Ca' Foscari, Venezia, Italy
[3]Department of Business Administration, University of Verona, Verona, Italy

Background: Functional Motor Disorders (FMD) are a prevalent and highly disabling condition affecting young adults who often are relegated to a dependent life [1]. Essential advancements have occurred in the past decades in pathophysiology understanding, clinical correlates, and evidence-based treatment options identification [2-3]. However, the number of health services consulted before the correct diagnosis and the related direct cost of illness is largely unknown.

Objective: This study aimed to report the number of diagnostic examinations, specialist visits, hospitalization and rehabilitation services, and the related costs in a cohort of FMD patients before receiving the correct diagnosis.

Material and Methods: This retrospective observational study involved 40 patients with a clinically definite diagnosis of FMD referred to the specialized Parkinson's Disease and Movement Disorders Unit (AOUI Verona, Italy). The total number of health services consulted in up to five years before FMD diagnosis was retrospectively collected and categorized into five groups (diagnostic examinations, specialist visits, Emergency Room services (ERs) access, hospitalization, rehabilitation). Direct medical costs for each of the five health services categories were calculated using the Italian healthcare reference prices (IBM® SPSS® Statistics version 26.0 for Macintosh).

Results: On average, the patients had 15 investigations (7.7 diagnostic examinations, 7.5 specialist visits) before the correct diagnosis of FMD (range 5-38 visits per person) and incurred per-patient annual costs of 2,301 euros of those 1,524 Euros for SSN (CI 1,214-1,834 Euros) and 778 Euros for the patient (CI 606-960 Euros). A higher number of ERs admissions, especially in the two years preceding the diagnosis.

Conclusions: We show that the Odyssey of FMD patients before the correct diagnosis is associated with many health care services resulting in substantial direct costs. These preliminary findings are relevant for health care decision-makers to allocate funds for disease-specific healthcare pathways implementation.

References:

[1] A J Espay et al., Current concepts in diagnosis and treatment of functional neurological disorders, JAMA Neurol., vol. 75, no. 9, pp. 1132–1141, 2018, DOI:10.1001/jamaneurol.2018.1264.
[2] D L Perez, M J Edwards, G Nielsen, K Kozlowska, M Hallett, and W C Lafrance, Decade of progress in motor functional neurological disorder: Continuing the momentum, J. Neurol. Neurosurg. Psychiatry, pp. 1–10, 2021, DOI: 10.1136/jnnp-2020-323953.
[3] M Tinazzi et al., Clinical Correlates of Functional Motor Disorders: An Italian Multicenter

Study, Mov. Disord. Clin. Pract., vol. 7, no. 8, pp. 920–929, 2020, DOI: 10.1002/mdc3.13077.

P15

Hypoglycemic encephalopathy with hemichorea-hemiballismus and contralateral cortical fronto-parietal brain lesions: a case report

Francesco Pasini[1], A. Karantzoulis[1], G. Fanella[1], F. Brovelli[1], D. Iacobucci[1], V. Aprea[1], B. Storti[1], F. Santangelo[1], F. Canonico[2], P. Remida[2], C. Ferrarese[1], L. Brighina[1]

[1]Department of Neurology, San Gerardo Hospital, ASST Monza, University of Milano-Bicocca, School of Medicine & Surgery, Monza, Italy
[2]Department of Neuroradiology, San Gerardo Hospital, ASST Monza, Monza, Italy

Background: Severe hypoglycemia is associated with a broad range of neurological deficits and alterations on cerebral magnetic resonance imaging (MRI). Typically, hypoglycemic encephalopathy causes bilateral lesions in the neostriatum and diffuse cortical involvement, the latter being usually correlated with a poor functional outcome.

Methods (case description): A 71-year-old man was admitted to hospital for acute hypoglycemic coma in poorly controlled type 2 diabetes mellitus. He promptly regained consciousness after intravenous glucose administration but during hospitalization he developed prominent intermittent ballistic movements of his right limbs intermixed with rare distal choreic movements. The involuntary movements did not respond to anticonvulsants and subsided within 20 days since admission in parallel with the improvement of the patient's glycemic control. Four months later, his neurological examination was normal.

Results: Serial CT brain scans were normal. EEGs registered during the atypical movements failed to detect any epileptic activity. Brain MRI showed left fronto-parietal corticalsubcortical lesions, with cingulate gyrus involved. On DWI, T2 and T2-FLAIR sequences they were hyperintense, while ADC was reduced. Follow-up MRI imaging showed progressive regression of the abnormalities. After 80 days, cerebral MRI was normal.

Conclusions: This is the first evidence of hemichorea-hemiballismus syndrome associated with focal contralateral fronto-parietal lesions induced by an episode of severe hypoglycemia. This case suggests that patients with limited cortical involvement due to hypoglycemic encephalopathy may present a good clinical outcome if normal glycemic levels are promptly restored.

P16

Impact of Covid-19 on essential tremor and dystonic tremor: experience of an Italian centre

Salvatore Bertino, S.M. Cartella, I.G. Arena, C. Terranova, A. Quartarone, P. Girlanda

Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Objective: To assess the impact of Covid-19 on essential and dystonic tremor.

Background: Covid-19 had a negative impact on movement disorders [1-2-4], but there are no studies on ET and DT. The only present studies regard the management of DBS and of botulinum toxin
[3-5].

Methods: Self-administered survey, based on Hamilton Depression and Anxiety Rating Scale, SARA scale, Hospital Anxiety and Depression Scale. Motor evaluation (TETRAS) before and after lockdown. We compared transcranial magnetic stimulation-evoked cortical potentials (TEPs) from the M1 and SMA between 15 PD patients tested off (OFF) and on (ON) medication and 12 healthy controls (HCs) and investigated possible correlations with bradykinesia tested clinically.

Results: We analysed 26 patients (20 ET, 6 DT). Depression worsened in 57,7% of them whereas anxiety in 26,9% and sleep quality in 34,6%, as well as fear. For 15,4% sexual life worsened. All these features are related between them and with the patient's level of education: 80-100% of patient who felt more depressed and had a worse sleep quality have a high level of education. Sleep quality is related to an increase in depression as well (88,9%). 19,2% of patients felt their difficulty in concentration increased during lockdown. This is related to the increase in anxiety (71,4%). None of the features is related to TETRAS score or to years of age or of disease, nor to the type of disease. A minority of patients had difficulty in finding their doctors, or their drugs. 38,4% of patients know what telemedicine is, but only 15,3% used it for a teleconsultation. 15,3% of patients said their health decreased, whereas 42,3% said quality of life did. 15,3% managed to practice physiotherapy during lockdown, and no one started playing videogames in substitution. Only one patient followed a physiotherapy video lesson. For most patients (15,3%) the major problems during lockdown were the impossibility to go to the hospital and the lack of social relationships.

Conclusions: Despite the little number of patients analysed, we can highlight Covid-19 had a negative impact on non-motor symptoms of ET and DT, with quality of life repercussions.

References:

[1] S.M. Papa, P. Brundin, V.S.C. Fung, U.J. Kang, D.J. Burn, C. Colosimo, H.L. Chiang, R.N. Alcalay, C. Trenkwalder. MDS Scientific Issues Committee, Impact of the Covid-19 Pandemic on Parkinson's Disease and Movement Disorders, Mov Disord 2020 May; 35(5): 711-715.
[2] A. Fasano, E. Cereda, M. Barichella, E. Cassani, V. Ferri, A.L. Zecchinelli, G. Pezzoli. Covid-19 in Parkinson's Disease Patients Living in Lombardy, Italy. Mov Disord. 2020 Jul;35(7):1089-1093.
[3] A. Fasano, A. Antonini, R. Katzenschlager, P. Krack, P. Odin, A.H. Evans, T. Foltynie, J. Volkmann, M. Merello. Management of Advanced Therapies in Parkinson's Disease Patients in Times of Humanitarian Crisis: The Covid-19 Experience. Mov Disord Clin Pract. 2020 May 4;7(4):361-372.

[4] https://www.movementdisorders.org/MDS/About/Committees--Other-Groups/Telemedicine-in-Your-Movement-Disorders-Practice-A-Step-by-Step-Guide.htm.
[5] D. Dressler, F. Adib Saberi. Botulinum toxin therapy in the SARS-CoV-2 pandemic: patient perceptions from a German cohort. J Neural Transm (Vienna). 2020 Sep;127(9):1271-1274.

P17

Unconventional therapy for acute-onset post-stroke hemiballism: a care report

Giulia Di Rauso[1], S. Coniglio[1], N. Orlandi[1], M. Jacopetti[2], G. Bigliardi[3], F. Antonelli[3], S. Meletti[1,3], V. Rispoli[3]

[1]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Rehabilitation Medicine, Department of Neuroscience, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

Introduction: Cerebrovascular diseases are the most common causes of secondary hypokinetic or hyperkinetic movement disorders [1]. Among acute-onset hyperkinetic movement disorders, hemiballism is the most frequent one [2]. Involuntary movements may severely compromise patients' quality of life and expose them to the risk of injuries. In these cases, symptomatic treatments are required: typical and atypical neuroleptics as well as tetrabenazine represent therapy of choice. On the other hand, anecdotal reports of antiseizures medications effectiveness have been rarely described [1-3].

Case presentation: A 78 years-old man with an history of vascular parkinsonism and undetermined generalized seizures, came to our attention for an acute-onset left hemiballism with homolateral hemiparesis. Brain CT scan showed a right thalamo-mesencefalic hemorrhage, while blood exams revealed acute renal failure secondary to severe rhabdomyolysis. Due to the persistence of severe hemiballism causing interference even with sitting balance and any rehabilitation approach together with the ongoing rhabdomyolysis, symptomatic therapy was required. Nevertheless, consistently prolonged QT interval at electrocardiograms and renal function impairment limited the dosage of neuroleptics and benzodiazepines, respectively. One month after hospital admission the left-sided involuntary movements remained disabling, despite several combined approaches including tetrabenazine, low-dose of quetiapine, clonazepam and diazepam. Thus, the patient received botulin neurotoxin injections in his left upper limb muscles (Botox 200 UI: biceps brachii, triceps brachii, teres major, deltoid) and low-dose of topiramate (37.5 mg/die) in up-titration, that were followed by the gradual reduction of hyperkinetic movements.

Conclusions: The present case highlights the effectiveness of unconventional therapeutic options in disabling acute onset post-stroke hemiballism when first-line therapies are contraindicated.
In selected cases, second and third-line agents might be combined with good functional outcome.

References

[1] Caproni et al.,2017.Expert Rev Neurother; 17(5):509-519.
[2] Bansil et al.,2012.Tremor Other Hyperkinet Mov (N Y); 2:tre-02-42-195-1.
[3] Mehanna et al.,2013.Lancet Neurol;12(6):597-608.

P18

Clinical overlap between functional neurological disorders and autism spectrum disorders: a preliminary study

Benedetta Demartini[1,2,3], V. Nisticò[1,2], D. Goeta[1], A. Iacono[1], R. Tedesco[1], B. Giordano[1], R.Faggioli[3], A. Priori[1,2,4], O. Gambini[1,2,3]

[1]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milano, Italy
[2]"Aldo Ravelli" Research Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[3]Unità di Psichiatria 52, Presidio San Paolo, ASST Santi Paolo e Carlo, Milano, Italy
[4]III Clinica Neurologica, Presidio San Paolo, ASST Santi Paolo e Carlo, Milano, Italy

Introduction: Functional Neurological Disorders (FNDs) and Autism Spectrum Disorders (ASDs) share some common features, in terms of deficits in emotion regulation and recognition, sensory sensitivity and interoception [1-5]; however, few studies have assessed their overlap.

Objectives: To assess the prevalence of autistic traits in a sample of adult patients with FNDs, and the prevalence of Functional Neurological Symptoms (FNS) in a sample of adult individuals with High Functioning ASDs (HF-ASDs). Furthermore, the association between sensory sensibility and FNS was investigated in the HF-ASDs group.

Methods: 21 patients with FNDs, 30 individuals with HF-ASDs and 45 neurotypical controls (NC) completed the Autism Quotient (AQ); the Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R); an ad-hoc questionnaire assessing FNS. HF-ASDs participants also completed the Sensory Perception Quotient - Short Form (SPQ-SF), assessing sensory sensibility.

Results: In the FNDs group, no patient scored above the clinical cut-off at the AQ and 19% scored above the cut-off at the RAADS, a prevalence comparable to the one found in the NC group (15.6%; both $p > 0.05$). Conversely, 86.7% of participants with ASDs reported at least one FNS, a prevalence significantly higher than the one in the NC group (35.6%, $p < 0.001$). In the HF-ASDs group, the Total Score at SPQ-SF and the total number of FNS negatively correlated, suggesting that the higher the sensibility was, the higher the number of FNS was. In particular, tactile hypersensitivity was found to be a risk factor for the development of functional weakness (OR = 0.74, $p = 0.033$) and paraesthesia (OR = 0.753, $p = 0.019$).

Conclusions: FNDs individuals did not present autistic traits more than NC. On the other hand, HF-ASDs individuals presented a higher number of FNS than NC, and this rate was associated with a higher sensory sensibility, especially in the touch domain.

References

[1] American Psychiatric Association: Diagnostic and statistical manual of mental disorders (5th ed.), Washington, DC: Author, 2013.
[2] Cai et al., 2018. Autism Research, DOI: 10.1002/aur.1968.
[3] Demartini et al., 2014, J Neurol Neurosurg Psychiatry, DOI: 10.1136/ jnnp- 2013-307203 11.
[4] Quattrocki & Friston 2014, Neurosci Biobehav Rev, DOI:10.1016/j.neubiorev.2014.09.012.
[5] Ricciardi et al. 2016 Biol psychol. DOI: 10.1016/j.biopsycho.2015.10.009.

P19

Sociodemographic characteristics and psychopathological assessment in 13 paediatric patients with functional neurological disorders: a preliminary report

Benedetta Demartini[1,2,3], V. Nisticò[1,2], V. Paleari[1,4], G. Zorzi[4], N. Nardocci[4], M.P. Canevini[5], A. Priori[1,2,6], O. Gambini[1,2,3]

[1]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milano, Italy
[2]"Aldo Ravelli" Research Center for Neurotechnology and Experimental Brain Therapeutics, Università degli Studi di Milano, Milano, Italy
[3]Unità di Psichiatria 52, ASST Santi Paolo e Carlo, Presidio San Paolo, Milano, Italy
[4]U.O. Neuropsichiatria Infantile, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italia
[5]U.O. Neuropsichiatria Infantile, ASST Santi Paolo e Carlo, Presidio San Paolo, Milano, Italy
[6]III Clinica Neurologica, ASST Santi Paolo e Carlo, Presidio San Paolo, Milano, Italy

Introduction: Functional neurological disorders (FND) are characterized by neurological symptoms that cannot be explained by typical neurological diseases or other medical conditions [1]. In the recent years, there has been a growing interest in FND in the paediatric age, whose prevalence and clinical manifestations are similar to the ones found in the adult population [2-3].

Objectives: To characterize, from a socio-demographic and psychopathological perspective, a sample of children diagnosed with FND.

Methods: Thirteen patients below 18 years old with FND, hospitalized at "Carlo Besta" Neurological Institute in Milan, completed a battery of anamnestic and neuropsychological tests, assessing: socio-demographic status, cognitive level, behavioural and emotional issues, depression, and anxiety. In adolescents, also alexithymic traits and dissociative symptoms were evaluated. Patients' parents completed the Child Behaviour Checklist (CBCL).

Results: Five patients presented movement disorders (tremor, myoclonus, gait disorder), three patients psychogenic non-epileptic seizures, and five patients sensitivity disturbances (pain, anaesthesia, paresthesia). Cognitive profile was normal in 11 patients; academic performance was good in 9 patients, whilst 3 had a diagnosis of Specific Learning Difficulty (SLD) and/or Attention Deficit Hyperactivity Disorder (ADHD). Precipitating events were found in 11 patients. At the self-report questionnaires, mean scores close to the clinical cut-off were documented with respect to affective and somatic problems. At the parent-report questionnaires, clinically significant mean scores were observed in the CBCL subscales assessing anxious-depressive symptoms and somatic complaints.

Conclusions: Demographic and anamnestic features of our sample were in line with the literature. Data about academic performance suggest that a screening for SLD or ADHD might be indicated for FND patients with concomitant school difficulties. With respect to the psychometric assessment, we might speculate that children with FND, although acknowledging the relevance of somatic symptoms, have difficulties in recognizing some internal emotional states (which, conversely, are easily recognized by their parents).

References

[1] American Psychiatric Association: Diagnostic and statistical manual of mental disorders (5th

ed.), Washington, DC: Author, 2013.
[2] Ani et al., 2013, Br J Psychiatry 202, 413-418, DOI: 10.1192/bjp.bp.112.116707.
[3] Carson & Lehn, 2016, Epidemiology. Handb Clin Neurol., 139, 47-60.

P20

The impact of surgical masks on emotion recognition in patients with movement disorders

Natale Maiorana[1], M. Dini[1], M.R. Reitano[1], B. Demartini[1,2], V. Nisticò[1], M. Guidetti[1], A. Averna[1], T. Bocci[1,2], A. Priori[1,2], R. Ferrucci[1,2]

[1]Department of Health Science, "Aldo Ravelli" Research Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[2]III Neurology Clinic, ASST-Santi Paolo e Carlo, Milan, Italy

Introduction: Studies have shown that the use of surgical masks to contrast the spread of the Covid-19 pandemic makes it difficult to read emotions on other people's faces [1]. To date, little is known about the impact of surgical masks on emotion recognition in patients with movement disorders.

Objective: The aim of the experiment was to evaluate the different impact of surgical masks on emotion recognition in movement disorders patients.

Methods: 16 subjects (6 Male; aged 26-82), 5 Parkinson's disease patients (PD), 3 functional motor disorder patients (FMD) and 8 healthy controls (HC) were enrolled.
Two different Facial Emotion Recognition Tasks were administered: no masked face (NM), masked face (MF). Subjects had to respond by pressing a key to discriminate between neutral, sad, happy, or angry faces. The procedure consisted of two experimental blocks composed by 96 trials.

Results: Non-parametric analysis showed that patients made more errors in discriminating emotions in MF condition than HC [(Mean ± S.D.) Patients vs HC : 21.74 ± 8.15 vs 14.06 ± 4.72 $p < 0.05$]. In particular patients made more error in recognition of happiness (15.10 ± 8.60 vs 4.68 ± 4.69 $p < 0.05$). No significant differences were found in error rate in other emotions.

Conclusions: Emotional recognition deficits that patients with movement disorders have experienced during pandemic, might have greatly influenced their social cognition abilities and quality of life.

References

[1] Carbon CC. Wearing Face Masks Strongly Confuses Counterparts in Reading Emotions. Front Psychol. 2020;11(September):1–8.

P21

Pathophysiological mechanisms underlying sensory trick in cervical dystonia: an electroencephalogram- electromyography study

Nicoletta Manzo[1,2], G. Leodori[1,2], G. Ruocco[2], D. Belvisi[1,2], L. Rocchi[3], G. Fabbrini[1,2], A. Berardelli[1,2], A. Conte[1,2]

[1]IRCCS Neuromed, Pozzilli, (IS), Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]Department of Medical Sciences and Public Health, University of Cagliari, Monserrato, Italy

Introduction: A characteristic and unique feature of focal dystonia is the partial or complete improvement of dystonic symptoms due to the execution of a voluntary manoeuvre, referred to as sensory trick (ST) [1]. Although previous studies showed that ST modifies sensorimotor cortex activity and connectivity [2-3], the underlying neurophysiological mechanisms remain unclear.

Objective: In this study, we investigated whether and how ST modulates cortical oscillations. Moreover, we aimed to verify whether the effectiveness of ST on dystonic symptoms reflects touch-related changes in oscillations over the sensorimotor cortex.

Methods: We recorded electroencephalography (EEG) activity before, during, and after ST execution in patients with cervical dystonia (CD) with effective ST. We also recorded electromyography (EMG) activity over the sternocleidomastoid (SCM) muscle bilaterally. Touch-related EEG spectral perturbation over sensorimotor areas was recorded in 8 CD patients with effective ST, defined as reduced EMG activity in the affected SCM muscle. Data were compared to those obtained in 9 CD patients with ineffective ST. Independent sample t-test comparisons were applied to test event-related spectral perturbation (ERSP) differences between patients with and without effective ST before, during, and after the ST touch. Bonferroni correction for multiple comparisons was used as a post hoc t-test.

Results: ERSP analysis in patients with effective ST showed bilateral event-related desynchronization (ERD) in the mu (8-13) band in sensorimotor cortical regions that was present only during the execution of ST ($p= 0.001$) and was directly related to reduced EMG activity in the dystonic muscle

Conclusions: Our results suggest that oscillatory activity changes in the mu band over the sensorimotor cortex are involved in the pathophysiology of ST. Our findings may also provide useful information regarding the role of abnormal sensorimotor integration in the pathophysiology of dystonia.

References:

[1] Patel N, Hanfelt J, Marsh L, and Jankovic J for the members of the Dystonia Coalition. Alleviating manoeuvres (sensory tricks) in cervical dystoniaJ Neurol Neurosurg Psychiatry. 2014. 85:882-4.
[2] Naumann M, Magyar-Lehmann S, Reiners K, Erbguth F and Leenders KL. Sensory Tricks in Cervical Dystonia: Perceptual Dysbalance of Parietal Cortex Modulates Frontal Motor Programming. Ann Neurol. 2000. 7: 322-8.
[3] Sarasso E, Agosta N, Piramide N, Bianchi F, Butera C, Gatti R, Amadio S, Del Carro U, Filippi M. Sensory trick phenomenon in cervical dystonia: a functional MRI study. J Neurol. 2020; 267:

1103-1115.

P22

Motor and non-motor subtypes of cervical dystonia

Matteo Costanzo[1], D. Belvisi[1,2], I. Berardelli[3], A. Maraone[1], F. D'Antonio[1], V. Baione[1], A. Toscano[1], G. Ferrazzano[1], M. Pasquini[1], A. Conte[1,2], G. Fabbrini[1,2], G. Defazio[4], A. Berardelli[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli (IS), Italy
[3]Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy
[4]Department of Medical Sciences and Public Health, University of Cagliari, Monserrato (CA), Italy

Introduction: Cervical dystonia (CD) is a heterogeneous condition [1]. However, while motor subtypes of CD have recently been identified, it is still unknown whether and how non-motor symptoms contribute to CD heterogeneity [2-4]. In the present cross-sectional study, we aimed to identify clinical CD subtypes on the basis of motor and non-motor symptoms by using a hypothesis-free data-driven
approach.

Methods: Fifty-seven patients with CD participated in the study. Patients underwent a clinical evaluation that assessed motor and non-motor features of CD with standardized clinical scales. We investigated five clinical domains, including motor symptoms, psychiatric disturbances, sleep disorders, cognitive impairment and pain. These domains were used as variables in a k-means cluster analysis with two-, three-, and four-cluster solutions.

Results: The two-cluster solution best fits our sample. Cluster I (n=32) included patients who were younger and had less severe non-motor symptoms and a lower disability level than patients included in Cluster II (n=25). The two clusters showed similar sex distribution and disease duration. Similarly, the type of motor pattern and the occurrence of tremor and sensory trick were equally distributed in the two subtypes.

Conclusions: We identified two clinical subtypes of CD. The two subtypes shared similar motor features but were characterized by different non-motor symptom severity. These findings suggest that motor network dysfunction is a common pathophysiological feature of CD, whereas the extent of non-motor network involvement may differ in CD, with age acting as a possible modulating factor.

References

[1] HA Jinnah, V Neychev, EJ Hess, The Anatomical Basis for Dystonia: The Motor Network Model, Tremor Other Hyperkinet. Mov. (N Y). 7 (2017) 506
[2] WH Jost, L Tatu, S Pandey et al. Frequency of different subtypes of cervical dystonia: a prospective multicenter study according to Col-Cap concept, J. Neural. Transm. (Vienna). 127 (2020) 45-50.
[3] F Di Biasio, R Marchese, G Abbruzzese et al. Motor and Sensory Features of Cervical Dystonia Subtypes: Data From the Italian Dystonia Registry, Front. Neurol. 11 (2020) 906.
[4] SA Norris, HA Jinnah, AJ Espay et al. Clinical and demographic characteristics related to onset site and spread of cervical dystonia: Onset Site and Spread Of Cervical Dystonia, Mov. Disord. 31 (2016) 1874–1882.

P23

Time to onset and duration of botulinum toxin efficacy in dystonia and sialorrhea

Claudia Ledda[1,2], C.A. Artusi[1,2], A. Tribolo[1,2], M. Zibetti[1,2], L. Lopiano[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Torino, Italy
[2]Neurology 2 Unit, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy

Introduction: The botulinum neurotoxin (BoNT) is a valuable option in neurological patients. Time-to-onset and duration of BoNT efficacy may vary according to doses, type of toxin, injection sites, but only a few studies aimed at analyzing these aspects.

Objectives: We aimed to analyze time-to-onset and duration of BoNT efficacy in different movement disorders and the impact of different demographic and clinical features.

Methods: We enrolled 193 patients treated with BoNT for the following neurological conditions: blepharospasm, cervical dystonia, facial hemispasm, oromandibular dystonia, focal limb dystonia, sialorrhea. Patients were interviewed and answers analyzed by Kruskall-Wallis, Spearman correlation, and multivariate linear regression tests. Clinical and demographic factors taken into consideration in the model were: dosages and types of botulinum toxin type A, sex, age, and years of treatment. Dosages were compared with the assumption that 1U of OnabotulinumtoxinA corresponds to 1U of IncobotulinumtoxinA and 3U of AbobotulinumtoxinA.

Results: Overall mean time-to-onset of efficacy was 6.7 days ± 5 (range 1-30) and duration of treatment 78.8 days ± 29.4 (range 15-180). We found no significant difference in time-to-onset and duration of BoNT efficacy between different neurological diseases. Both time-to-onset and duration of efficacy were correlated to BoNT doses ($p=0.007$ and $p=0.02$). Multiple regression analysis demonstrated that sex, years of toxin treatment, type of toxin, age, and doses explained 73% of the variability of time-to-onset, with doses (beta: 0.154; $p=0,086$) and age (beta: -0.278; $p=0,001$) being the significant factors; the same variables explained 53% of the variability of the BoNT duration of efficacy, with doses (beta: -0.319; $p<0,001$) and type of toxin (beta: 0.236; $p=0,018$) being the most significant factors.

Conclusions: Our findings suggest that age, type of toxin, and especially doses may account for the variability of BoNT efficacy in terms of time-to-onset and duration.

P24

Spread of segmental/multifocal idiopathic adult-onset dystonia to a third body site

Tommaso Ercoli[1], R. Erro[2], G. Fabbrini[3,4], R. Pellicciari[5], P. Girlanda[6], C. Terranova[6], L. Avanzino[7,8], F. Di Biasio[7], P. Barone[2], M. Esposito[9], G. De Joanna[9], R. Eleopra[10], F. Bono[11], L. Manzo[11],
A.R. Bentivoglio[12,13], M. Petracca[12], M.M. Mascia[1], A. Albanese[14], A. Castagna[15], R. Ceravolo[16], M.C. Altavista[17], C. Scaglione[18], L. Magistrelli[19,20], M. Zibetti[21], L. Bertolasi[22], M. Coletti Moja[23], M.S. Cotelli[24], G. Cossu[25], B. Minafra[26], A. Pisani[26,27], S. Misceo[28], N. Modugno[4], M. Romano[29], D. Cassano[30], A. Berardelli[3,4], G. Defazio[1]

[1]Department of Medical Science and Public Health, Institute of Neurology, University of Cagliari, Cagliari, Italy
[2]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Baronissi (SA), Italy
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[4]IRCCS Neuromed, Pozzilli (IS), Italy
[5]Department of Basic Science, Neuroscience and Sense Organs, Aldo Moro University of Bari, Bari, Italy.
[6]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[7]Ospedale Policlinico San Martino - IRCCS, Genoa, Italy
[8]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[9]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[10]SOC Neurologia, AOU S. Maria della Misericordia; Neurological Unit 1, Fondazione IRCSS. Istituto Neurologico “Carlo Besta”, Milan, Italy
[11]Center for Botulinum Toxin Therapy Neurologic Unit. A.O.U. Mater Domini, Catanzaro, Italy
[12]Fondazione Policlinico Universitario Agostino Gemelli - IRCCS, Rome, Italy
[13]Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[14]Department of Neurology, IRCCS Istituto Clinico Humanitas, Rozzano, Milan, Italy
[15]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[16]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[17]Neurology Unit, San Filippo Neri Hospital ASL Roma 1, Roma, Italy
[18]IRCCS Institute of Neurological Sciences, Bologna, Italy
[19]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[20]University of Insubria, Varese, Italy
[21]Department of Neuroscience Rita Levi Montalcini, University of Turin, Turin, Italy
[22]Neurologic Unit, University Hospital, Verona, Italy
[23]Mauriziano Hospital Umberto I, Torino, Italy
[24]Neurology Unit, ASST Valcamonica, Esine, Italy
[25]Neurology Service and Stroke Unit, Department of Neuroscience, A.O. Brotzu, Cagliari, Italy
[26]IRCCS Mondino Foundation, Pavia, Italy
[27]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[28]Neurologic Unit, San Paolo Hospital, Bari, Italy
[29]Neurology Unit, AOOR Villa Sofia Cervello, Palermo, Italy
[30]Unit of Neurology, Ospedale Maria Vittoria, Turin, Italy

Introduction: Adult-onset focal dystonia can spread to involve one, or less frequently, two additional body regions [1]. Spread of focal dystonia to a third body site is not fully characterized.

Objective: The aim of the study is to fully characterize the spread of segmental/multifocal dystonia to a third body site in idiopathic adult-onset patients.

Materials and Methods: We retrospectively analyzed data from the Italian Dystonia Registry [2], enrolling patients with segmental/multifocal dystonia involving at least two parts of the body or more. Survival analysis estimated the relationship between dystonia features and spread to a third body part.

Results: We identified 340 patients with segmental/multifocal dystonia involving at least two body parts. Spread of dystonia to a third body site occurred in 42/241 patients (17.4%) with focal onset and 10/99 patients (10.1%) with segmental/multifocal dystonia at onset. The former had a greater tendency to spread than patients with segmental/multifocal dystonia at onset. Gender, years of schooling, comorbidity, family history of dystonia/tremor, age at dystonia onset, and disease duration could not predict spread to a third body site. Among patients with focal onset in different body parts (cranial, cervical, and upper limb regions), there was no association between site of focal dystonia onset and risk of spread to a third body site.

*Conclusion***:** Spread to a third body site occurs in a relative low percentage of patients with idiopathic adult-onset dystonia affecting two body parts. Regardless of the site of dystonia onset and of other demographic/clinical variables, focal onset seems to confer a greater risk of spread to a third body site in comparison to patients with segmental/multifocal dystonia at onset.

References:

[1] BD Berman, CL Groth, SH Sillau, S Pirio Richardson, SA Norris, J Junker, N Brüggemann, P Agarwal, RL Barbano, AJ Espay, JA Vizcarra, C Klein, T Baümer, S Loens, SG Reich, M Vidailhet, C Bonnet, E Rose, HA Jinnah, JS Perlmutter, Risk of spread in adult-onset isolated focal dystonia: A prospective international cohort study, J. Neurol. Neurosurg. Psychiatry. (2019) 1–7.

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

P25

A thematic framework analysis of nationwide survey on needs and perceptions of people living with dystonia during the first wave of Covid-19 pandemic in Italy

Vittorio Rispoli[1], M.E.D. Crescitelli[2], G. Di Rauso[5], S. Coniglio[5], F. Cavallieri[3,4], F. Antonelli[1], S. Meletti[1,5], L. Ghirotto[2], F. Valzania[4]

[1]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero - Universitaria di Modena, Modena, Italy
[2]Qualitative Research Unit - AUSL – 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, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy

Introduction: The unprecedented situation forced governments to quickly pose into action a number of countermeasures to prevent the Covid-19 spread and to tackle SARS-COV2-related syndromes. The daily life of people suffering from choric diseases was negatively impacted and routine medical care faced a sudden shortening. This is even true for rare disease, such as dystonia. During the ongoing pandemic, dystonic patients' medical care is at risk of not being taken into consideration as before. Moreover, pandemic might play a direct or indirect role in modifying motor and non-motor symptoms.

Objective: To explore the feelings and issues of people living with dystonia, the possible consequences of pandemic countermeasures on their daily and working-life, clinics remodulation and patients' relationship with healthcare centers, and to uncover needs at risk of not being met.

Methods: A nationwide survey was publicly posted online for incentive-free selfenrolment. The survey focused on demographic and clinical features, neurological service as well as contact provision, perceptions about virus infection and healthcare-related needs, job questions, support-seeking during the first-wave of the ongoing pandemic. The collected data were analysed with descriptive statistics and thematic framework analysis.

Results: People affected by dystonia highlighted the detrimental condition experienced during the first-wave of this pandemic, mainly due to social isolation and treatment session withdrawal (i.e. botulinum neurotoxin injection clinics). They felt "abandoned" in dealing with dystonia with a worsening of dystonia related features, which had negatively impacted on daily functioning and fueled stigmatization. So, people living with dystonia sought information and support via a number of means. Nevertheless, relevant needs remained unmet.

Conclusions: These findings may foster future actions to guarantee a standard of care for people suffering from dystonia even during worldwide emergencies and to contribute to awareness-raising campaign on this rare disease.

P26

A comparison of level of disability (LoD) in patients with blepharospasm between the Covid19 lockdown and the unlock period

Assunta Trinchillo[1], G. De Joanna[2], F. Iorillo[2], F. Habetswallner[2], M. Esposito[2]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, "Federico II" University, Naples, Italy
[2]Clinical Neurophysiology Unit, "A. Cardarelli" Hospital, Naples, Italy

Introduction: Blepharospasm (BS) is a focal dystonia presenting involuntary eyelid closure, and it exacerbates with stressful conditions and with light exposure. [1-3].

Objectives: We investigated the impact of lockdown (LD) for the Covid 19 pandemic on disability due to BS.

Materials and Methods: The level of disability (LoD) was assessed by using four items of the Blepharospasm Disability Index (4iBSDI): reading, whatching TV, walking, everyday activities. Driving and shopping items were not applicable because of the restrictions due to Covid19. A pool of 50 consecutive patients affected by BS, referred to the botulinum toxin (btx) clinic of Cardarelli Hospital of Naples, was investigated on the LoD during the lockdown (LD) and unlock (UL) period. We compared scores from 4iBSDI during the LD period, when patients missed the scheduled injection, and scores obtained during the following UL phase at least three months after the last injection. [4-5].

Results: BSDI scores were calculated at the LD and UL time (LDt, ULt). 4iBSDI Mean scores ± SD was 3.82±3.571 at LDt and 5.53±3.319 at ULt. Mean distribution was not normal therefore values were analyzed by Paired T-student test after logarithmic transformation. Statistical analysis showed a significant difference between 4iBSD mean scores at LDt and ULt (Mean=1.09; CI -1.26, -0.93; $p<0.001$).

Discussion: Our results show that patients with BS could present a lower LoD due to dystonia during the LD period in comparison to the UL phase. During the LD time patients with BS were less exposed to outdoor light and especially to social interaction.

Conclusions: People with dystonia present clinical worsening with physical and emotional stress. Our study shows that BS may be extremely affected by emotional factors like social embarrassment. The lack of social interaction experienced during the LD period could have protected BS patients from stressful conditions and alleviate symptoms of dystonia.

References:

[1] EL Peckham, G Lopez, EA Shamim, SP Richardson, S Sanku, R Malkani, M Stacy, P Mahant, A Crawley, A Singleton et al.Clinical features of Meige's disease (idiopathic orofacial dystonia): A report of 17 cases. Arch. Neurol. 1981, 38, 147–151. 13.
[2] AAN Updates Guidelines on the Uses of Botulinum Neurotoxin. Am Fam Physician. 2017 Feb 1;95(3):198-199.

[3] EL Peckham, G Lopez, EA Shamim, S Pirio Richardson, S Sanku, R Malkani, M Stacy, P Mahant, A Crawley, A Singleton, M Hallett. Clinical features of patients with blepharospasm: a report of 240 patients. Eur. J. Neurol. 2011, 18, 382–386.
[4] DM Simpson, M Hallett, EJ Ashman, CL Comella, MW Green, GS Gronseth, MJ Armstrong, D Gloss, S Potrebic, J Jankovic et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology 2016, 86, 1818–1826
[5] MD Joseph Jankovic, C Kenney, S Grafe, R Goertelmeyer and G Comes. Relationship Between Various Clinical Outcome Assessments in Patients with Blepharospasm, Movement Disorders Vol. 24, No. 3, 2009, pp. 407–41.

P27

Action-based modulations of somatosensory processing in professional musicians with focal hand dystonia: novel insights for neurorehabilitation

Francesco Marenco[*], C.C. Derchi[*], M. Ramella, A. Mazza, A. Viganò, E. Saibene, R.M. Converti, A. Castagna[#], A. Comanducci[#]

IRCCS Fondazione Don Gnocchi, Milan, Italy

[*]*These authors equally contributed to this work*
[#]*These authors equally contributed to this work*

Introduction: Focal task-specific dystonia is a rare movement disorder that may affect musicians while playing instruments. An impaired sensorimotor integration has been shown to explain the impairment of voluntary control of highly-skilled movements in musicians [1,2]. Furthermore, sensory training based on visual input seems able to modulate this pathologic sensorimotor integration playing a key role for rehabilitation [3].

Objective: To determine how somatosensory processing is modulated during variants of a simple hand motor task in musicians affected by focal hand dystonia (FHD).

Methods: We enrolled 5 professional musicians with a selective FHD and recorded somatosensory evoked potentials (SEP) independently from the affected and the non-affected hand in 4 randomized conditions: 1. at rest 2. during a self-paced motor task (i.e. finger tapping) without action observation 3. during motor imagery of the same task 4. during finger tapping with action observation. We analyzed SEP to verify whether they are specifically modulated across different task modalities in the affected compared to the non-affected hand.

Results: A self-paced motor task, such as finger tapping performed without action observation, led to a suppression of SEP amplitude which resulted to be significantly greater in the dystonic hand compared to the control one. The imagery of the same motor task led to a mild SEP attenuation without differences in the two hands. More interestingly, the action observation of the same task seemed effective in attenuating differences between hands due to a milder suppression of SEP in the dystonic hand up to the level of the control hand.

Conclusion: These findings further corroborate the hypothesis for a leading role of somatosensory dysfunction in FHD. Furthermore, the impact of action observation on SEP during a motor task may be interpreted as a novel evidence for explaining the effect of rehabilitation based on mirror therapy in patients with FHD.

References:

[1] Byl, & Priori, 2012. In Music, Motor Control and the Brain, Oxford University Press.
[2] Abbruzzese & Berardelli, 2003. Mov Disord Mar;18(3):231-40.
[3] Ramella et al, 2021. Medical Problems of Performing Artists.

P28

Sudden onset, fixed dystonia and acute peripheral trauma as diagnostic clues for functional dystonia

Tommaso Ercoli[1], G. Defazio[1], C. Geroin[2], E. Marcuzzo[2], G. Fabbrini[3,4], F. Bono[5], A. Mechelli[5], R. Ceravolo[6], L.M. Romito[7], A. Albanese[8], A. Pisani[9,10], M. Zibetti[11], M.C. Altavista[12], L. Maderna[13], M. Petracca[14], P. Girlanda[15], M.M. Mascia[1], A. Berardelli[3,4], M. Tinazzi[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy.
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[4]IRCCS Neuromed, Pozzilli (IS), Italy
[5]Botulinum Toxin Center, Neurology Unit A.O.U. Mater Domini, Catanzaro, Italy
[6]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy
[7]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[8]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano Milan, Italy
[9]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[10]IRCCS Mondino Foundation, Pavia, Italy
[11]Department of Neuroscience - Rita Levi Montalcini, University of Turin, Turin, Italy
[12]UOC di Neurologia, Ospedale San Filippo Neri, ASL Roma 1, Roma, Italy
[13]Department of Neurology-Stroke Unit and Laboratory of Neurosciences, Istituto Auxologico Italiano, IRCCS, Milan, Italy
[14]Fondazione Policlinico Universitario Agostino Gemelli - IRCCS, Rome, Italy
[15]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Introduction: The differentiation of functional dystonia from idiopathic dystonia may be clinically challenging [1].

Objective: To identify clinical features suggestive of functional dystonia in order to guide physicians to distinguish functional dystonia from idiopathic dystonia.

Methods: Patient data were extracted from the Italian Registry of Functional Motor Disorders [2] and the Italian Registry of Adult Dystonia [3], supported by the Fondazione LIMPE and the Accademia LIMPE-DISMOV RADAC project. Patients with functional and idiopathic dystonia were followed up at the same clinical sites, and they were similar for age and sex.

Results: We identified 113 patients with functional dystonia and 125 with idiopathic dystonia. Sudden onset of dystonia, evidence of fixed dystonia, and acute peripheral trauma prior to dystonia onset were more frequent in the functional dystonia group. No study variable alone achieved satisfactory sensitivity and specificity, whereas combination of variables yielded 85% sensitivity and 98% specificity. A diagnostic algorithm was developed to reduce the risk of misclassifying functional dystonia.
*Conclusions***:** Our findings extend the current diagnostic approach to functional dystonia by showing that clinical information about symptom onset, fixed dystonia, and history of peripheral trauma may provide key clues in the diagnosis of functional dystonia.

References:

[1] J. Stone, A. Carson, M. Sharpe. Functional symptoms in neurology: management. J Neurol Neurosurg Psychiatry. 2005;76
[2] M. Tinazzi, F. Morgante, E. Marcuzzo et al. Clinical Correlates of Functional Motor Disorders: An Italian Multicenter Study. Mov Disord Clin Pract. 2020;7(8):920-929.
[3] G. Defazio, M. Esposito, G. Abbruzzese et al. The Italian Dystonia Registry: rationale, design and preliminary findings. Neurol Sci. 2017;38(5):819-825.

P29

Correlates of the discrepancy between objective and subjective cognitive functioning in non-demented patients with Parkinson's disease

Mattia Siciliano[1,2], L. Trojano[2], R. De Micco[1], V. Sant'Elia[2], A. Giordano[1], A. Russo[1], L. Passamonti[3,4], G. Tedeschi[1], C. Chiorri[5], A. Tessitore[1]

[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]Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
[4]Institute of Molecular Bioimaging and Physiology, CNR, Milan, Italy
[5]Department of Educational Sciences, University of Genova, Genova, Italy

Background: Subjective complaints of cognitive deficits are not necessarily consistent with objective evidence of cognitive impairment in Parkinson's disease (PD) [1-3]. Here we examined the factors associated with the objective-subjective cognitive discrepancy.

Methods: We consecutively enrolled 90 non-demented patients with PD who completed the Parkinson's Disease Cognitive Functional Rating Scale (subjective cognitive measure) and the Montreal Cognitive Assessment (MoCA; objective cognitive measure). The patients were classified as "Overestimators", "Accurate estimators", and "Underestimators" on the basis of the discrepancy between the objective vs. subjective cognitive measures. To identify the factors distinguishing these groups from each other, we used Chi-Square tests or one-way Analyses of Variance, completed by logistic and linear regression analyses.

Results: Forty-nine patients (54.45%) were classified as "Accurate estimators", 29 (32.22%) as "Underestimators", and 12 (13.33%) as "Overestimators". Relative to the other groups, the "Underestimators" scored higher on the Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), and Parkinson Anxiety Scale ($p<0.01$). Logistic regression confirmed that FSS and BDI scores distinguished the "Underestimators" group from the others ($p<0.05$). Linear regression analyses also indicated that FSS and BDI scores positively related to objective-subjective cognitive discrepancy ($p<0.01$). "Overestimators" scored lower than other groups on the MoCA's total score and Attention and Working Memory subscores ($p<0.01$).

Conclusions: In more than 45% of consecutive non-demented patients with PD, we found a 'mismatch' between objective and subjective measures of cognitive functioning [2-3]. Such discrepancy, which was related to the presence of fatigue and depressive symptoms and frontal executive impairments, should be carefully evaluated in clinical setting.

References:

[1] I Litvan, JG Goldman, AI Tröster, BA Schmand, D Weintraub, RC Petersen, B Mollenhauer, CH Adler, K Marder, CH Williams-Gray, D Aarsland, J Kulisevsky, MC Rodriguez-Oroz, DJ Burn, RA Barker, M Emre. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord 27:349-356 (2012).
[2] JN Copeland, A Lieberman, S Oravivattanakul, AI Tröster. Accuracy of Patient and Care Partner Identification of Cognitive Impairments in Parkinson's Disease-Mild Cognitive Impairment. Mov Disord 31:693-698 (2016).
[3] R Purri, L Brennan, J Rick, SX Xie, BL Deck, LM Chahine, N Dahodwala, A Chen-Plotkin,

JE Duda, JF Morley, RS Akhtar, JQ Trojanowski, A Siderowf, D Weintraub. Subjective Cognitive Complaint in Parkinson's Disease Patients with Normal Cognition: Canary in the Coal Mine? Mov Disord 35:1618-1625 (2020).

P30

CSF tau biomarkers and structural brain MRI measures in frontotemporal lobar degeneration

Giuseppe Fenu[1], V. Oppo[1], G. Serra[1], L. Lorefice[2], F. Di Stefano[1], D. Deagostini[1], C. Mancosu[2], E. Fadda[2], C. Melis[2], P. Siotto[3], E. Cocco[2], M. Melis[1], G. Cossu[1]

[1]Department of Neuroscience, A.O. Brotzu, Cagliari, Italy
[2]Multiple Sclerosis Centre, University of Cagliari, Cagliari, Italy
[3]Radiology Unit, A.O. Brotzu, Cagliari, Italy

Introduction: In recent years, in the field neurodegenerative diseases, increasing attention has been pointed to CSF biomarkers and their integration with neuroimaging [1]. Frontotemporal lobar degeneration (FTLD) refers to a heterogeneous group of clinical syndromes with different underlying
proteinopathies including tau pathology [2]. CSF biomarkers have been proposed as diagnostic and prognostic factors [3].

Objective: Aim of our study was to evaluate the relationship between CSF tau biomarkers and structural MRI brain measures in FTLD.

Materials and Methods: We included early FTLD patient. All included patients underwent lumbar puncture to evaluate amyloid, total-tau (t-tau), phospho-tau 181 (p-tau); p-tau/t-tau ratio was also calculated; brain MRI was performed to estimate whole brain volume, volume of principal deep grey matter structures and regional cortical thickness using FreeSurfer software version 7.1.1 (http://surfer.nmr.mgh.harvard.edu). The principal clinical and demographic features were also recorded.

Results: Demographic characteristics of the 28 included patients were as follows: female/male: 9/19; mean±SD age: 67.9±7.7 years. The p-tau/t-tau ratio was significantly correlated with whole brain volume ($r=0.77$; $p < 0.001$), brain-stem volume ($r=0.41$; p: 0.04), left putamen volume ($r=0.57$ p: 0.006) left pallidum volume ($r=0.41$; p: 0.04), right accumbens volume ($r=0.47$; p: 0.02). P-tau/t-tau ratio showed also a significant correlation with cortical thickness of left temporal lobe ($r=0.74$; $p < 0.001$) and left caudal middle frontal cortex ($r=0.45$; p: 0.03). Linear regression showed a significant relationship between p-tau/t-tau ratio and left temporal pole ($p = 0.001$; r^2: 0.60) after controlling for age and gender.

Conclusions: Our data suggest that CSF biomarkers, especially p-tau/t-tau ratio, could play a role as prognostic factor in FTLD. Further longitudinal investigations are needed to confirm these findings.

References:

[1] LH Meeter, LD Kaat, JD Rohrer, JC van Swieten. Imaging and fluid biomarkersin frontotemporal dementia. Nat Rev Neurol. 2017 Jul;13(7):406-419.
[2] S Abu-Rumeileh, N Mometto, A Bartoletti-Stella, B Polischi, F Oppi, R. Poda, M Stanzani-Maserati, P Cortelli, R. Liguori, S Capellari, P Parchi. Cerebrospinal Fluid Biomarkers in Patients with Frontotemporal Dementia Spectrum: A Single-Center Study. J Alzheimers Dis.;66: 551-563. doi: 10.3233/JAD-180409 (2018).
[3] YA Pijnenburg, NA. Verwey, WM van der Flier, P Scheltens, CE Teunissen. Discriminative and prognostic potential of cerebrospinal fluid phosphoTau/tau ratio and neurofilaments for frontotemporal dementia subtypes. Alzheimers Dement (Amst). 14;1: 505-12 (2015).

P31

Qualitative aspects of Rey-Osterrieth Complex Figure Test performance in patients with Progressive Sopranuclear Palsy

Luca Tommasini[1], J. Bonaccorsi[1], E. Del Prete[2], S. Mazzucchi[2], S. Cintoli[1], G. Tognoni[1], R. Ceravolo[1,2]

[1]Department of Medical Specialties, Neurology Unit, AOUP, Pisa, Italy
[2]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy

Introduction: Copy of Rey-Osterrieth Complex Figure (ROCF) is a drawing test considered a complex neuropsychological task requiring multiple cognitive abilities (e.g. visuo-spatial, executive function, attention, fine-motor coordination). The scoring system commonly used is the quantitative 36-point scoring system. Recently some studies showed that this score was able to differentiated Progressive Sopranuclear Palsy (PSP) from Parkinson's disease (PD) patients [1,2], however without providing information about underling impaired cognitive process. In this context, qualitative analyses of ROCF may be relevant.

Objectives: Our work aimed at examining which qualitative aspects of ROCF copy is the most useful in discriminating PSP-Richardson Syndrome (PSP-RS) from PD and healthy control (HC). Furthermore, we were interested in evaluating the predictive validity of PSP-RS diagnosis according to different scoring system (quantitative vs qualitative).

Methods: Thirty PSP-RS subjects, 30 PD patients and 30 HC matched for age, education and gender were enrolled. No differences in disease duration between PSP-RS and PD were found (respectively 3.2±1,7; 2.9±1.7). All subjects underwent a neuropsychological evaluation; ROCF copy were evaluated with quantitative and qualitative (Boston Qualitative Scoring System-BQSS) scoring system.

Results: PSP-RS performed worse in ROCF quantitative score, as expected, and in different BQSS scores ($p<.05$). Using a logistic regression model, the most suitable scores discriminating PSP-RS from PD and from HC were "Perseveration" and "Vertical Expansion". These BQSS scores showed better predictive validity of PSP-RS diagnosis than standard quantitative score.

Conclusions: We found that "Perseveration" and "Vertical Expansion" BQSS scores are useful in discriminating PSP-RS from PD and HC. These scores could be underlined by a motor inhibitory deficit distinctive of PSP-RS patients. "Perseveration" and "Vertical Expansion" BQSS scores could be included in the cognitive evaluation along with quantitative scores when PSP diagnosis is considered.

References

[1] G. Santangelo, S. Cuoco, M.T. Pellecchia, R. Erro, P. Barone, M. Picillo. (2018). Comparative cognitive and neuropsychiatric profiles between Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. *Journal of neurology*, *265*(11), 2602-2613.
[2] C. Pellicano, F. Assogna, N. Cellupica, F. Piras, M. Pierantozzi, A. Stefani, G. Spalletta. (2017). Neuropsychiatric and cognitive profile of early Richardson's syndrome, Progressive Supranuclear Palsy-parkinsonism and Parkinson's disease. *Parkinsonism & related disorders*, *45*, 50-56.

P32

Efficacy of transcranial direct current stimulation on cognition in Parkinson's disease

Arianna Cappiello[1], M. Picillo[1], P. Barone[1], M.T. Pellecchia[1], S. Cuoco[1], R. Erro[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience Section, University of Salerno, Salerno, Italy

Objective: Parkinson's disease (PD) comprises a wide range of cognitive deficits from the earliest stage [1]. Since cognitive impairment significantly contribute to worse health-related quality of life (HRQoL) and there are no efficacious treatment options, there is the need for alternative approaches. The aim of this study is to provide an overview of the effects of tDCS on cognition in PD.

Materials and methods: We systematically reviewed the literature published on the use of tDCS for cognition in PD, identifying 17 eligible studies.

Results: A summary of the included studies is displayed [1]. In most studies (71%) tDCS was applied on the dorsolateral prefrontal cortex (DLPFC), while alternative stimulated areas included primary motor cortex, medial frontal cortex and the cerebellum. Although the majority of studies demonstrated an improvement of specific neuropsychological tests, especially exploring the executive functions, in most cases results were modest.

Discussion: Because cognitive impairment in PD most commonly involve executive functions [2], most studies focused on DLPFC stimulation, showing some modest results on executive outcomes. However, there is few consistency across the observed results and discrepancies between different studies have been identified and there is suggestion that the improvement also depend on the baseline cognitive status of patients. Studies are also heterogeneous in terms sample size, patients' characteristics, stimulation protocol and outcome measures.

Conclusions: tDCS could be efficacious in PD, perhaps in association with other interventions such as neurocognitive rehabilitation. However, more homogeneous studies, with larger samples and longer follow-up evaluations are necessary.

References

[1] Hasmet A., Hanagasi H.A., Tufekcioglu Z., Emre M. Dementia in Parkinson's disease. J Neurol Sci. 2017 Mar 15; 374:26-31.
[2] Ding W., Ding L.-J., Li F.-F., Han Y., Mu L. Neurodegeneration and cognition in Parkinson's disease: a review. Eur Rev Med Pharmacol Sci. 2015 Jun;19(12):2275-81.

P33

The language profile in multiple system atrophy: an exploratory study

Sofia Cuoco[1], M. Picillo[1], I. Carotenuto[1], R. Erro[1], E. Catricalà[2], S. Cappa[2,3], M.T. Pellecchia [1], P. Barone[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience section, University of Salerno, Salerno, Italy
[2]University School for Advanced Studies IUSS Pavia, Pavia, Italy
[3]IRCCS Fondazione Mondino, Pavia, Italy

*Background***:** The evidence about the language performance profile of multiple system atrophy (MSA) is limited [1], but its definition may lead to a more comprehensive characterization of the disorder and contribute to clarify the involvement of the basal ganglia in language abilities [2].

*Objective***:** The objectives of the study were: 1) to evaluate the reliability of the Screening for Aphasia in NeuroDegeneration (SAND) [3] in MSA patients; 2) compare the linguistic profiles among MSA and Parkinson's disease (PD) patients and healthy controls (HC), and 3) assess relationships between language impairment and cognitive status and MSA motor subtypes.

*Methods and results***:** Forty patients with a diagnosis of MSA, 22 HC and 17 patients with PD were enrolled in the present study. By excluding the writing task that showed a poor acceptability, we showed that the MSA-tailored SAND Global Score is an acceptable, consistent and reliable tool to screen language disturbances in MSA. MSA patients performed worse than HC, but not than PD, in MSA-tailored SAND Global Score, repetition, reading and semantic association tasks. We did not find significant differences between MSA phenotypes. MSA patients with mild cognitive impairment multiple domain presented worse language performances as compared to MSA patients with normal cognition and mild cognitive impairment-single domain.

*Conclusions***:** The MSA-tailored SAND Global Score is a consistent and reliable tool to screen language disturbances in MSA. Language disturbances characterize MSA patients irrespective of disease phenotype, and parallel the decline of global cognitive functions.

References

[1] I Stankovic, F Krismer, A Jesic, A Antonini, T Benke, RG Brown, DJ Burn, JL Holton, H Kaufmann, VS Kostic, H Ling, WG Meissner, W Poewe, M Semnic, K Seppi, A Takeda, D Weintraub, GK Wenning, Movement Disorders Society MSA (MODIMSA) Study Group. Cognitive impairment in multiple system atrophy: a position statement by the Neuropsychology Task Force of the MDS Multiple System Atrophy (MODIMSA) study group. Moviment Disorders, 29(7) (2014) 857-67. doi:10.1002/mds.25880. Epub 2014 Apr 18. Review. PubMed PMID: 24753321.
[2] JF Cardona, O Gershanik, C Gelormini-Lezama, AL Houck, S Cardona, L Kargieman, N Trujillo, A Arévalo, L Amoruso, F Manes, A Ibáñez, Action-verb processing in Parkinson's disease: New pathways for motorelanguage coupling. Brain Structure and Function, 218(6) (2013) 1355e1373. Doi: 10.1007/s00429-013-0510-1.
[3] E Catricalà, E Gobbi, P Battista, A Miozzo, C Polito, V Boschi, V Esposito, S Cuoco, P Barone, S Sorbi, SF Cappa, P Garrard, SAND: a Screening for Aphasia In NeuroDegeneration. Development and normative data. Neurological Science, 38(8) (2017) 1469-1483. doi: 10.1007/s10072-017-3001-y. Epub 2017 Jun 4. PubMed PMID: 28578483.

P34

Serum lipids fractions and executive functioning in Parkinson's disease: a possible sex-effect. Findings from the PACOS study

Antonina Luca[1], R. Monastero[2], C.E. Cicero[1], R. Baschi[2], G. Mostile[1], G. Donzuso[1], M. Davì[2], L. Di Giorgi[2], M. Caccamo [2], M. Zappia[1], A. Nicoletti[1]

[1]Department of Surgical and Medical Sciences Advanced Technologies "G.F. Ingrassia", University of Catania, Catania, Italy
[2]Department of Experimental Biomedicine and Clinical Neuroscience (BioNeC), University of Palermo, Palermo, Italy

Background: The association between dyslipidemia and cognitive performance in Parkinson's disease (PD) patients has not been properly investigated.

Aims: Aims of the present study were: 1) to evaluate the presence of possible associations between mild cognitive impairment (PD-MCI) and lipids levels; 2) to evaluate possible correlations between scores obtained at tests assessing executive functioning and serum lipids; 3) to explore sex-specific contribute of these lipid fractions on cognition.

Methods: Patients from the PACOS cohort, who underwent a complete serum lipid profile measures (total cholesterol-TC, low-density lipoprotein cholesterol-LDL, high-density lipoprotein cholesterol-HDL and triglycerides-TG) were selected. PD-MCI was diagnosed according to MDS-level II criteria. Executive functioning was assessed with the Frontal Assessment Battery (FAB) and the Raven's Colored Progressive Matrices (RCPM).

Results: Three hundred forty-eight PD patients (148 women; age 66.5±9.5 years; disease duration 3.9±4.9 years) were enrolled. Women presented significantly higher TC, LDL and HLD than men. In the whole sample, any association between lipid profile measures, MCI, FAB and RCPM was found. Among woman, at univariate analysis, a positive association between pathological TG and pathological FAB score was found (OR 3.4; 95%CI 1.29-9.03; p-value 0.013). In women, a statistically significant negative correlation was found between FAB score and triglyceride serum levels (r= -0.226; p-value:0.005). Differently, among men, a statistically significant negative association between pathological TC and pathological FAB score (OR 0.4;95%CI 0.17-0.84; p-value 0.018) and between pathological LDL and pathological FAB score (OR 0.4;95%CI 0.18-0.90; p-value 0.027) were found.

Conclusions: Our data suggest a sex-specific different role of lipids in executive functioning.

References

[1] R Monastero, CE Cicero, R Baschi, M Davì, A Luca, V Restivo, C Zangara, B Fierro, M Zappia, A Nicoletti. Mild cognitive impairment in Parkinson's disease: the Parkinson's disease cognitive study (PACOS). J Neurol. 2018;265(5):1050-1058.

[2] X Huang, SY Ng, NS Chia, S Acharyya, F Setiawan, Z Lu, YJ Tan, E Ng, MC Wen, A S L Ng, K Y Tay, WL Au, EK Tan, LC Tan. Higher serum triglyceride levels are associated with Parkinson's disease mild cognitive impairment. Mov Disord. 2018;33(12):1970-1971.
[3] A Nicoletti, R Vasta, G Mostile, G Nicoletti, G Arabia, G Iliceto, P Lamberti, R Marconi,

L Morgante, P Barone, A. Quattrone, M Zappia. Gender effect on non-motor symptoms in Parkinson's disease: are men more at risk? Parkinsonism Relat Disord. 2017;35:69-74.

P35

Influence of drugs on mild cognitive impairment in Parkinson's disease: Evidence from the PACOS Study

Calogero Edoardo Cicero[1], R. Monastero[2], C. Terravecchia[1], G. Donzuso[1], A. Luca[1], R. Baschi[2], M. Caccamo[2], G. Mostile[1], L. Giuliano[1], M. Zappia[1], A. Nicoletti[1]

[1]Department G.F. Ingrassia, Neuroscience Section, University of Catania, Catania, Italy
[2]Department of Biomedicine, Neuroscience and Advanced Diagnostics, University of Palermo, Palermo, Italy

Background: Polytherapy and the anticholinergic activity of several drugs negatively influence cognition in the elderly. However, little is known on the effect on Mild Cognitive Impairment (MCI) in Parkinson's disease (PD).

Methods: Patients with PD belonging to the baseline PACOS cohort with full pharmacological data, have been included in this study. MCI diagnosis was made according to the MDS level II criteria. Polytherapy was defined as patients assuming ≥6 drugs. Anticholinergic burden has been calculated using the Anticholinergic Drug Scale (ADS). Molecules have been classified according to the ATC classification. Association with MCI has been assessed with a multivariate logistic regression analysis considering MCI as the dependent variable.

Results: Pharmacological data was available for 238 patients (mean age 64.7±9.7). One hundred (42.0%) were diagnosed as MCI. In the full multivariate model (correcting for age, sex, disease duration, education, UPDRS-ME) no association was found with either polytherapy or the ADS. Concerning drug classes, anti-hypertensive medications increased the risk of PD-MCI (OR 2.03;95%CI 1.06-3.91; p=0.032) while gastroprotective agents had a protective effect (OR 0.51; 95%CI 0.27-0.98; p=0.046).

Conclusions: The magnitude of polytherapy and anticholinergic drugs burden does not appear to modulate MCI risk in PD, probably due to cautious prescription patterns. The protective effect of gastroprotective agents needs further confirmations.

P36

Could cognitive and emotional information processing influence obstacle negotiation in patients with Parkinson's disease and freezing of gait?

Susanna Mezzarobba[1], M. Grassi[2], E. Pelosin[1], P. Manganotti[3], P. Bernardis[2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genova, Genova, Italy
[2]Department of Life Sciences, University of Trieste, Trieste, Italy
[3]Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy

Freezing of gait (FoG) causes a transient inability to generate an effective forward stepping. The underlying pathophysiology is still not fully understood: an emerging hypothesis explain FoG episodes as a processing overload of information produced by faulty basal ganglia control of cognitive, limbic and motor networks [1].
In order to study the cognitive and emotional information processing influence on FoG genesis, we used emotional images (from the International Affective Picture System - IAPS) and cognitive inputs (visual perturbation in obstacle crossing tasks) during an obstacle negotiation task. 12 Parkinson's patients with FoG, 11 without, and 15 healthy elderly controls underwent neurological, neuropsychological, and affective assessments. 20 different images were used as emotional stimuli; the cognitive stimulus consisted in an obstacle with a light placed at its top. Standing participants were asked to look at a screen (where the IAPS images were presented) and to walk and step over the obstacle in the middle of the walkway. In half trials, when the subject began the last step before overcoming the obstacle, the light placed on the top was turned on randomly. When the unpleasant images were presented, PD-FoG group showed slow reaction times ($p=0.028$), longer times to approach ($p=0.012$) and cross ($p=0.023$) the obstacle, and lower step clearance ($p=0.020$) when the light was off. A similar slowing was present in the mean velocity of the crossing step in response to unpleasant images ($p=0.044$). Our data support the hypothesis that the increase of cognitive and emotional information processing could affect FoG.

References

[1] D. Weiss, A. Schoellmann, M.D. Fox, N.I. Bohnen, S.A. Factor, A. Nieuwboer, M. Hallett, S.J.G. Lewis. Freezing of gait: understanding the complexity of an enigmatic phenomenon. Brain. 2020 Jan 1;143(1):14-30.

P37

Pareidolic illusions in advanced non-demented Parkinson's disease

Elisabetta Belli, E. Del Prete, L. Tommasini, A. Francesconi, E. Benevento, R. Ceravolo

Neurology Unit, Clinical and Experimental Medicine Department, University of Pisa, Pisa, Italy

Introduction: Pareidolias are visual illusions of meaningful objects arising from ambiguous forms embedded in visual scenes. Pareidolias and visual hallucinations (VHs) have been suggested to have a common underlying neural mechanism; pareidolia tests have been investigated as marker of VHs in patients with cognitive impairment [1].

Objective: We investigated pareidolia in advanced non-demented Parkinson's disease (PD).

Method: Neuropsychological tests including MMSE, MOCA, incomplete letters (IL), semantic fluency, phonemic fluency and pareidolia battery [2] (scene and noise tests) were administered to PD patients and healthy controls (HCs). Pareidolia score was calculated for noise, for scene and as the total sum of illusory responses. For PD total MDS-UPDRS III, MDS-UPDRS 1.2 for VHs, Daily Levo-dopa Dose Equivalent Total (LEDD-T) and for Dopamine Agonists (LEDD-DA) at time of tests were evaluated, as well as side effects of DA, RBD and motor complications during disease course.

Results: Fourty-nine subjects were recruited, 36 with PD (age 69.1±10.6 years, mean disease duration 10.5±7.3 years, MMSE 27.9±0.5) and 13 HCs (age 67.5±8.6 years). PD patients showed higher pareidolia scores (p=0.036), higher noise test scores (p=0.006) and worst performance in phonemic fluency (p=0.001) than HCs. Pareidolia total score was inversely correlated with MMSE (r=-0.49), MOCA (r=-0.35), LEDD-DA (r=-0.33), and directly with IL (r=0.02), LEDD-T (r=0.48), MDS-UPDRS 1.2 (r=0.332), and disease duration (r=0.68). Noise test showed direct correlation with LEDD-T (r=0.50) and disease duration (r=0.69). Four patients developed dementia one year after evaluation; they all produced illusory responses in pareidolia test.

Conclusions: This is the first study assessing both noise and scene pareidolia in advanced non-demented PD patients. Pareidolic illusions, especially noise ones, are more frequent in PD patients than HCs, and they correlates with disease duration, dopaminergic therapy and VHs. Longitudinal studies are needed to investigate the predictive role of pareidolia for dementia.

References

[1] M Uchiyama, Y Nishio, K Yokoi et al. Pareidolias: Complex visual illusions in dementia with Lewy bodies. *Brain*. 2012;135(8): 2458-2469. doi:10.1093/brain/aws126.
[2] Y Mamiya, Y Nishio, H Watanabe et al. The pareidolia test: A simple neuropsychological test measuring visual hallucination-like illusions. *PLoS One*. 2016;11(5). doi:10.1371/journal.pone.0154713.

P38

Effects of dopaminergic medication on reactive and proactive inhibitory control

Giovanni Mirabella[1,2], C. Mancini[1], E. Olivola[2], N. Modugno[2]

[1]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]IRCCS Neuromed, Pozzilli (IS), Italy

Objective: Inhibitory control plays a crucial role in decision-making, allowing behavioral flexibility in a continually changing world [1]. This executive function is severely impaired in Parkinson's disease (PD), [2-5], dramatically impacting patients' ability to pursue future-oriented goals. Paradoxically, even though it is well known that the midbrain's dopamine neurons have a key role in decision making [6-7], the effects of dopaminergic medication on inhibition are still largely unclear. However, understanding the impact of dopamine on inhibitory control has crucial clinical implications.

Methods: To shed light on this issue, we took into consideration two aspects previously almost neglected. First, we compared the stop-signal task performance in early- (Hoehn and Yahr stage1.5/2, n=20) versus moderate-to-advanced (Hoehn and Yahr stage-2.5/3, n=20) PD patients both in ON and in OFF medication. Second, we evaluated both neuropsychological domains of inhibitory control for each cohort of patients, i.e., reactive (the ability to react to a stop signal) and proactive inhibition (the ability to adapt the motor strategies according to the current context flexibly). The latter domain has never been studied in such a context.

Results: We found that medication benefited proactive and reactive inhibitory control in patients with shorter disease duration differently from moderate-to-advanced patients.

Conclusions: Such findings indicate that in a more advanced stage of PD the efficacy of dopaminergic drugs is diminished possibly because there are few remaining dopaminergic cells for the drugs to operate on. Thus, the effect of dopaminergic drugs on inhibitory control could potentially provide critical insights into the state of the disease.

References

[1] Mirabella Front Syst Neurosci. 2014 Nov 3;8:206
[2] Mirabella et al. Cereb Cortex. 2012 May;22(5):1124-32
[3] Mirabella et al. PLoS One. 2013 May 3;8(5):e62793
[4] Mirabella et al. Neuropsychologia. 2017 Jul 28;102:177-189
[5] Mancini et al. Front Neurol. 2019 Jan 7;9:1149.
[6] Montague et al. Nature. 2004 Oct 14;431(7010):760-7
[7] Ryterska et al. Neurosci Biobehav Rev. 2013 Dec;37(10 Pt 2):2836-46

P39

Non-motor symptoms assessment in Parkinson's disease patients carrying GBA gene mutations

Sandra Perillo[1], G.R. Palmieri[1], C. Pane[1], F.M. Di Canio[1], C.D.P. Dello Iacovo[1], S. Petrucci[2,3], E.M. Valente[4,5], F. Saccà[1], G. De Michele[1], G. De Michele[1], A. De Rosa[1]

[1]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy
[3]Department of Clinical and Molecular Medicine, S. Andrea University Hospital, Rome, Italy
[4]IRCCS Mondino Foundation, Pavia, Italy
[5]Department of Molecular Medicine, University of Pavia, Pavia, Italy

Introduction: Glucocerebrosidase (GBA) mutations are the most common genetic risk factor of Parkinson's disease (PD), present in about 5-10% of Caucasian patients.

Objective: We aimed to assess GBA mutations prevalence in a case series of PD patients from Campania (Southern Italy). We also attempted to characterize GBA-related PD in comparison to idiopathic PD (iPD), by assessing motor (MS) and non-motor symptoms (NMSS) through standardized scales.

Methods: We enrolled 207 (126 M and 81 F) unrelated PD patients. GCase activity was measured with fluorometric assay in 149 patients. Next Generation Sequencing was used to detect GBA mutations. MS were assessed in GBA carriers and iPD matched controls with Unified Parkinson's Disease Rating Scale (UPDRS)-section III, Freezing of Gait Questionnaire, and Wearing off questionnaire. NMSS were evaluated by Mini-Mental State Examination, SCOPA-AUT Questionnaire, Apathy Evaluation Scale, Non-Motor Symptoms Scale, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's disease, Beck Depression Inventory, Epworth Sleepiness Scale, Restless Legs Syndrom Rating Scale, Parkinson Psychosis Rating Scale.

Results: Fourteen patients (5 M and 9 F) carried a heterozygous GBA mutation (overall prevalence of 6.7%). L444P mutation was found in four subjects, three of whom had early dementia. Any significant differences were found in the presence and severity of apathy, depression, psychosis, self-reported olfaction, sleep, and autonomic disorders between 11 GBA-PD patients and 11 iPD controls. However, familial history for PD, dementia, dyskinesias, and higher UPDRS-III scores were more common in GBA carriers than iPD patients ($p=0.035$, $p=0.035$, $p=0.033$, and $p=0.035$, respectively).

Conclusions: Our results confirm that GBA gene mutations are common among PD patients and L444P mutation is associated with early-onset dementia. As previously described, the prevalence of cognitive impairment and familial history for PD is significantly higher in GBA carriers. Furthermore, GBA-PD patients had a more severe disease course and more dyskinesias than iPD controls. These findings suggest that GBA mutation carriers may have a more severe disease course.

P40

Dissecting the role of TWNK in Parkinson's disease: a comparative perspective between Movement Disorders and Neuromuscular Diseases Centers

Marco Percetti[1,2], G. Franco[1,3], E. Monfrini[1,3], L. Caporali[4], C. La Morgia[4,5], I. Palmieri[6,7], M.L. Valentino[4,5], R. Minardi[4], D. Ottaviani[8], M. Vizziello[1,3], A. Cocco[9,10], A. Albanese[10], B. Giometto[8], E.M. Valente[6,7], V. Carelli[4,5], A.B Di Fonzo[1,3]

[1]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Neurology Unit, San Gerardo Hospital, ASST Monza, Monza, Italy
[3]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[4]IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Clinica Neurologica, Bologna, Italy
[5]Unit of Neurology, Department of Biomedical and NeuroMotor Sciences (DIBINEM), University of Bologna, Bologna, Italy
[6]IRCCS Mondino Foundation, Pavia, Italy
[7]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[8]Neurology Unit, Rovereto Hospital, Azienda Provinciale per i Servizi Sanitari (APSS) di Trento, Trento, Italy
[9]University of Milan, Milan, Italy
[10]Department of Neurology, Istituto di Ricovero e Cura a Carattere Scientifico Humanitas, Research Hospital, Milan, Italy

Introduction: Parkinsonian features have been described in patients with mutations in nuclear genes encoding for proteins involved in mtDNA metabolism, such as *POLG*, *TWNK*, *OPA1*, *SLC25A46* and *DGUOK*. However, the precise link between Parkinson's disease (PD) and dysfunction of these proteins is largely unknown.

Aim of the study: To look for the role of *TWNK* variants in a large cohort of PD patients and the presence of parkinsonism in a chronic progressive external ophtalmoplegia (cPEO) patients carrying *TWNK* mutations. To describe the clinical phenotypes, video-oculography, neuroimaging, and the effect of *TWNK* variants on mtDNA.

Methods: Genomic DNA was analyzed with a targeted customized gene panel for genes associated to PD and parkinsonism, including nuclear genes involved in mtDNA metabolism (i.e. *POLG*, *TWNK*, *OPA1*, *SLC25A46*). Genetic and clinical data of patients carrying TWNK mutations from a Neuromuscular Diseases Center were retrospectively analyzed.

Results: 317 patients with PD (196 males, 62%; 121 females, 38%) were consecutively analyzed. 6 patients (1.9%) with PD alone or in combination with bilateral palpebral ptosis carried a very rare heterozygotic mutation of *TWNK* (c.500T>C, p.L167P; c.1112G>A, p.R371Q; c.1381G>A, p.E461K; c.1618G>A, p.G540R; c.1966A>C, p.K656Q; c.2010G>C, p.Q670H). Considering cPEO patients with *TWNK* mutations (n=18), 5 had parkinsonism. Detailed phenotypic features were compared among all patients. The role of other genetic factors for the risk of PD was assessed.

Conclusions: TWNK variants seem to be a not so rare finding in patients with PD, even in absence of clinical evidence of cPEO. Identifying the genetic modifiers of PD risk in *TWNK* patients will shed a light on the link of PD pathogenesis and mitochondrial impairment.

P41

GBA mutations and Parkinson's disease. What happens in Southern Italy?

Francesca Spagnolo[1], A. Quarta[2], E. Leopizzi[1], D. Pastore[2], A.M. Rini[1]

[1]Department of Neurology, A. Perrino's Hospital, Brindisi, Italy
[2]Department of Haematology, A. Perrino's Hospital, Brindisi, Italy

Objectives: GBA1 mutations represent the most common genetic risk factor for developing Parkinson's disease (PD) [1]. However, many aspects of this association need to be clarified, especially to identify specific clinical or biological markers capable to distinguish parkinsonian carriers of GBA1 mutations. Glucosylsphingosine (Lyso-GB1), a deacylated form of glucosylceramide, is degraded by the ß-glucocerebrosidase enzyme. Lyso-Gb1 was proved to be a highly sensitive and specific biomarker for diagnosis and monitoring of patients with GD [2]. This is the first study reporting the possible role of Lyso-GB1 for detecting the state of GBA1-heterozygosity in a relatively large cohort of subjects suffering from PD.

Materials and Methods: Sixty consecutive PD-subjects attending our Movement Disorders Unit were included in this study. Dried blood spots were collected on filter cards (CentoCard®) and ß-glucocerebrosidase activity, Lyso-GB1 analysis and GBA1 gene sequencing were carried out in Centogene, Rostock, Germany [2]. Subjects with PD were further divided in two groups, according to the presence (PD-GBA+) or absence (PD-GBA-) of GBA1 mutations. Difference in clinic-demographic characteristics between GBA1- carriers *vs* non-carriers were further analyzed.

Results: Thirteen PD-subjects resulted GBA1-carriers (21%), disclosing a surprisingly high prevalence of GBA1 mutations in the PD-population of this geographic area. GBA1 mutations were, namely, Asn409Ser (7 subjects), Leu483Pro (4 subjects), Glu365Lys (1 subject), Val414Ala (1 subject). There was no statistically significant difference in age, gender, disease duration, Hoehn & Yahr Stage, positive familial history for PD and Total Levodopa Equivalent Daily Dose between PD-GBA+ and PD-GBA-. Tremor-dominant PD was significantly more common in the PD-GBA- than in PD-GBA+ group (51% *vs*23%; *p=0.04*). Moreover, the two groups significantly differed in the use of device-aided therapies, showing an higher utilization in the PD-GBA+ group (5/13 subjects, 38%; namely 4 Deep Brain Stimulations-DBS, 1 Levodopa-carbidopa intestinal gel-LCIG) than in the PD-GBA- group (4/47 subjects, 8.5%; 4 DBS; *p=0.007*). A significant difference was also observed in ß-glucocerebrosidase activity and Lyso-GB1 levels between the two groups, with PD-GBA+ subjects showing a lower enzymatic activity and higher Lyso-GB1 concentrations (ß-glucocerebrosidase: 2.8 ± 0.6 *vs* 3.2 ± 0.6, *p=0.04*; Lyso-GB1 5.8 ± 1.8*vs*4.7 ± 1.4, *p=0.03*, respectively for PD-GBA+ and PD-GBA-groups).

Discussion: GBA1 mutations in PD-populations are probably underreported and an analysis of their impact in different geographical areas should be performed. In our study PD-GBA1 carriers showed a lower ß-glucocerebrosidase activity associated with higher Lyso-GB1 substrate accumulation. These data further support the "loss-of-function" hypothesis of GBA1 mutation carriers, leading to lysosomal substrate accumulation, disruption of autophagic-lysosomal function, and induction of alpha-synuclein pathology responsible for PD. Interestingly PD-GBA1 subjects seem to require more frequently complex, device-aided therapies. This should be keep in mind examining long-term follow-up data about DBS and LCIG efficacy.

Conclusions: The association between GBA1 gene mutations and Parkinson's disease has provided critical clues into PD-etiology and will hopefully change the therapeutic approach of several neurodegenerative conditions in the near future.

References

[1] LN Clark, BM Ross, Y Wang, H Mejia-Santana, J Harris, E D Louis, LJ Cote, H Andrews, S Fahn, C Waters et al. 2007; Mutations in the glucocerebrosidase gene are associated with early-onset Parkinson disease. Neurology. 69:1270–1277.

[2] A Rolfs, AK Giese, U Grittner, D Mascher, D Elstein, A Zimran, T Bottcher, J Lukas, R Hubner, U Golnitz et al. Glucosylsphingosine is a highly sensitive and specific biomarker for primary diagnostic and follow-up monitoring in Gaucher disease in a non-Jewish, Caucasian cohort of Gaucher disease patients. PLoS ONE 2013; 8, e79732.

P42

Genetic screening for GBA mutations in parkinsonian patients from Campania

Gianluigi Rosario Palmieri[1], G. De Michele[1], I. Ferrara[1], T. Fico[1], B. Tomasz[2], P. Bauer[2], G. De Michele[1], A. De Rosa[1]

[1]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2]CENTOGENE AG, Rostock, Germany

Introduction: Mutations of the Glucocerebrosidase (GBA) gene are the most important genetic risk factor yet discovered for Parkinson's disease (PD), found in about 5-10% of Caucasian patients [1]. The most common mutations reported among PD patients are N370S and L444P. Both mutations are associated with a faster disease course and higher frequency of dementia than in the idiopathic form.

Objective: We assessed *GBA* gene variations frequency in a cohort of PD patients from Campania.

Methods: We studied 169 (108 M and 61 F) unrelated PD patients. At the time of screening, mean age ± SD of the patients was 67.7 ±8.9 years, and disease onset was 59.6 ± 10.7 years. GBA activity determination was performed by Dried blood spots (DBSs) on standard filter paper. Whole blood from DBSs was analyzed by fluorometric assay. The individuals with positive metabolic screening underwent genetic confirm by Sanger sequencing.

Results: Nine patients (3 M and 6 F) carried a heterozygous *GBA* mutation, with an overall prevalence of 5.3%. L444P was found in 4 subjects, three of whom presented with early dementia. We compared the whole sample of idiopathic PD(iPD) patients with the mutation carriers. We did not find any significant difference about age at exam, age at onset, subtype (tremor-dominant orakinetic-rigid), familial history for PD, presence of apathy, depression, hallucinations, self-reported olfaction, sleep and autonomic disorders, motor fluctuations, and dyskinesias. However, dementia and anxiety disorder were more significantly frequent among the carriers than iPD ($p=0.014$ and $p=0.039$, respectively).

Conclusions: Our results confirm that *GBA* mutations are common among PD patients. Furthermore, as previously described [1-2], the prevalence of cognitive impairment and anxiety resulted significantly higher among the carriers than iPD. We also confirmed that L444P represents the mutation most often associated with early onset of dementia.

References

[1] Schapira AH. Glucocerebrosidase and Parkinson disease: Recent advances. Mol Cell Neurosci. 2015;66:37-42
[2] Swan M, Doan N, Ortega RA, Barrett M, Nichols W, Ozelius L, et al. Neuropsychiatric characteristics of GBA-associated Parkinson disease. J Neurol Sci. 2016;15;370:63-69

P43

Corpus callosum hypoplasia and parkinsonism with poor response to levodopa in DYNC1H1 mutation

Marta Filidei[1], N. Tambasco[2], P. Prontera[1,2], G. Cappelletti[1], S. Simoni[1,2], P. Nigro[1], L. Parnetti[1,2]

[1]Università degli Studi di Perugia, Perugia, Italy
[2]Ospedale S. Maria della Misericordia di Perugia, Perugia, Italy

Background: Mutations in the cytoplasmic dynein 1 heavy chain 1 gene (DYNC1H1) are associate with autosomal dominant lower extremity-predominant spinal muscular atrophy [1-2], neuromuscular [3-4] and neurodevelopmental disorders [5], and hereditary spastic paraplegia. To the best of our knowledge, only one case was reported of DYNC1H1 haploinsufficiency with associated parkinsonian features responding to levodopa [6].

Aim and Methods: Case presentation and literature review.

Results: A 58-years-old caucasian man developed progressive motor slowing in right limbs. His medical history revealed diabetes mellitus type 2 and arterial hypertension. His family was non-consanguineous, his brother suffered from intellectual disability, epilepsy and interatrial septum aneurysm. Patient's occipitofrontal circumference was 58,5 cm (>97°c). He presented strabismus, antiverse nares, long philtrum, fleshy lips. The patient was partially cooperative, presented hypomimic face, rest tremor at right hand, rigidity and bradikynesia predominant in right limbs. He walked in shuffling gate with reduced arm swing in both sides. 123I-FP-CIT SPECT imaging showed decreased tracer uptake in both the striatum bilaterally. A brain MRI scan displayed corpus callosum hypoplasia. The neuropsychological evaluation revealed a globally poor cognitive performance at the frontal battery, and cognitive slowing. Routine laboratory work ups were unremarkable. A levodopa challenge test showed no improvement on the Unified Parkinson's Disease Rating Scale motor scores. Poor response to long-term L-dopa therapy was observed. The molecular analysis for fragile -X syndrome (FMR1 gene) and array-CGH resulted normal. Next generation sequencing of customized panel targeting 63 genes associated with neurodevelopmental disorders and macrocephaly detected variant c.13783C>T (p.Gln4595Ter) in heterozygosis of DYNC1H1 gene.

Conclusions: Unlike a previous described case with DYNC1H1 mutation and parkinsonism [6], our patient was unresponsive to the dopaminergic therapy and showed corpus callosum hypoplasia. The mutation found has never been described before. Further studies are required to define the effect of this mutation and its possible causative role in parkinsonism.

References:

[1] MB Harms, P Allred, R Gardner Jr, JA Fernandes Filho, J Florence, A Pestronk et al. Dominant spinal muscular atrophy with lower extremity predominance: linkage to 14q32. Neurology. 2010;75:539–46.
[2] MG Marzo, JM Griswold, KM Ruff, RE Buchmeier, CP Fees, SM Markus. Molecular basis for dyneinopathies reveals insight into dynein regulation and dysfunction. Elife. 2019;8:e47246.
[3] AV Strickland, M Schabhuttl, H Offenbacher, M. Synofzik, NS Hauser, M. Brunner-Krainz et al. Mutation screen reveals novel variants and expands the phenotypes associated with DYNC1H1. J Neurol. 2015;262:2124–34.

[4] MN Weedon, R Hastings, R Caswell, W Xie, K Paszkiewicz, T Antoniadi et al. Exome sequencing identifies a DYNC1H1 mutation in a large pedigree with dominant axonal Charcot-Marie-Tooth disease. Am J Hum Genet. 2011;89:308–12.
[5] MH Willemsen, LE Vissers, MA Willemsen, BW van Bon, T Kroes, J de Ligt et al. Mutations in DYNC1H1 cause severe intellectual disability with neuronal migration defects. J Med Genet. 2012;49:179–83.
[6] K Szczałuba, K Szymańska, M Rydzanicz, E Ciara, A Walczak, D Piekutowska-Abramczuk, J Kosińska, A Jacoszek, K Czerska, A Biernacka, M Laure-Kamionowska, P Gasperowicz, E Pronicka, R Płoski. A de novo loss-of-function DYNC1H1 mutation in a patient with parkinsonian features and a favourable response to levodopa. Clin Genet. 2018 May;93(5):1107-1108.

P44

Clinical and instrumental characterization of GBA-related Parkinson's disease: focus on cardiovascular and sudomotor autonomic dysfunction and other non-motor features. Does the type of mutation matter?

Giulia Straccia [1,2*], G. Devigili[1*], A. Fedeli[1], E. Cereda[3], S. Prioni[1], E. Bocchi[1], S. Piacentini[1], S. Bonvegna[1], A.E. Elia[1], N.G. Andreasi[1], L.M. Romito[1], B. Garavaglia[4], R. Eleopra[1§], R. Cilia[1§]

**These authors contributed equally to this work*
§These authors share senior authorship"

[1]Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Department of Medical Sciences and Advanced Surgery, University of Campania "Luigi Vanvitelli", Napoli, Italy
[3]Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[4]Medical Genetics and Neurogenetics Unit, Foundation IRCCS Carlo Besta Neurological Institute, Milan, Italy

Background and aims: Some non-motor features (e.g. dementia) present more frequently in glucocerebrosidase-associated Parkinson's disease (GBA-PD). What is the autonomic profile in GBA-PD compared to PD non-carriers (iPD)? Is there any difference between carriers of severe (GBA-SM) *vs.* mild (GBA-MM) mutations?

Methods: Motor and non-motor features, including instrumental evaluation of cardiovascular and sudomotor autonomic functions, were compared between 21 GBA-PD (11 GBA-SM, 10 GBA-MM) and 24 iPD of similar sex, age and disease duration. Autonomic tests were additionally compared those of Dementia with Lewy Bodies (DLB, n=7).

Results: GBA-PD had greater motor complications and worse non-motor symptoms (mainly GBA-SM) than iPD, including orthostatic hypotension, sweat disturbances, pain, and cognitive dysfunction (mainly attentive/executive tasks, verbal memory, visuo-spatial abilities). At cardiovascular autonomic testing: (1) heart rate variability and blood pressure (BP) responses during phase IV of Valsalva Maneuver were lower in GBA-PD; (2) BP response during isometric exercise was selectively impaired in GBA-SM; (3) the pattern of baroreflex dysfunction at tilt test overlapped between GBA-PD and DLB (occurring earlier in DLB) and differed from iPD; (4) GBA-PD had reduced sweat output at the Dynamic Sweat Test. The severity of cardiac denervation in GBA-PD was intermediate between iPD and DLB.

Conclusions: Our data support the notion that GBA-PD is characterized by a more widespread pathology than iPD, with a greater impairment of cardiac parasympathetic system and of cardiac, muscular and sudomotor sympathetic system. Concerning cardiac denervation, GBA-PD places midway in the continuum between iPD and DLB, with GBA-SM (mainly L444P) more similar to DLB.

P45

Oligomeric α-Synuclein and SNARE complex proteins in peripheral neural-derived extravesicles (NDEs) differentiate Parkinson's disease from healthy controls

Mario Meloni[1], C. Agliardi[1], F.R. Guerini[1], M. Zanzottera[1], F.L. Saibene[1], A.V. Milner[1], J. Navarro[1], M. Clerici[1,2]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Introduction: Blood-based biomarkers are needed to be used as easy, reproducible, and non-invasive tools for the diagnosis and prognosis of chronic neurodegenerative disorders including Parkinson's Disease (PD). In PD, aggregated toxic forms of α-Synuclein (α-Syn) accumulate within neurons in the brain and cause neurodegeneration; α-Syn interaction with SNARE proteins also results in synaptic disfunction [1].

Objective: The objective of this study was to measure oligomeric α-Syn and presinaptic SNARE complex proteins (STX-1A; VAMP-2 and SNAP-25) levels in peripheral neural derived extravesicles (NDEs) in a group of PD patients and sex- and age-matched healthy controls (HC).

Methods: NDEs were isolated from peripheral serum samples of 32 PD patients and 40 HC by immunocapture with L1CAM antibody. Oligomeric α-Syn, SNAP-25, VAMP-2 and STX-1A levels were measured in NDEs protein extracts by sandwich enzyme-linked immunosorbent assay (ELISA).

Results: Oligomeric α-Syn was significantly augmented whereas STX-1A and VAMP-2 were significantly reduced in NDEs of PD patients compared to HC ($p < 0.001$ in all cases). ROC curve analyses confirmed the discriminatory ability of NDEs oligomeric α-Syn, STX-1A and VAMP-2 levels to distinguish between PD patients and HC. Oligomeric α-Syn NDEs concentration also positively correlated with disease duration and severity of PD.

Conclusions: These results are promising and confirm that NDEs cargoes likely reflect core pathogenic intracellular processes in their originating brain cells and could serve as novel easily accessible biomarkers. Further studies are needed to confirm these results and eventually for testing drug treatments and rehabilitation programs.

References

[1] Bong-Kyu Choi et al. Proc Natl Acad Sci U S A. 2013 Mar 5; 110(10): 4087–4092.

P46

Prokineticin-2 levels are increased in serum of patients with Parkinson's disease

Tommaso Schirinzi[1], D. Maffei[2], N.B. Mercuri[1,3], R. Lattanzi[2], C. Severini[4]

[1]Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]Department of Physiology and Pharmacology "Vittorio Erspamer", Sapienza University of Rome, Rome, Italy
[3]IRCCS Fondazione Santa Lucia, Rome, Italy
[4]Department of Biochemistry and Cell Biology, National Research Council of Italy, Rome, Italy

Introduction: Prokineticin-2 (PK2) is a chemokine involved in many CNS functions. Parkinson's disease (PD) animal models showed that PK2 is highly expressed in early phases of nigrostriatal degeneration to mediate a neuroprotective response. However, to date, there are no data from PD patients.

Objective: To perform a pilot assessment of PK2 in serum of PD patients in order to estimate its value in clinical perspective.

Methods: PK2 levels were measured in serum of 31 PD patients and 14 control subjects, also providing ROC curve analysis. In the PD group, a correlation analysis was run with main clinical parameters, including UPDRS III and Hoehn and Yahr scale, MMSE adjusted score, Non Motor Symptoms Scale, and levodopa equivalent daily dose. In five patients the associations with CSF levels of lactate, albumin CSF/serum ratio, amyloid-β-42, total-tau and phosphorylated-tau were also explored.

Results: Serum PK2 was significantly higher in PD patients (mean±dev.st.: 6.3±3.6 ng/ml) than controls (3.1±1.7), and differentiated the groups with moderate accuracy (AUC=0.75; Sensitivity=71%; Specificity=64%). Serum PK2 levels were directly associated with amyloid-β-42 (R=0.96, p=0.008), even independently from age and sex; moreover, an inverse association with lactate resulted (R= -0.89, p=0.04).

Conclusions: We demonstrated that PK2 pathway was activated at systemic level in PD patients, probably in a defensive manner. These findings, although preliminary, focus attention on PK2 in PD either as a disease biomarker of early neuronal damage or as a novel target for disease-modifying treatments. Future studies are now needed for confirmation.

P47

Corticobasal syndrome and Parkinson's disease at the beginning: usefulness of different asymmetrical patterns for early diagnosis

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

Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, Catania, Italy

Introduction: Differential diagnosis between Parkinson's Disease (PD) and Cortico-basal syndrome (CBS) could be challenging, especially at the early stage, due to the asymmetric onset of the diseases [1]. Despite the clinical overlap, the anatomical circuits involved in the occurrence of these disorders are different.

Objectives: To evaluate R2 Blink Reflex Recovery Cycle (R2BRRC) and cortical thickness in drug-naïve PD patients and in CBS patients for characterizing pathophysiological mechanisms underlying these conditions.

Methods: Patients with diagnosis of PD and CBS were recruited. R2BRRC was evaluated bilaterally at interstimulus intervals (ISIs) of 100-150-200-300-400-500-750 ms. Asymmetry index (AI) of R2BRRC for each ISI was computed [2]. Patients underwent a structural brain MRI using a 3-D T1-weighted and cortical thickness and MRI-AI was calculated.

Results: Fourteen drug-naïve PD patients and 10 patients with early CBS diagnosis were enrolled. R2BRRC of PD patients showed an increased brainstem excitability for less affected side (LAS) stimulation at ISIs of 100 and 150 ms ($p<0.001$) compared to most affected side (MAS), whereas no differences between LAS and MAS were found in CBS. R2BRRC-AI at ISI of 100 ms showed significant difference between groups, being higher in PD. Cortical thickness analysis showed significant differences between groups in left medialorbitofrontal, superiorfrontal and superiorparietal gyri, and conversely, MRI-AI was significantly higher in CBS group.

Conclusions: Drug-naïve PD patients exhibited an asymmetric pattern of brainstem excitability, compared to CBS. Conversely, CBS patients showed an asymmetric pattern of cortical atrophy. This opposite pattern of neurophysiological and structural abnormalities involving cortical and subcortical brain structures could highlight the different pathophysiological mechanisms underlying these neurodegenerative disorders

References:

[1] M.M. Correia, T. Rittman, C.L. Barnes, I.T. Coyle-Gilchrist, B. Ghosh, L.E. Hughes, J.B. Rowe. Towards accurate and unbiased imaging-based differentiation of Parkinson's disease, progressive supranuclear palsy and corticobasal syndrome. Brain Commun. 2020;2(1):fcaa051. doi: 10.1093/braincomms/fcaa051.

[2] G. Sciacca, G. Mostile, I. Disilvestro, G. Donzuso, R. Manna, G. Portaro, C. Rascunà, S. Salomon, F. Drago, A. Nicoletti, M. Zappia. Asymmetry index of Blink Reflex Recovery Cycle differentiates Parkinson's disease from atypical Parkinsonian syndromes. J Neurol. 2020 Jun;267(6):1859-1863. doi: 10.1007/s00415-020-09900-6.

P48

Dysfunction of EEG resting-state networks in *de novo* Parkinson's disease patients

Matteo Conti[1], R. Bovenzi[1], R. Cerroni[1], E. Garasto[1], M. Pierantozzi[1], M. Spanetta[2], N.B. Mercuri[2], A. Stefani[1]

[1]Parkinson Centre, Department of System Medicine, Policlinico Tor Vergata, Rome, Italy
[2]Neurology Unit, Department of System Medicine, Policlinico Tor Vergata, Rome, Italy

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by a progressive synucleinopathy that should begin in the brainsteam and spread rostrally. However, theories of a primary subcortical pathology are not easy to reconcile with PD heterogeneous clinical manifestations. Dysfunction of selective brain networks could explain this phenomenon. Connectivity analysis may be performed by functional magnetic resonance imaging (fMRI), but also by electroencephalography (EEG) [1], with the advantage of direct measuring of electrical activity with high temporal resolution.

Objective: To analyze the differences in EEG resting-state networks (RSNs) between *de novo* PD patients and healthy controls.

Methods: 21 PD patients and 20 controls were, so far, enrolled and matched. The analyses used custom-written scripts on the Matlab platform, combined with high-level functions of Fieldtrip toolbox [2]. First, we proceeded to the EEG cortical source localization, through the resolution of forward and inverse problems. Secondly, we calculated the connectivity matrices in the five frequency bands of the EEG (δ, θ, α, β, γ), based on the imaginary part of coherency [3].
Then, we applied the Newman clustering algorithm to subdivide the connectome into nonoverlapping networks. Finally, we compared RSNs between PD patients and controls through T-test.

Results: We identified four main RSNs among those classically described in literature (default-mode, visual, sensorimotor, frontoparietal networks). We found severe dysfunctions in *de novo* PD patients compared to controls in sensorimotor, default-mode and frontoparietal networks, mainly in θ and α frequency bands. No differences were observed in visual network.

Conclusions: This study showed that PD is associated with dysfunctions of RSNs since the earliest stages. We indeed demonstrated that not only sensorimotor network, as we expected, but also default-mode and frontoparietal networks are altered. These results contrast with the ascendent theory of the disease and can be useful to better understand the pathophysiology of PD.

References

[1] X Zhang, X Lei, T Wu, and T Jiang, "A review of EEG and MEG for brainnetome research", *Cogn. Neurodyn.*, vol. 8, no. 2, pp. 87–98, 2014, doi: 10.1007/s11571-013-9274-9.
[2] R Oostenveld, P Fries, E Maris, and J M. Schoffelen, "FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data," *Comput. Intell. Neurosci.*, vol. 2011, 2011, doi: 10.1155/2011/156869.
[3] G Nolte, O Bai, L Wheaton, Z Mari, S Vorbach, and M Hallett, "Identifying true brain interaction from EEG data using the imaginary part ofcoherency," *Clin. Neurophysiol.*, vol. 115, no. 10, pp. 2292–2307, 2004, doi: 10.1016/j.clinph.2004.04.029.

P49

Cortical motor network excitability changes in Parkinson's disease

Giorgio Leodori[1,2], M.I. De Bartolo[1], A. Guerra[1], A. Fabbrini[2], L. Rocchi[3,4], A. Latorre[3], G. Paparella[1], D. Belvisi[1,2], A. Conte[1,2], K.P. Bhatia[3], J.C. Rothwell[3], A. Berardelli[1,2]

[1]IRCCS Neuromed, Pozzilli (IS), Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, University College London, London, UK
[4]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy

Background: Bradykinesia in Parkinson's disease (PD) reflects changes in the basal ganglia-thalamo-cortical circuit converging on the primary motor cortex (M1) and supplementary motor area (SMA).

Objectives: To assess motor cortical network excitability in PD patients and their relation to dopaminergic status and bradykinesia.

Methods: We compared transcranial magnetic stimulation-evoked cortical potentials (TEPs) from the M1 and SMA between 15 PD patients tested off (OFF) and on (ON) medication and 12 healthy controls (HCs) and investigated possible correlations with bradykinesia tested clinically.

Results: OFF PD patients compared to HCs had smaller P30 responses from the M1s contralateral (M1+) and ipsilateral (M1-) to the most bradykinetic side, reduced N45 from the M1+, and increased N40 from the SMA. OFF PD patients showed a significant correlation between the amplitudes of the M1+ P30 and the SMA N40. Dopaminergic therapy normalized the amplitude of the M1+ and M1- P30 responses as well as the SMA N40. We found a positive correlation between M1+ P30 amplitude and bradykinesia in OFF PD patients.

Conclusions: Changes in M1 P30 and SMA N40 in PD suggest that M1 excitability is reduced on both sides while SMA excitability is increased. The effect of dopaminergic therapy and the clinical correlation suggest that these cortical changes may reflect abnormal basal ganglia-thalamocortical activity related to bradykinesia. The N45 reduction in PD patients suggests additional excitability changes in the most affected M1, which are dopamine independent and not directly correlated with bradykinesia. TMS-EEG provides a novel insight into motor cortical network changes related to the pathophysiology of PD.

P50

Interrogating cortical excitability with TMS-EEG to explain motor impairment in patients with Parkinson disease

Angela Comanducci[1], A. Mazza[1], C.C. Derchi[1], F.L. Saibene[1], M.A. Colombo[2], A.V. Milner[1], A. Viganò[1], F. Baglio[1], J. Navarro[1], M. Meloni[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milan, Italy

Introduction: In recent years, a novel brain-stimulation technique which combines MRI-navigated TMS with high-density EEG (TMS-EEG) has emerged as a powerful tool to non-invasively probe brain circuits, allowing for the assessment of several cortical properties such as excitability and connectivity and adding a new dimension to the functional study of the human brain. Indeed, a previous TMS-EEG study unveiled the change of excitability induced by an acute dopamine intake in the premotor cortex of Parkinson's disease (PD) patients [1].

Objective: To investigate the TMS-evoked potentials (TEP) obtained by targeting occipital and premotor cortex in PD patients without dementia and to evaluate their association with motor impairment and cognitive performance.

Methods: 12 subjects with a diagnosis of PD according to the MDS Clinical Diagnostic Criteria were enrolled. We measured the EEG responses to TMS obtained by targeting the supplementary motor area and occipital cortex. We also recorded resting high-density EEG both in the eyes open and closed conditions. In addition to the MDS-UPDRS Part III, a comprehensive neuropsychological assessment were performed. TEP were analyzed to compute latency, area and slope of statistically significant peaks with respect to the baseline. We also detected alpha peak and power of resting EEG. A correlation analysis of neurophysiological measures, neuropsychological scores and MDS-UPDRS Part III was performed.

Results: We found that the MDS-UPDRS Part III is significantly positively associated with the latency of occipital TEP and negatively associated with the latency of premotor TEP. Furthermore, the performance at Rey-Osterrieth complex figure is negatively associated with eyes-closed alpha peak in resting EEG.

Conclusions: Our findings support the use of TMS-EEG as a non-invasive tool to probe the role of different cortical regions in the pathophysiology of PD and further disclose the functional impairment of premotor and occipital cortical areas with potential implications for rehabilitation targets.

References:
[1] S. Casarotto. Brain Stimul. Jan-Feb 2019;12(1):152-160

P51

Fatigue in Parkinson's disease: neurophysiological correlates

Ilaria Di Vico[1], G. Cirillo[1,2], M. Venturelli[1], M.E. Andani[1], F. Morgante[3,4], M. Tinazzi[1]

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Division of Human Anatomy - Laboratory of Morphology of Neuronal Network, Department of Mental, Physical Health and Preventive Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy
[3]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's, University of London, London, U.K.
[4]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy

Background: Fatigue is frequent and highly disabling in neurological illnesses and occurs in 50% of patients with Parkinson's disease (PD) [1-2]. It is an overwhelming sense of tiredness, lack of energy or need for increased effort and it negatively impacts quality of life [1-3]. Yet, its pathophysiology is still far to be understood and no objective biomarkers exist. In Multiple Sclerosis (MS), fatigue was correlated to the lack of pre-movement facilitation (PMF), implying a dysfunction of movement preparation [4].

Aim: We tested the hypothesis that reduced pre-movement facilitation (PMF) could be an objective biomarker of fatigue in PD.

Methods: In this preliminary study, we enrolled 10 patients with a diagnosis of PD in the absence of cognitive impairment or neuropsychiatric symptoms and 10 healthy subjects (HS). Fatigue severity was measured with the Fatigue Severity Scale (FSS). We assessed PMF during a simple reaction time (RT) motor task using transcranial magnetic stimulation (TMS). RT was calculated as the mean time for electromyography (EMG) onset (thumb abduction) after a visual go signal. TMS was delivered within RT at 150, 100 and 50 ms.

Results: In PD, MEP amplitude increased significantly, compared to MEP at rest, only when TMS pulse was delivered at 50 ms (P=0,013) and not at 100 or 150 ms. In HS, MEP amplitude significantly increased during all the timings of the TMS protocol (all, p£0.002). In PD, the mean amplitude of MEP obtained at 50, 100 and 150 ms before the estimated EMG burst in a simple RT paradigm, resulted inversely correlated with FSS values (p=0.03; R=-0.27; Rsq=0.07).

Conclusions: PD patients showed reduced PMF compared to HS. Moreover, reduced PMF was greater in PD patients with higher degrees of fatigue, suggesting that it might be associated to a dysfunction in the cerebral circuits involved in the planning and preparation of the movement.

References:
[1] B.M. Kluger, K. Herlofson, K.L. Chou, J.S. Lou, C.G. Goetz, A.E. Lang, D. Weintraub, J. Friedman .2016. Parkinson's disease-related fatigue: A case definition and recommendations for clinical research. Mov. Disord. 31, 625–631. https://doi.org/10.1002/mds.26511.
[2] B.M. Kluger, L.B. Krupp, R.M. Enoka. 2013. Fatigue and fatigability in neurologic illnesses. Neurology 80, 409–416.

[3] F. Morgante, V. Dattola, D. Crupi, M. Russo, V. Rizzo, M.F. Ghilardi, C. Terranova, P. Girlanda, A. Quartarone. 2011. Is central fatigue in multiple sclerosis a disorder of movement preparation? J. Neurol. 258, 263– 272. https://doi.org/10.1007/s00415-010-5742-x.

P52

Neural oscillations modulation during working memory in premanifest and early Huntington's disease

Gaia Bonassi[1], M. Semprini[2], P. Mandich[3,4], L. Trevisan[4], R. Marchese[3], G. Lagravinese[3,4], F. Barban[2,5], E. Pelosin[3,4], M. Chiappalone[2,5], D. Mantini[6,7], L. Avanzino[3,8]

[1]S.C. Medicina Fisica e Riabilitazione Ospedaliera, ASL4, Azienda Sanitaria Locale Chiavarese, Italy
[2]Rehab Technologies, Istituto Italiano di Tecnologia, Genoa, Italy
[3]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[4]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[5]Dept. of Informatics, Bioengineering, Robotics and Systems Engineering, University of Genoa, Genoa, Italy
[6]Research Center for Motor Control and Neuroplasticity, Leuven, Belgium
[7]Brain Imaging and Neural Dynamics Research Group, IRCCS San Camillo Hospital, Venice, Italy
[8]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy

Objective: To identify neuronal oscillations in specific frequency bands in patients with Huntington's disease (HD), pre-symptomatic and early symptomatic, and in a control group, during a working memory (WM) task with high-density electroencephalography (hdEEG) coupled to source localization.

Background: We recently [1] demonstrated specific spectral signatures associated with updating of memory information, working memory maintenance and readout, with relatively high spatial resolution by means of hdEEG. WM is the ability to keep in mind information and retrieve them after a short period of time, and is one of the first cognitive functions to decline in early-HD and also in pre-HD [2].

Methods: Participants had to respond to an n-back WM task (with n = 2, 3), with a button press when the currently presented letter (stimulus) corresponded to the letter presented n trials earlier (probe). We examined modulation of neural oscillations during the task by event-related desynchronization and synchronization (ERD/ERS) of θ, β, gamma low, γLOW and γHIGH EEG bands in a-priori selected large fronto-parietal network, including the insula and the cerebellum. Results: (i) Reduced θ oscillations in HD with respect to controls in almost all the areas of the WM network during the update and readout phases; (ii) Reduced β oscillations in HD with respect to controls in DLPFC-L and InsCl-L; (iii) For γHIGH oscillations, HD showed decreased oscillation compared to controls during maintenance in the PFC-R in both 2-back and 3-back tasks and decreased γHIGH oscillation in PM L and PPC L during the 3-back task, in the maintenance phase. Finally, in HD patients, brain oscillations during WM task correlated with CAG repeat length.

Conclusions: HD patients showed reduced phase-specific modulation of oscillations, even in the presence of preserved dynamic of modulation. Correlations between phase-specific modulations of neural oscillations and CAG repeat lengths suggest that decreased EEG oscillations are linked to HD
pathology.

References:

[1] M. Semprini, G. Bonassi, F. Barban, E. Pelosin, R. Iandolo, M. Chiappalone et al. Modulation of neural oscillations during working memory update, maintenance, and readout: An hdEEG study .Hum Brain Mapp. 2020.

[2] A.D. Lawrence, J.R. Hodges, A.E. Rosser, A. Kershaw, C. Ffrench-Constant, D.C.Rubinsztein et al. Evidence for specific cognitive deficits in preclinical Huntington's disease. Brain. 1998;121(7):1329–41.

P53

Molecular chaperones and Parkinson's disease: exploring the role of clusterin in the dynamic process of alpha-synuclein aggregation

Ileana Ramazzina[1,2,3], L. Chiara[1,4], F. Rizzi[1,2,3]

[1]Department of Medicine and Surgery, University of Parma, Parma, Italy
[2]Centre for Molecular and Translational Oncology (COMT), University of Parma, Parma, Italy
[3]Biostructures and Biosystems National Institute (INBB), Rome, Italy
[4]B-Cell Neoplasia Unit, Division of Experimental Oncology, San Raffaele Scientific Institute, Milan, Italy

Introduction: The integrity of the proteostasis network (PN) is essential to assure cell viability, as its failure leads to abnormal protein aggregation that is associated with different human neurodegenerative disease, e.g. Parkinson's disease (PD). Under proteostasis impairment, α-Synuclein (αSyn) forms toxic aggregates in neurons that represent the hallmarks of PD [1]. Key effectors of PN are molecular chaperones and hence the modulation of their expression represents a compelling PD therapeutic strategy [2]. Clusterin (CLU) is chaperone predominantly expressed in brain and reproductive tissues. At present, the role of CLU has been characterized in relation to Alzheimer's disease [3]. However, its role in PD has not yet been extensively elucidated.

Objective: The focus of the research was to explore the involvement of CLU in the cellular response caused by both αSyn up-regulation and aggregation process.

Methods: We used the SH-SY5Y neuron-like cells overexpressing αSyn, either in absence or in presence of MG132, to induce mild or strong proteostasis impairment. In these experimental models, we performed CLU loss-of-function studies, by using CLU siRNA sequences.

Results: We demonstrated that the overexpression of αSyn causes up-regulation of CLU expression, without affecting Hsp27, Hsp70 and Hsp90 levels, which are the chaperones recognized to be able to counteract αSyn burden. Following MG132 treatment, we showed an increase of CLU levels in the fraction where oligomeric and high molecular weight forms of αSyn were detected. We also provided
evidence that CLU down-regulation favors or exacerbates αSyn aggregation. Finally, we found that CLU and αSyn co-localize inside the cell and that the two proteins exhibit a direct molecular interaction.

References

[1] Goedert et al., 2017. J Parkinsons Dis; 7:S53-S71
[2] Brundin et al., 2017. Exp Neurol; 298:225-235
[3] Foster et al., 2019. Front Neurosci; 13, 1-27

P54

Assessment of cardiovascular dysautonomia in GBA-associated Parkinson's disease

Tiziana De Santis[1], L. Bresciani[2], A. Cocco[1], P. Amami[1], A. Albanese [1,2]

[1]IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy
[2]Humanitas University, Pieve Emanuele, Milano, Italy

We aimed to assess whether the prevalence of cardiovascular dysautonomia is higher in Parkinson's disease (PD) patients carrying heterozygous β-glucocerebrosidase (GBA) mutations compared to non-mutated PD (NM-PD) patients and to establish the relative involvement of the sympathetic or parasympathetic cardiac autonomic branches. GBA mutations are the most common genetic risk factor predisposing to PD. PD patients carrying GBA mutations (GBA-PD) present with several non-motor features, including cognitive decline, depression, anxiety, hallucinations, REM sleep behavior disorder (RBD) and dysautonomia [1, 2]. Cardiovascular dysautonomia is one of the most disabling manifestations of autonomic dysfunction. An increased prevalence of cardiovascular dysautonomia in GBA-PD patients has been suggested by studies based on clinical questionnaires or clinical rating scales. These data need to be confirmed via clinical laboratory testing.
Thirty-four patients with clinically definite PD were included in the study: one group encompassed 17 GBA-PD patients, the other one 17 non-mutated PD patients (NM-PD). The two groups were matched for sex, age at onset, disease duration and total levodopa equivalent daily dose (LEDD). All patients underwent a standard laboratory assessment to evaluate the cardiovascular autonomic function: head-up tilt test, isometric hand grip and the Valsalva overshoot allowed to assess cardiac sympathetic function; the cold test, deep breathing and the Valsalva ratio were used to evaluate cardiac parasympathetic function. Between group comparisons were performed by the Fisher's exact test for categorical variables and by the Mann Whitney test for continuous variables. The statistical level was set at $p < 0.05$.
There were no between-group statistical differences either in tests of sympathetic or of parasympathetic function. GBA-PD patients presented a tendency to higher prevalence of pathological responses compared to NM-PD patients in all tests assessing cardiac sympathetic function. These data are considered preliminary, as we are continuing to recruit patients. They do not suggest a difference between the GBA-PD group and the wild-type NM-PD group.

References

[1] K Brockmann, K Srulijes, AK Hauser *et al.* GBA-associated PD presents with nonmotor characteristics. *Neurology*. 2011 77: 276-280.
[2] S Jesus, I Huertas, I Bernal-Bernal *et al.* GBA Variants Influence Motor and Non-Motor Features of Parkinson's Disease. *PLoS One*. 2016 11: e0167749.

P55

Circadian rhythm in Parkinson's disease, from chronotype to phenotype: a clinical and biological study

Massimo Marano[1,2], F. Motolese[1], M. Rossi[1], A. Magliozzi[1], M. Iannizzotto[1], G. Sergi[1], A. Casamassa[3], A.L. Vescovi[3], V. Di Lazzaro[1], J. Rosati[3]

[1]Neurology, Neurophysiology and Neurobiology Unit; University Campus Bio-Medico of Rome, Rome, Italy
[2]Fondazione Alberto Sordi, Rome, Italy
[3]CSS Mendel Institute of Human Genetics, IRCCS Casa Sollievo della Sofferenza, Rome, Italy

Introduction: Alterations of the circadian rhythm might play a role in the pathobiology of neurodegenerative diseases. Symptoms of sleep and wakefulness impairment are prominent in Parkinson's disease (PD), being also crucial disease milestones. However, the relationship between the circadian cycle and the clinical and biological disease profile has not been fully elucidated so far [1].

Objective: To explore the relationship between the PD chronotype and the phenotype in a clinical and biological translational setting.

Methods: 50 non demented PD patients entered a cross-sectional and longitudinal study collecting data on chronotype (MEQ-SA), sleep and wakefulness quality (PDSS, RBDQ, ESS), motor and non-motor performances (UPDRS, Hoehn & Yahr, NMSQ, PDQ39), heart rate variability as an index of autonomic nervous system functioning and prospective PD associated events (eg, falls). Five samples of skin fibroblasts obtained by PD patients were cultured and compared to 5 matched controls in a case-control study exploring the expression of the circadian rhythm genetic regulators and the cell growth [2].

Results: PD patients manifested 2 main chronotypes: "moderate morningness" (n=28) and "intermediate" (n=16). No clear association intercurred between the chronotype, the sleep and the wakefulness quality. The "intermediate" group showed (i) a higher Hoehn & Yahr and a worse disease profile overall in various motor and non-motor parameters, (iii) a higher rate of falls after 1 month of follow-up and (iii) a lower HRV parasympathetic activity. Cultured fibroblasts showed a different pattern of expression of the CLOCK-BMAL1 system compared to controls.

Conclusions: Our observations suggest that there is a fascinating interplay between the chronotype and the PD phenotype, which deserves further attention. Moreover, the presence of an altered CLOCK-BMAL1 pattern in fibroblasts is a cue that points toward a role of the circadian rhythm deregulation in the molecular pathobiology of the disease. A study replication on neuronal tissue is warranted.

References:
[1] Pacelli C, et al., 2019. Int J Mol Sci. 2019;20 (11):2772.
[2] Leng Y, et al. 2020 JAMA Neurol. 77 (10):1270-1278.

P56

Effect of smell and taste stimuli on pain perception in patients with chronic oral burning pain: an exploratory study

Angela Sandri[1], M.P. Cecchini[2], A. Zanini[2], R. Nocini[3], F. Boschi[4], G. Zanette[5], M. Fiorio[6], M. Tinazzi[1]

[1]Neurology Unit, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Anatomy and Histology Section, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]Otolaryngology Section, Department of Surgery, Dentistry, Paediatrics and Gynaecology, University Hospital of Verona, Verona, Italy
[4]Department of Computer Science, University of Verona, Verona, Italy
[5]Italian Scientific Society of Clinical Hypnosis in Psychotherapy and Humanistic Medicine, SIPMU, Verona, Italy
[6]Movement Sciences Section, Department of Neurosciences, Biomedicine and Movement Sciences, University Hospital of Verona, Verona, Italy

Introduction: Oral burning pain is usually associated to the "Burning Mouth Syndrome", a painful status where the oral pain has no causative reasons [1]. It mainly affects menopausal and post-menopausal women, and the incidence and prevalence are not well-established [2]. Growing evidence on multisensory integration states that different smell and taste substances exert an effect on experimentally induced pain, but in a clinical context results are still preliminary [3]. In patients with chronic oral burning pain, to our knowledge, a systematic evaluation is absent.

Objective: We decided to perform an exploratory study on chronic oral burning pain patients to evaluate multisensory interaction, namely the effect of different olfactory and gustatory substances on pain perception.

Methods: Twenty-two patients with chronic oral burning pain were tested with different olfactory and gustatory substances, of pleasant, neutral and unpleasant valences, in multisensory interaction. Pain intensity and unpleasantness were collected on a numerical rating scale from 0 to 10 at baselines and immediately after each substance administration, similar to our previous works [4,5].

Results: The unpleasant smell and taste stimuli increased the perception of pain unpleasantness compared to pleasant and neutral ones. No effect was detected on pain intensity. Pain modulation for both intensity and unpleasantness correlates with the subjectively valence of the smell substances: the more they were disliked, the more they increased the pain, and the more they were liked the more they decreased the pain.

Conclusions: These preliminary data highlight that the valence of a chemosensory stimulus might impact chronic oral burning pain perception. Future studies are necessary to unravel the role of chemosensory stimuli on this chronic and disabling pain condition.

References

[1] Headache Classification Committee of the International Headache Society. The international Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38(1): 1-211.
[2] Teruel and Patel 2019. Gen Dent; 67(2), 24-29.

[3] Sandri et al., 2021. Pain Ther; 10: 245-268.
[4] Riello et al., 2019. Eur J Pain; 23(10): 1790-1800.
[5] Cecchini et al., 2020. Eur J Pain; 24(10): 1946-1955.

P57

Structural and functional cerebellar alterations in Parkinson's disease with postural instability and gait disorders

Andrea Gardoni[1], E. Sarasso[1], S. Basaia[1], M.A. Volontè[2], M. Filippi[1-5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Neurology Unit, RCCS 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

Introduction: Brain structures other than basal ganglia are likely to be involved in the pathophysiological process of Parkinson's disease (PD). The role of cerebellum in PD has been explored during motor tasks involving the hand, while few studies investigated its activity during gait-simulating tasks and dual-task situations.

Objectives: This study aimed at assessing structural and task-based functional cerebellar alterations in PD patients with postural instability and gait disorders (PD-PIGD).

Methods: Twenty-one PD-PIGD patients and 23 age and sex-matched healthy controls underwent clinical, structural and functional MRI, including a motor-task (foot anti-phase movements) and a dual-task (foot anti-phase movements while counting backwards by three). Regional grey matter cerebellar volumes were assessed automatically using an atlas propagation and label fusion strategy based on the freely available human cerebellum template and probabilistic atlas (SUIT). FMRI images were co-registered with structural images and cerebellar fMRI analysis was performed.

Results: PD-PIGD patients showed reduced volumes in several cerebellar motor and non-motor areas relative to controls. During the fMRI motor-task, patients showed greater activation of cognitive cerebellar areas (lobule VI and crus I-II) relative to healthy subjects. During the fMRI dual-task, PD-PIGD showed increased activity of cognitive areas (crus II) and a reduced activity of motor areas (lobules I-IV). Structural alterations of cerebellum were correlated with the increased activity of cerebellar cognitive areas. Moreover, the increased recruitment of cognitive areas during the fMRI motor task correlated with a better motor performance in PD-PIGD patients.

Conclusions: The increased activity of non-motor cerebellar areas might be a consequence of grey matter atrophy or an attempt to compensate the functional failure of cerebellar motor areas. Structural and functional MRI metrics focusing on cerebellum are useful to characterize brain correlates of motor and dual-task abilities in PD-PIGD patients.

P58

Striatal dopamine transporter imaging in Parkinson's disease drug-naïve patients: focus on sexual dysfunction

Elena Contaldi[1,2], L. Magistrelli[3], I. Campini[1], C. Comi[1]

[1]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[2]PhD Program in Medical Sciences and Biotechnology, University of Piemonte Orientale, Novara, Italy
[3]PhD Program in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy

Introduction: Sexual dysfunction is one of the most disabling yet poorly investigated non-motor symptoms in PD [1]. Even though dopaminergic mechanisms have been involved in the pathogenesis, evidence from dopaminergic imaging studies is still lacking.

Objective: To evaluate whether the 123I-FP-CIT striatal uptake differs in Parkinson's disease (PD) drug-naïve patients with and without sexual dysfunction.

Methods: 20 drug-naïve newly diagnosed parkinsonian patients (9 females and 11 males, aged 66.4±7.8 years) underwent both 123I-FP-CIT SPECT and complete motor and non-motor symptoms
evaluation through UPDRS-III score, H&Y staging, Mini-Mental State Examination (MMSE), Addenbrooke's Cognitive Examination (ACE), Beck Depression Inventory (BDI)-II, Zung's Anxiety
Scale, and Non-Motor Symptoms Scale (NMSS). During regular follow-up visits, a diagnosis of idiopathic PD was established for all patients according to current criteria. Based on NMSS sexual function scores, we identified patients with (WSC, score ≥1) and without (NoSC, score=0) sexual concerns. The ratios of striatal to occipital binding for the entire striatum (tSBR), putamina, and caudate were calculated in the basal ganglia using the *BasGan* software [2].

Results: 8 WSC and 12 NoSC were identified. No statistically significant differences were found among groups regarding gender, age, H&Y, UPDRS-III, disease duration, scores in MMSE, ACE, Zung, BDI-II, and use of antidepressants. 123I-FP-CIT SPECT analysis revealed that WSC display significantly lower uptake values in the entire striatum (p=0.035), particularly in both putamina (p=0.029, p=0.023).

Conclusions: To the best of our knowledge, this is the first study exploring striatal DAT binding in relation to sexual symptoms in PD. These findings further suggest that nigrostriatal system denervation (especially involving the putamina) is a key feature of PD altered sexual behavior, probably by disrupting the connections to the medial preoptic area, the paraventricular nucleus, and the nucleus accumbens.

References:

[1] G. Meco, A. Rubino, N. Caravona, M. Valente. Sexual dysfunction in Parkinson's disease. Parkinsonism Relat Disord. 2008 Aug;14(6):451-6. doi: 10.1016/j.parkreldis.2007.10.008. Epub 2008 Mar 3. PMID: 18316235.
[2] P. Calvini, G. Rodriguez, F. Inguglia, A. Mignone, U.P. Guerra, F. Nobili. The basal ganglia matching tools package for striatal uptake semi-quantification: description and validation. Eur J Nucl Med Mol Imaging. 2007 Aug;34(8):1240-53. doi: 10.1007/s00259-006-0357-2.

P59

Incidental evidence of hypointensity in brain grey nuclei on routine MR imaging: when to suspect a neurodegenerative disorder?

Maurizio Morelli[1,2], A. Quattrone[1], G. Arabia[1,2], B. Vescio[3], M.G. Vaccaro[4], A. Mechelli[1], F. Rocca[4], A. Gambardella[1,4], A. Quattrone[2,4]

[1]Institute of Neurology, Department of Medical and Surgical Sciences, Magna Graecia University, Catanzaro, Italy
[2]Neuroscience Centre, Magna Graecia University, Catanzaro, Italy
[3]Biotecnomed, S.C.aR.L, Catanzaro, Italy
[4]Neuroimaging Research Unit, Institute of Molecular Bioimaging and Physiology, National Research Council, Catanzaro, Italy

Introduction: Deep grey nuclei of the human brain accumulate minerals both in aging and in several neurodegenerative diseases. Mineral deposition produces a shortening of the transverse relaxation time which causes hypointensity on magnetic resonance (MR) imaging. The physician often has difficulties in determining whether the incidental hypointensity of grey nuclei seen on MR images is related to aging or neurodegenerative pathology.

Methods: We investigated the hypointensity patterns in globus pallidus, putamen, caudate nucleus, thalamus and dentate nucleus of 217 healthy subjects (ages, 20-79 years; men/women, 104/113) using 3T MR imaging.

Results: Hypointensity was detected more frequently in globus pallidus (35.5%) than in dentate nucleus (32.7%) and putamen (7.8%). A consistent effect of aging on hypointensity ($p < 0.001$) of these grey nuclei was evident. Putaminal hypointensity appeared only in elderly subjects whereas we did not find hypointensity in the caudate nucleus and thalamus of any subject.

Conclusions: The evidence of hypointensity in the caudate nucleus and thalamus at any age or hypointensity in the putamen seen in young subjects should prompt the clinician to consider a neurodegenerative disease.

P60

Cognitive profiles based on MRI ventricular size measurements in patients with idiopathic normal pressure hydrocephalus and Alzheimer disease. Implications for a diagnostic approach

Roberta Terranova[1], A. Luca[1], G. Donzuso[1], G. Mostile[1,2], R. Manna[1], C. D'Agate[1], C. Terravecchia[1], C. Rascunà[1], C.E. Cicero[1], A. Nicoletti[1], M. Zappia[1]

[1]University of Catania, Department of Medical and Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Catania, Italy,
[2]Department of Neurology I.C., Oasi Research Institute-IRCCS, Troina (EN), Italy

Background and Aims: To evaluate the association between ventricular size measurements and cognitive performances in patients with cognitive complains validating measurements with confirmed clinical diagnosis.

Methods: We identified patients with cognitive impairment who underwent both standardized neuropsychological evaluation and MRI study demonstrating cerebral ventricular enlargement. Evans' Index (EI), Temporal Ratio (TR) and Parieto-Occipital Ratio (POR) were calculated based on neuroimaging. After the diagnostic workup, a diagnosis of idiopathic Normal Pressure Hydrocephalus (iNPH) or Alzheimer Disease (AD) was made. Considering discriminating cut-off! values of each index, cognitive performances between patients were compared. Sensitivity and specificity of computed indices in discriminating iNPH from AD were estimated.

Results: Fifty-two patients were identified. Regardless clinical diagnosis, 27 patients with normal EI had statistically-significant lower score on Rey Auditory Verbal Learning Test (RAVLT), both immediate ($p=0.22$) and delayed recall ($p<0.001$) as compared to 25 patients with abnormal EI. Thirteen patients with normal TR had statistically-significant lower score at the RAVLT-delayed recall ($p<0.027$) as compared to 38 patients with abnormal TR. No statistically-significant differences in cognitive performances were found between identified two groups on POR (8 pathological vs 44 normal). Twenty-six patients were diagnosed as iNPH (20 probable iNPH, 6 possible iNPH). Twenty-six patients received a diagnosed of probable AD. Sensitivity and specificity of MRI measures in differentiating iNPH vs AD were respectively: 84%(95%CI:65.1-95.6) and 87%(95%CI:60.6-93.4) for EI; 100%(95%CI:86.3-100) and 50%(95%CI:29.9-70) for TR; 30.7%(95%CI:14.3-51.8) and 100%(95%CI:86.7-100) for POR.

Conclusions: EI and TR measures differentiated amnestic patterns among study subjects. EI demonstrated the best accuracy in distinguish iNPH from AD.

P61

Sex differences in cortical hemodynamic response to levodopa in Parkinson's disease patients: a functional NIRS study

Gennarina Arabia[1], A. Quattrone[1], R. Vasta[2], V. Gramigna[2], G. Olivadese[2], M. Morelli[1], A. Gambardella[1], A. Quattrone[1]

[1]Clinica Neurologica, Università "Magna Graecia" di Catanzaro, Campus Germaneto, Catanzaro, Italia
[2]Unità di Neuroimmagini, Istituto di Bioimmagini e Fisiologia Molecolare, CNR, Campus Germaneto, Catanzaro, Italia

Objective: The aim of this study was to investigate sex differences in hemodynamic response of the cortical motor system after levodopa intake, in patients affected by Parkinson's disease (PD) with levodopa-induced dyskinesias (LID), by means of functional near-infrared spectroscopy (fNIRS).

Patients and Methods: Patients fulfilling UK Brain Bank criteria for PD, referring to the Movement Disorders Center of the University "Magna Graecia" of Catanzaro, were consecutively recruited. Main inclusion criteria were a) presence of LID; b) duration of levodopa treatment greater than 6 months; c) stable dosages of levodopa treatment for at least 4 weeks. All patients were evaluated by means of motor UPDRS and AIMS scale at baseline (T0), after 1 (T1), and 2 (T2) hours from levodopa intake. NIRS study was performed at the same time-points.

Results: Nine PD patients with LID were included. Four were females (age: 60.83 ± 4.17 years, mean ± SD) and five were males (age: 61.00 ± 14.00 years; p=0.978). In NIRS study, in men a gradual increase in oxygenated-hemoglobin (HbO) concentrations of motor cortex was observed at T1 and T2, in comparison to T0. By contrast, women showed a reduction in HbO concentrations at T1 in comparison to T0, followed by a return to baseline hemodynamic activation levels after 2 hours from levodopa intake.

Discussion and Conclusions: Our preliminary results of this fNIRS study showed a significant difference in the motor cortical haemodynamic responses to levodopa intake in male and female patients with PD and dyskinesias. Further studies on sex-disaggregated data to interpret differential cortical activation in PD are needed.

P62

Negative DAT-SPECT in old onset Parkinson's disease: an additional pitfall?

Giovanni Palermo[1], S. Giannoni[1], T. Depalo[2], D. Frosini[1,3], D. Volterrani[2], D. Paoli[1,3], U. Bonuccelli[3], R. Ceravolo[1,3]

[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]Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Introduction: Scans without evidence of dopaminergic deficit (SWEDD) refer to patients clinically diagnosed with Parkinson's disease (PD), but showing normal findings on dopamine transporter single-photon emission computed tomography (DATSPECT). SWEDD remains a heterogeneous and highly debated entity and there are some indications that a few patients with SWEDD could truly have PD implying that, at least in the early stage of PD, a DAT-SPECT scan may be normal. Interestingly, it is acknowledged that compensatory downregulation of DAT in the early stages of PD seems to be less efficient in older-onset than in young-onset patients. Recent findings suggesting that DAT-SPECT does not reflect either nigral cell bodies or striatal fibers of dopaminergic nigrostriatal neurons might improve our understanding of this phenomenon.

Methods: We report eight patients with old-age PD diagnosis (mean age at onset was 80.8±2.9 years), confirmed during a long-term clinical follow-up and with a positive response to levodopa in which baseline DAT-SPECT was normal both visually and semiquantitatively. Two subjects demonstrated an abnormal scan when repeated later.

Conclusions: Our study suggests that old onset PD could account for some patients with SWEDD because of the co-occurrence of an age-related failure of striatal compensatory strategies to counteract striatal dopamine decline in the early stages of PD.

P63

Long-term modulation of glutamatergic transmission in Parkinson's disease patients with and without L-dopa-induced dyskinesia

Andrea Guerra[1,2], F. Asci[1], V. D'Onofrio[2], A. Zampogna[2], G. Fabbrini[1,2], A. Berardelli[1,2], A. Suppa[1,2]

[1]IRCCS Neuromed, Pozzilli (IS), Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

Introduction: Abnormal glutamatergic neurotransmission in the primary motor cortex (M1) contributes to the pathophysiology of Parkinson's disease (PD) and is crucially related to L-dopa-induced dyskinesias (LID). The short-term modulation of glutamatergic neurotransmission improves the abnormally enhanced short-interval intracortical facilitation (SICF) in PD patients.

Objective: To examine whether the long-term modulation of SICF has beneficial effects on clinical measures, including LID severity, and whether these changes parallel an improvement in cortical plasticity mechanisms in PD.

Methods: We tested SICF before (S0) and after short- (14 days - S1) and long-term (12 months - S2) treatment with safinamide 100 mg/day, a drug with anti-glutamatergic properties, in patients with and without LID. Possible changes in M1 plasticity were assessed using intermittent theta-burst stimulation (iTBS). Finally, we correlated safinamide-related neurophysiological changes with possible modifications in clinical scores.

Results: SICF was abnormally enhanced at S0, and prominently in patients with LID. Safinamide normalized SICF at S1 and this effect persisted at S2. The iTBS-induced plasticity was impaired at S0 and safinamide restored this alteration at S2. There was a significant correlation between the degree of SICF and the amount of iTBS-induced plasticity at S0 as well as at S2. In patients with LID, the degree of SICF at S0 and S2 correlated with long-term changes in LID severity.

*Conclusion***:** SICF alteration contributes to M1 plasticity impairment in PD. Safinamide-related long-term modulation of glutamatergic neurotransmission ameliorates both SICF and M1 plasticity. The abnormality in SICF-related circuits plays a relevant role in LID pathophysiology and its long-term modulation may prevent LID worsening over time in PD.

P64

Correlates of psychological distress in patients with Parkinson's disease during the Covid-19 outbreak

Sara Satolli[1], R. De Micco[1], M. Siciliano[1,2], V. Sant'Elia[1,2], A. Giordano[1], A. Russo[1], G. Tedeschi[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

Background: Following the severe consequences of the Covid-19 outbreak, on March 9, 2020, the Italian government implemented extraordinary measures to limit viral transmission, including restrictive quarantine measures. This resulted in a rapid and profound change of people's daily lives.

Objective: We assessed the psychological impact of the 40-day quarantine in a large cohort of patients with Parkinson's disease (PD) and caregivers. Moreover, we analyzed whether prelockdown clinical features may be associated with subjective response of patients with PD to this traumatic event.

Methods: A total of 94 patients with PD were enrolled in the study. The impact of event scale-revised, the Kessler Psychological Distress Scale, and the 12-item Zarit Burden Inventory were obtained from patients and caregivers by email. A multivariate regression analysis was performed to determine whether prelockdown clinical motor and nonmotor features were associated with the psychological impact of lockdown.

Results: Regression analyses showed that prelockdown levels of anxiety, treatment-related motor complications, patients' quality of life, and lockdown hours per day were significantly associated with psychological impact measures of the 40-day quarantine. In addition, we showed that caregiver burden was correlated with overall patient autonomy and attention/memory impairment.

Conclusions: We identified specific PD motor and nonmotor features potentially predisposing to higher psychological impact of stressful situations, such as quarantine. This may help guide postpandemic interventions and preventive strategies to avoid further impairment of psychological well-being in patients with PD.

P65

Effect of oxytocin on response inhibition in Parkinson´s disease: a pilot study

Federico Carbone[1], P. Ellmerer[1], S. Spielberger[1], M. Peball[1], V. Sidoroff[1], M. Ritter[2], K. Seppi[1], W. Poewe[1], A. Djamshidian[1]

[1]Department of Neurology, Medical University Innsbruck, Innsbruck, Austria
[2]Interactive Graphics and Simulation Group, University of Innsbruck, Innsbruck, Austria

Introduction: Cumulating evidence has shown the role of the neuropeptide OXT in social behavior and cognition [1]. Recent studies have also revealed that OXT has a modulatory role on inhibitory control [2-3]. The overlap pro-saccade task and anti-saccade task are two established saccadic paradigms that allow for an objective assessment of response inhibition, which is known to be impaired in PD patients.

Objective: To observe the effect of oxytocin (OXT) on response inhibition in Parkinson´s disease (PD) patients using dedicated saccadic tasks.

Methods: This was a randomized, placebo-controlled, double blind, crossover, monocentric pilot study. We recruited 11 male PD patients. Participants received 24 IU of a synthetic OXT nasal spray or placebo before saccadic assessment, consisting of an overlap pro-saccade and an anti-saccade task. Eye movements were recorded using an eye tracker (Tobii TX300).

Results: Participants made less anticipatory errors in the overlapping pro-saccade task ($p= 0.003$) after intake of OXT compared to placebo. Reaction time in correctly performed anti-saccade task were shorter after OXT intake, although this did not reach significance ($p= 0.07$). There were no differences in error rate in the antisaccade task after OXT or placebo intake ($p>0.05$).

Conclusions: Our results show a significant reduction of the anticipatory error rate in the overlapping pro-saccade task after intake of intranasal OXT. This is in line with previously shown correlation of OXT with behavioral performance, specifically impulsivity control [2-3]. The improvement in motor impulsivity described in this eye tracking study may be reflected by a clinical improvement of overall impulsivity, particularly in PD patients with addictive behaviors. Ours is a small pilot study, and these results warrant further validation in bigger cohorts.

References

[1] T.M. Love, Oxytocin, motivation and the role of dopamine, Pharmacol. Biochem. Behav. 119 (2014) 49–60. https://doi.org/10.1016/j.pbb.2013.06.011.
[2] S. Hayashi, A. Tsuru, F. Kishida, Y.K. Kim, S. Higuchi, Y. Motomura, ERP study on the associations of peripheral oxytocin and prolactin with inhibitory processes involving emotional distraction, J. Physiol. Anthropol. 38 (2019) 1–12. https://doi.org/10.1186/s40101-019-0196-z.
[3] E. Demirci, S. Özmen, D.B. Öztop, Relationship between impulsivity and serum oxytocin in male children and adolescents with attention-deficit and hyperactivity disorder: A preliminary study, Noropsikiyatri Ars. 53 (2016) 291–295. https://doi.org/10.5152/npa.2015.10284.

P66

Visual attention and Pisa Syndrome: simple correlation or cause-effect relationship?

Nicolò Baldini[1], L. Pepa[3], L. Tisara[1], E. Andrenelli[1], M. Capecci[1,2], M.G. Ceravolo[1,2]

[1]Department of Experimental and Clinical Medicine, Politecnica delle Marche University, Ancona, Italy
[2]Neurorehabilitation Clinic, University Hospital "Azienda Ospedali Riuniti di Ancona", Ancona, Italy
[3]Department of Information Engineering, Politecnica delle Marche University, Ancona, Italy

Background and Aims: Pisa Syndrome (PS) is a highly disabling postural deformity, with a strong impact on patients' quality of life. However, it can be reversible if diagnosed and treated at an early stage. The neuropsychological profile is characteristic: reduced performance on visuospatial abilities, attention and language. This study aims to analyze PS from a different perspective: the ocular behavior, through the Eye Tracking methodology. The ultimate goal is to shed light on the association between PS and visuospatial and attention impairment functions, looking into clinical predictors of PS evolution.

Methods: This cross sectional study compared the behavior reactions and the pattern of visual scanning in a group of pwPD – with (PS+)(n=34), or without (PS-)(n=22) trunk postural deviation - and a group of healthy age-matched people (HC)(n=11). To this scope, the Benton Judgment of Line Orientation Test (BJLOT) was used to create a set of stimuli consecutively presented on the screen, while tracking patients' gaze, by means of the eye tracker EyeLink 1000.

Results: PS+ subjects show significantly worse performances on the BJLOT and MoCA tests. Congruent, they show a characteristic pattern of visual scanning, which is significantly different from the one exhibited by PS- subjects and age-matched healthy subjects, with special impairment in the ability to process stimuli in the left hemifield. On a logistic regression analysis, the performance on the BJLOT is significantly ($p<.0001$) related to the severity of attention deficit (e.g. latency of first fixation of the visual stimulus and MoCA subitem score) and the severity of axial symptoms (e.g. UPDRS-III posture and freezing subitem scores).

Conclusions: We confirm the association between visuospatial and attention disorders and PS; the role of cognitive disorders as early predictors of the risk for developing severe trunk abnormalities is to be sought in prospective studies on large cohorts of pwPD.

P67

Young-onset Parkinson's disease: role of head trauma and sport practice

Piergiorgio Grillo[1], G. Di Lazzaro[1,2], H. Zenuni[1], K. Dams-O'Connor[3], G.M. Sancesario[4], N.B. Mercuri[1,5], A. Pisani[6,7], T. Schirinzi[1]

[1]Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]Neurology Unit, IRCCS Fondazione Policlinico Universitario A. Gemelli, Rome, Italy
[3]Department of Rehabilitation and Human Performance, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, USA
[4]Biobank Unit, IRCCS Fondazione Santa Lucia, Rome, Italy
[5]Experimental Neuroscience Unit, IRCCS Fondazione Santa Lucia, Rome, Italy
[6]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[7]IRCCS Mondino Foundation, Pavia, Italy

Introduction: Head Trauma (HT) may be responsible for the earlier onset of neurodegenerative diseases such as Amyotrophic Lateral Sclerosis and dementia. However, no studies examined the potential contribution of HT in young onset cases (YOPD, age at onset <50) of Parkinson's disease (PD), a condition whose environmental risk factors have not been identified yet.

Objectives: To assess HT history in a cohort of PD patients to estimate the associated risk, the impact on age of onset, and the effect on both clinical and biochemical features of the disease.

Methods: 94 PD patients (31 with YOPD, monogenic forms excluded) and 70 healthy controls, were screened for HT history using the Brain Injury Screening Questionnaire (BISQ), which investigates number, severity, and circumstances of HT across lifespan, calculating the associations with different clinical groups (case vs controls, YOPD vs late-onset PD). In all PD patients, HT history features were correlated with motor and non-motor scores, and to CSF levels of α-synuclein, amyloid-β42, total and phosporiled-181 tau, lactate, CSF/serum albumin into a subgroup.

Results: Positive HT history increased the risk for PD overall and for YOPD specifically. Sport-related HTs resulted a specific risk factor for YOPD, although the prolonged sporting life delayed PD onset. The individual number of HTs ("trauma score", TS) was higher in PD patients than controls, proportionally increasing the risk for PD. TS directly correlated with CSF t-tau in PD group, but not in the YOPD subgroup.

Conclusions: This study confirms HT as "dose-dependent" risk factor for PD overall, but specifically indicates its role in favoring YOPD. Sport-related HT is the most risky for YOPD, although the longer sporting life delays PD onset, protecting from YOPD. Contribution of HT in PD pathogenesis may involve tau-mediated mechanisms, which have greater relevance in those cases with later onset but not in YOPD.

P68

The effects of Levodopa Challenge Test on eye movements in Parkinson's disease: insights from a de novo cohort

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

Introduction: Clinical eye movement quantitative assessment represents a promising non-invasive tool to investigate both pathophysiology and clinical aspects of neurodegenerative disorders. In Parkinson's disease (PD), eye movements abnormalities involving both saccadic and smooth pursuit
movements were described and investigations about the effects of antiparkinsonian drugs on eye motility provided conflicting evidences. Notably, only few studies with small sample sizes assessed Levodopa (LD) effects on a drug-naïve population through a standardized Levodopa Challenge Test (LCT). Moreover, few data are available about vertical eye movements after LD administration.

Objective: We aimed to widely investigate eye motility effects of LCT in a large de novo PD population.

Methods: Patients fulfilling UK-Brain-Bank criteria for PD were enrolled. Eye movement were recorded by Eyelink 1000 Plus. Horizontal and vertical visually guided saccades, horizontal and vertical smooth pursuit movements (SPM) were assessed at baseline and after 2 hours from the administration of Levodopa/Carbidopa 250/25 mg.

Results: Forty de novo PD patients were enrolled [23 Men (57.5%); mean age 64.5±6.9 years; mean disease duration 1.7±1.1 years; baseline UPDRS-ME 25.8±8.3; peak UPDRS-ME 21.3±8.3]. We found an improvement in saccadic velocities and accuracy as well as reduced horizontal latencies after LD administration. Moreover, an increased vertical SPM gain was demonstrated.

Conclusions: Our findings from a de novo population partially confirmed literature evidences, enlighting interesting insights about acute LD effects on SPM and saccadic latencies.

P69

Exploring the relationship between eye movements and levodopa long duration response in drug-naïve Parkinson's disease patients

Giovanni Mostile[1,2], C. Terravecchia[1], C.G. Chisari[1], A. Luca[1], R. Terranova[1], G. Donzuso[1], C. Rascunà[1], C.E. Cicero[1], G. Sciacca[1], A. Nicoletti[1], M. Zappia[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

Introduction: In Parkinson's disease (PD) eye movement quantitative assessment demonstrated both saccadic and smooth pursuit movements abnormalities. Levodopa treatment exerts a reciprocally influenced Short and Long Duration Response (SDR and LDR). To date, only the effects of SDR on eye motility was investigated, reporting conflicting results.

Objective: Aim of this pilot study was to investigate possible associations between eye movement parameters evaluated during SDR assessment and later achievement of sustained LDR.

Methods: In drug-naïve PD patients, SDR and LDR were assessed using a standardised protocol. Eye movements were recorded by Eyelink-1000 Plus. Horizontal and vertical visually-guided saccades as well as horizontal and vertical smooth pursuit movements were assessed at baseline and after 2-hours from administration of Levodopa/Carbidopa 250/25 mg. Both baseline and peak-ofdose eye movements parameters on SDR were compared between patients who have and have not achieved LDR (LDR+ and LDR-) after 2- weeks of continuative levodopa therapy.

Results: Forty PD patients were enrolled [23 (57.5%) Men; age 64.5±6.9 years; disease duration 1.7±1.1 years; baseline UPDRS-ME 25.8±8.3; peak UPDRSM E 21.3±8.3]. Out of them, 20 (50%) were LDR+. Patients LDR+ had a significantly higher horizontal pursuit gain at SDR peak-of-dose than patients LDR-.

Conclusions: Horizontal pursuit gain at SDR peak-of-dose assessment may predict LDR achievement in de novo PD patients.

P70

Evaluation of serum tau and β-amyloid peptides in Parkinson's disease

Henri Zenuni[1], P. Grillo[1], G. Guerrera[2], L. Battistini[2], N.B. Mercuri[1,2], G.M. Sancesario[2], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Pathological events occurring at brain level can reflect at peripheral level; accordingly, blood tissue could represent a potential easy-accessible source for reliable biomarkers. Indeed, the measurement of neurodegerationrelated blood biomarkers is gaining clinical relevance in Alzheimer's disease field; however, data on Parkinson's disease (PD) are still scarce.

Objective: To provide a pilot case-control study assessing serum levels of classical neurodegeration-related biomarkers in PD, looking at correlations with both the respective CSF content and the main clinical parameters.

Methods: The study involved 22 PD patients and 10 control subjects. Classical neurodegeration-related biomarkers (total tau protein, amyloid-β-42 and amyloid- β-40 peptides) were measured by an ultrasensitive methodology of single molecule array (SiMoA) in serum, and by electrochemiluminescence immunoassay (ECLIA) in CSF. Standard motor (UPDRS part III) and non-motor scores (NMSS and MoCA) were collected for each patient, together with LEDD calculation. Serum biomarkers were compared between patients and controls, and correlated with their CSF content and clinical data separately in each group.

Results: Serum biomarkers did not differ between patients and controls. In PD patients but not in controls, serum tau and amyloid-β-42 directly correlated with their respective CSF levels. In addition, serum tau inversely correlated with cognitive performances (MoCA score).

Conclusions: This pilot study showed that in PD neurodegeneration-related biomarkers change in serum in parallel to CSF. Accordingly, they may represent an easy-accessible source for clinically-informative markers, as the correlation with clinical score also suggest. However, further confirmatory studies are now needed.

P71

Rehabilitation program care for outpatients of Sandro Pertini Hospital Parkinson Center

Steno Rinalduzzi[1], Antonella Biasiotta[1], S. Almonti[1], I.F. Pestalozza[1], F. Gilio[1], F. Gragnani[1], S. Taloni[2], A.M. Attisano[2], C. Sales[2], A.M. Servadio[2]

[1]UOC Neurology and Neurophysiopathology, Sandro Pertini Hospital, Rome, Italy
[2]UOS Rehabilitation, Sandro Pertini Hospital, Rome, Italy

Introduction: Non-pharmacological interventions are essential in the management of motor impairments in Parkinson's disease [1]. The success and benefit of motor rehabilitation relies both on therapy adherence and training intensity achieved. Moreover, it is crucial to apply non-pharmacological interventions in an individualized and evidence-based manner.

Objective: To build rehabilitation pathways program care for outpatients of Sandro Pertini Hospital, ASLROMA2, Parkinson Center**.**

Methods: During the first visit, each parkinsonian patient undergoes the neurological examination by a neurologist, followed by the functional evaluation by a therapist. The functional evaluation assesses how often people affected by Parkinson's experience difficulties across 8 dimensions of daily living including relationships, social situations and communication. It including a global evaluation as well as a quality of life and a motor section UPDRS score, Tinetti scale, pain numerical rating scale and PDQ39 scale that assesses the impact of Parkinson's on specific dimensions of functioning and wellbeing. Neurologist and therapist build together the best rehabilitation program for the patient; they consider potential factors influencing effectiveness of non-pharmacological intervention on motor impairments as well as motor and non-motor symptoms, availability of the caregiver, co-morbidities, environment factors, etc. They ponder if each patient can perform only home exercise program by themselves [2] or with intervention of a therapist or in the hospital with therapist intervention. Finally, home exercise session of patients by themselves will be monitored by inhome
virtual video calls [3].

Results: The therapist and neurological examination performed together allowed a better formulation of personalized and differentiated rehabilitation programs. Home exercise programs to be performed by themselves made access to rehabilitation programs possible at low cost for an increased number of patients. Furthermore, monitoring through telemedicine has increased adherence to treatment of patients.

Conclusion: The treatment of Parkinson's disease must include physiotherapy in addition to pharmacological treatments. Home exercises and telemedicine reduce costs and allow an increasing number of patients to access treatment. We encourage other centers to build rehabilitation pathways for their patients.

References

[1] L.A. King, F.B. Horak. Delaying mobility disability in people with Parkinson disease using a sensorimotor agility exercise program. Phys Ther. 2009;89:384-93.

[2] L.A. King et al. Effects of Group, Individual, and Home Exercise in Persons With Parkinson Disease: A Randomized Clinical Trial. J. Neurol. Phys. Ther. 2015; 39: 204-12.
[3] J.M. Hatcher et al. Telemedicine in neurology: Telemedicine Work Group of the American Academy of Neurology update. Neurology 2020; 94(1):30-38.

P72

Burden of Parkinson's disease in Sicily. A health administrative database study

Calogero Edoardo Cicero[1], S. Scondotto[2], A.V. Allotta[2], G. De Luca[2], G. Murolo[2], A. Nicoletti[1], M. Zappia[1]

[1]Department of Medical, Surgical and Advanced technologies G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[2]Health Activities and Epidemiologic Observatory Division, Health Department, Sicily Region

Introduction: Prevalence of Parkinson's disease (PD) increases with the advanced ages, representing a relevant health burden. Accurate prevalence estimates are of fundamental need in order to adjust the supply of health services for these patients. The availability of administrative health data from the National Health System provides a useful resource to assess the burden of diseases. Our aim was to evaluate the prevalence of PD through the use of administrative data in the Sicily region.

Methods: We have identified all the subjects affected by PD in Sicily in 2017 by gathering data from three regional health administrative databases: the hospital discharge records, the medical exemption databases and the pharmacological prescription database. Prevalence rates and 95% confidence intervals (CI) have been calculated across five-years age classes.

Results: PD patients identified through database searching were 24,674, giving a prevalence of 488/100,000 (95%CI 481.9-494.1) inhabitants. Prevalence was higher among men (514.5/100,000; 95%CI 505.6-523.6) and reached a peak in the 85-89 age class (3,203.8/100,000; 95%CI 3,095.2-3,315.1).

Discussion: Our prevalence estimates of PD were higher when compared to previous epidemiological surveys conducted in Sicily. These findings are, however, comparable to other studies conducted in Italy that identified cases through administrative databases. Using health databases is a feasible strategy to assess the burden of PD.

P73

Olfactory hallucinations in Parkinson's disease patients

Paolo Solla[1], C. Masala[2], I. Pinna[2], T. Ercoli[3], F. Loy[2], G. Orofino[3], L. Fadda[3], G. Defazio[3]

[1]Department of Neurology, University of Sassari, Sassari, Italy
[2]Department of Biomedical Sciences, University of Cagliari, Monserrato, Italy
[3]Movement Disorders Center, Department of Neurology, University of Cagliari, Cagliari, Italy

Introduction: Olfactory dysfunctions and hallucinations are considered common nonmotor symptoms in Parkinson's disease (PD). Visual and auditory hallucinations are well-known; however, olfactory hallucinations (OHs) are not fully investigated [1].

Objective: To evaluate OHs in PD patients, and their correlation to motor impairment, cognitive abilities, visual and auditory hallucinations, and olfactory and gustatory function.

Methods: A sample of 273 subjects was enrolled: 141 PD patients (mean age ± SD: 70.1 ± 9.5 years) and 132 healthy controls (mean age ± SD: 69.4 ± 9.6 years). In all patients, the following parameters were evaluated: motor symptoms (UPDRS-III), olfactory function, cognitive abilities, and occurrence of OH, gustatory hallucinations (GHs), and visual/auditory hallucinations.

Results: OHs were found only in PD patients with a percentage of 11.3%. Among PD patients with OHs, 2.8% also presented GHs. High significant frequencies of females, the presence of visual/auditory hallucinations, and a high mean UPDRS-III score were found in patients with OHs related to patients without them. Binary logistic regression evidenced the presence of visual/auditory hallucinations and sex as main variables predicting the presence of OHs.

Conclusions: Our data indicated that OHs occur frequently in PD patients, especially in women, and often concomitant with visual and auditory hallucinations, without any association with olfactory impairment.

References

[1] CV Kulick; KM Montgomery; MJ Nirenberg. Comprehensive identification of delusions and olfactory, tactile, gustatory, and minor hallucinations in Parkinson’s disease psychosis. Park. Relat. Disord. 2018, 54, 40–45.

P74

Orthostatic hypotension in Parkinson´s disease: do height and weight matter?

Nicole Campese[1,2], G. Goebel[3], L. Fabian[2], J.P. Ndayisaba[2], S. Eschlboeck[2], C. Kaindlstorfer[2], C. Raccagni[2,4], R. Granata[2], R. Ceravolo[1], S. Kiechl[2], K. Seppi[2], W. Poewe[2], G.K. Wenning[2], A. Fanciulli[2]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria
[3]Department of Medical Statistics, Informatics and Health Economics, Medical University of Innsbruck, Innsbruck, Austria
[4]Department of Neurology, Regional General Hospital Bolzano, Bolzano, Italy

Introduction: Orthostatic hypotension (OH) is a common non-motor feature in Parkinson´s disease (PD), being reported by every third PD patient [1]. Besides classic OH, transient forms of orthostatic hypotension occurring within the first minute upon standing (transient OH, tOH) have been recently described [2]. Pilot studies in Asian populations report an association between lower body mass index (BMI) and classic orthostatic hypotension (cOH) [3-5]. The impact of height and BMI on cOH and tOH in European PD patients has never been explored.

Objective: To investigate the association between height, BMI and the presence of laboratory-confirmed cOH or tOH in PD.

Methods: We performed a sub-analysis of a previously published cohort of 173 PD patients, who underwent cardiovascular autonomic function testing (CAFTs) at the Medical University of Innsbruck between 2007 and 2020, by collecting information on height and weight at the time of CAFTs.

Results: In our cohort, BMI did not differ in patients with either cOH, tOH or without any OH. Height also did not differ between female patients with or without any form of orthostatic blood pressure dysregulation. After adjusting for age, male patients with a height <172.5 cm showed a lower cOH burden [OR=0.141, (95% CI 0.030-0.663), p=0.013] compared to taller ones, despite other cardiovascular autonomic indices were equally impaired.

*Conclusions***:** While BMI does not seem to impact on the development of cOH or tOH, a shorter stature may represent a protective factor for cOH in male PD patients. Given that cardiovascular autonomic indices other than cOH were equally impaired in short and taller patients, we suggest an underlying hydrostatic mechanism, related to fluid shifts when changing from the supine to the upright position. Identifying individual and PD-related risk factors for OH will help developing tailored screening approaches for this overlooked condition.

References

[1] D.C. Velseboer et al., Prevalence of orthostatic hypotension in Parkinson's disease: A systematic review and meta-analysis. Parkinsonism & Related Disorders, 2011. 17(10): p. 724-729.
[2] A. Fanciulli et al., Association of transient orthostatic hypotension with falls and syncope in patients with Parkinson disease. Neurology, 2020. 95(21): p. e2854-e2865.
[3] Q. Wu et al., Sex differences in underweight and body mass index in Chinese early de novo patients with Parkinson's disease. Brain Behav, 2020. 10(12): p. e01893.

[4] T. Nakamura et al., Lower body mass index is associated with orthostatic hypotension in Parkinson's disease. J Neurol Sci, 2017. 372: p. 14-18.
[5] T. Umehara et al., Body weight and dysautonomia in early Parkinson's disease. Acta Neurol Scand, 2017. 135(5): p. 560-567.

P75

Nocturnal complex behaviors in Parkinson's disease: not always REM sleep behavior disorder

Luca Baldelli[1], G. Loddo[2], G. Mainieri[1,3], L. Sambati[3], F. Mignani[3], A. Montini[1], P. Cortelli[1,3], S. Capellari[1,3], G. Calandra-Buonaura[1,3], F. Provini[1,3]

[1]Dipartimento di Scienze Biomediche e Neuromotorie, Università di Bologna, Bologna, Italy
[2]Azienda USL di Bologna, Bologna, Italy
[3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Introduction: In Parkinson's disease (PD), Disorders of Arousal (DoA) have seldom been investigated in contrast with REM Sleep Behavior Disorder (RBD) [1-3]. DoA and RBD share some anamnestic features, although they have different clinical and therapeutic implications.

Objectives: To discuss clinical and video-polysomnographic (VPSG) findings of three PD patients (Pt) displaying nocturnal complex motor behaviors.

Methods: Three male PD patients (Pt1=65, Pt2=67 and Pt3=72yo) presenting sleep-related motor disorders with atypical features for RBD underwent one nocturnal VPSG.

Results: Pt1 (disease duration–dd=4y) had positive familial (brother) and personal history (since 24yo) of DoAs, Pt2 (dd=9y) and Pt3 (dd=5y) had a definite diagnosis of RBD and developed mild cognitive impairment during the disease course, with diurnal hallucinations. Pt2 had positive history for personal and bed-partner traumatic lesions during night-time.
At VPSG only Pt1 presented physiological REM atonia, his recording showed 10 behavioral episodes from NREM sleep suggestive of DoA. VPSG in Pt2 documented prolonged mixed states of light sleep and wakefulness manifesting with confusion and complex motor behaviors (i.e.shooting) instead. When questioned, the patient reported that he aimed at "some lights". Pt3 showed RBD, plus a prolonged episode following an early morning awakening from NREM where he sat on the bed looking around and moving his arms searching for something. When asked the patient reported having seen a "monster", however at the end of the episode he was amnesic.

Conclusions: In our case series, nocturnal VPSG revealed a wide range of non-RBD motor events, from DoA to confusional arousals/nocturnal visual hallucinations arising from a mixed EEG state of wake and sleep. A detailed history collection of nocturnal motor events shall raise the suspicion of non-RBD episodes even in PD patients and VPSG is crucial for their objective detection, characterization [4], and correlation with polygraphic parameters.

References

[1] PL Ratti, M Sierra-Peña, R Manni et al. Distinctive features of NREM parasomnia behaviors in parkinson's disease and multiple system atrophy. PloS one. 2015;10(3):e0120973.
[2] W Schrempf, MD Brandt, A Storch, H Reichmann. Sleep disorders in Parkinson's disease. J Parkinsons Dis. 2014;4(2):211-21.
[3] M Terzaghi, B Minafra, R Zangaglia, M Picascia, N Pozzi, R Cremascoli, D Arnaldi, M Versino, E Sinforiani, V Rustioni, C Pacchetti, R Manni. NREM sleep arousal-related disorders reflect cognitive impairment in Parkinson's disease. Sleep Med. 2020 Nov;75:491-496.
[4] A Fernández-Arcos, E Morenas-Rodríguez, J Santamaria, R Sánchez-Valle, A Lladó, C Gaig, A Lleó, A Iranzo. Clinical and video-polysomnographic analysis of rapid eye movement sleep behavior disorder and other sleep disturbances in dementia with Lewy bodies. Sleep. 2019 Jul 8;42(7):zsz086.

P76

Gait analysis may distinguish iatrogenic from neurodegenerative parkinsonism: a pilot study

Annamaria Landolfi[1], C. Ricciardi[2,3], G. D'Agostino[1], M. Picillo[1], C. Vitale[4], M.T. Pellecchia[1], S. Adamo[3], G. D'Addio[3], M. Cesarelli[2,3], P. Monteleone[1], P. Barone[1], R. Erro[1], M. Amboni[1,5]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Baronissi, Italy
[2]Department of Electrical Engineering and Information Technologies, University of Naples "Federico II", Naples, Italy
[3]Bioengineering Unit, Institute of Care and Scientific Research Maugeri, Pavia, Italy
[4]Department of Motor Sciences and Wellness, University Parthenope, Naples, Italy
[5]IDC Hermitage-Capodimonte, Naples, Italy

Introduction: Drug-induced parkinsonism (DIP) may be clinically indistinguishable from degenerative parkinsonism. Instrumental diagnostic tools, such as the ^{123}Ioflupane dopamine transporter (DaT) single-photon emission computer tomography (SPECT), are not always supportive in recognizing its etiology, since a number of drugs may interfere with DaT binding, affecting interpretation of results.

Objectives: The aim of our study is to find whether gait analysis may reveal typical patterns associated to iatrogenic parkinsonism compared to neurodegenerative parkinsonism (Parkinson Disease, PD).

Methods: Gait analysis is a 3D, computerized and non-invasive exam of walk; by elaborating signals obtained through a BTS Bioengineering system, spatial and temporal parameters of gait were computed and then analysed through a nonparametric statistical Mann Whitney test. We collected data from PD patients and patients affected by Bipolar Disorder (BD) with iatrogenic extrapyramidal signs. Each patient performed a normal gait task, a motor dual task and a cognitive dual task.

Results: Data were obtained from 8 BD and 8 PD patients, matched for age, sex, motor symptom duration and MDS-UPDRSIII scores. Parameters obtained during the normal gait task showed p-values almost significant in distinguishing PD and BD patients. Similarly, in the cognitive dual task, only step width showed a statistical significance difference between the two groups. Differently, in the motor dual task, stance phase, swing phase, mean velocity, cycle length, step length and step width showed a statistically significant difference (p-values <0.05) between PD and BD.

Conclusions: Gait analysis may reveal typical patterns associated with iatrogenic parkinsonism compared to neurodegeneration. Future perspectives include the comparison with a population of drug-exposed patients with concomitant neurodegeneration, in order to elucidate the relative contribution of the pharmacological treatment and the underlying conditions on the observed trends.

P77

Evaluation of Jebsen Taylor Hand Function Test in an Italian population with Parkinson disease

A. Berardi[1], *Giovanni Galeoto*[1,2], M. Tofani[3], F. Panuccio[4], G. Fabbrini[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCSS Neuromed, Pozzilli (IS), Italy
[3]Department of Public Health and Infection Disease, Sapienza University of Rome, Rome, Italy
[4]Department of Anatomical and Histological Sciences, Legal Medicine and Orthopedics, Sapienza University of Rome, Rome, Italy

Objective: The purpose of this study was to evaluate and validate the Italian version of the Jebsen Taylor Hand Function Test (JTHFT) in Italian people with Parkinson's Disease (PD) [1-3].

Methods: The test's reliability and validity were assessed by following international guidelines. Its internal consistency was evaluated with Cronbach's alpha, and intra-rater reliability was examined using the intraclass correlation coefficient. Its concurrent validity was evaluated using Pearson's correlation coefficient with the HAQ scale. It evaluated a cross-cultural validity between dominant hand and age, H&Y, diagnosis' years, gender, dyskinesia, motor fluctuation.

Results: The test was administered to 29 Italian people with PD. Cronbach's alpha (α) reported 0,59 for the non-dominant hand and 0,69 for the dominant hand. The test-retest analysis showed that the instrument is stable with ICC values between 0,754 and 0,988. Pearson's correlation coefficient showed significant correlations between JTHFT and HAQ. Finally, for PD's population, Pearson correlation showed statistically significant correlations between "handwriting" "hand turning pages" items of the JTHFT with age [3-5].

Conclusions: Jebsen Taylor Hand Function Test is a reliable tool to evaluate the upper limb and hand functionalities in PD patients [6].

References

[1] J.A. Opara, A. Małecki, E. Małecka T. Socha. Motor assessment in parkinson's disease. *Annals of Agricultural and Environmental Medicine* (2017) doi:10.5604/12321966.1232774.
[2] M. Tofani *et al.* Efficacy of Occupational Therapy Interventions on Quality of Life in Patients with Parkinson's Disease: A Systematic Review and Meta- Analysis. *Mov. Disord. Clin. Pract.* mdc3.13089 (2020) doi:10.1002/mdc3.13089.
[3] Savona *et al.* Evaluation of intra- and inter-rater reliability and concurrent validity of the Italian version of the Jebsen–Taylor Hand Function Test in adults with rheumatoid arthritis. *Hand Ther.* (2019) doi:10.1177/1758998319843554.
[4] Berardi et al. Internal consistency and validity of the Jebsen-Taylor hand function test in an Italian population with hemiparesis. *NeuroRehabilitation* (2019) doi:10.3233/NRE-192867.
[5] G. Culicchia *et al.* Cross-Cultural Adaptation and Validation of the Jebsen-Taylor Hand Function Test in an Italian Population. *Rehabil. Res. Pract.* (2016) doi:10.1155/2016/8970917.
[6]M.K .Y. Mak, E.T.L. Lau, V.W.K. Tam, C.W.Y. Woo, S.K.Y. Yuen. Use of Jebsen Taylor Hand Function Test in evaluating the hand dexterity in people with Parkinson's disease. *J. Hand Ther.* (2015) doi:10.1016/j.jht.2015.05.002.

P78

Effects of emotional auditory stimulation on anticipatory postural adjustments in Parkinson's disease

A.V. Milner[1], M. Meloni[1], *Francesca Lea Saibene*[1], A. Castagna[1], G. Fusaroli[1], M. Ferrarin[1], E. Pelosin[2,3], T. Lencioni[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy
[3]IRCCS Policlinico San Martino, Genoa, Italy

Introduction: The role of emotions on the Anticipatory Postural Adjustments (APA) in Parkinson's disease (PD) is still under debate [1], above all because their alterations are not studied outside the laboratory. Recently, a new method for quantifying APAs using an inertial measurements unit (IMU) was validated in elderly [2].

Objective: To investigate whether APA parameters from IMU after emotional stimuli differ between PD and controls subjects (CS).

Methods: Fourteen PD (71.1±5.7 years, mean UPDRS-III score 39.0±14.9) and eight agematched healthy controls stood wearing headphones and an IMU on the lower back and were asked to initiate gait in response to neutral, pleasant and unpleasant auditory stimuli. As baseline condition a voice saying "start" was used. Patients were on the "on" state. APA onset and APA duration were calculated from the acceleration data [2]. The differences were tested using a repeated-measures ANOVA (Group: PD/CS, Stimuli: Baseline/Neutral/Pleasant/Unpleasant). Correlation analysis was performed between the APA parameters and UPDRS Part III using the Pearson test. Fisher's post-hoc test was applied for multiple comparison analysis.

Results: APA duration was longer in PD patients than in controls (p=0.01) and it was positively correlated with UPDRS III (rho 0.60, p=0.02) only at baseline. The emotional valence of the auditory stimulation affected APA onset (p=0.05), with the shortest values registered after the unpleasant stimuli. APA onset after N/P/U stimulations was significantly different compared to the baseline one.

Conclusions: The longer APA duration confirms an impaired postural control in PD. In addition, comparable APA onset between PD and CS suggests that the emotions recognition from common auditory stimuli of daily life is preserved in PD.

References

[1] Avanzino L, *Gait Posture* (2018) 65:57–64.
[2] Gazit E, et al. *Gait Posture.* 2020;76:128-135.
[3] Callisaya ML, et al. Gait Posture, 49 (2016), pp. 19-24.

P79

Frequency of non-motor symptoms in Parkinson's patients with motor fluctuations

Claudio Liguori[1,2,3], M. Fernandes[1], M. Pierantozzi[2,3], A. Stefani[2,3], C. Cattaneo[4], E.A. Bonizzoni[5], R. Cerroni[3], N.B. Mercuri[3,6]

[1]Sleep Medicine Centre, Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]Neurology Unit, University Hospital of Rome Tor Vergata, Rome, Italy
[3]Parkinson's Disease Center, University Hospital of Rome Tor Vergata, Rome, Italy
[4]Medical Department, Zambon SpA, Bresso, Italy
[5]Department of Clinical Science and Community, Section of Medical Statistics and Biometry "GA Maccacaro", University of Milan, Milan, Italy
[6]IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Non-motor symptoms (NMS) including neuropsychiatric, sleep, autonomic, and sensory domains are an integral aspect of the clinical presentation of Parkinson disease (PD) and affect neurocognitive functioning as well as patients' and caregivers' well-being [1–3].

Objective: To describe the occurrence of NMS in PD patients with motor fluctuations in real-life condition.

Methods: The present study is a secondary analysis of a previous multinational, multicentre, retrospective-prospective cohort observational study (SYNAPSES). Patients with PD diagnosis and motor fluctuations aged ≥18 years who had started treatment with safinamide at the enrolment visit or in the previous 4 months were included. Data achieved at the baseline visit was used for this study and descriptive analyses were conducted to describe the distribution of NMS in motor-fluctuating PD patients distributed according to different clinical characteristics.

Results: Of the 1610 patients enrolled, 1589 were included for the analysis (978 Males and 611 Females), with a mean age of 68.4 (SD=9.6). The mean years from diagnosis was 7.94 (SD=5.40). Most patients had at least one NMS (88.5%). Sleep problems and psychiatric symptoms were the most prevalent NMS in motor fluctuating PD patients in all H&Y stages. Psychiatric disorders were more frequent in older patients and in patients with a larger number of years of PD diagnosis, while sleep problems were more preeminent in younger patients and with inferior disease duration.

*Conclusions***:** The present findings further support the high prevalence of NMS in PD patients with motor fluctuations, reinforcing thus the need to also considering NMS in clinical practice and taking into account their different prevalence across the stages of the disease, the influence of gender and the clinical PD characteristics.

References

[1] Chaudhuri et al., 2006. Lancet Neurol;5:235–45.
[2] Park et al., 2009. J Neurol;256:293–8.
[3] Martinez-Martin et al., 2011. Mov Disord;26:399–406.

P80

Emotional processing and response times in Parkinson's disease

Alessandro Botta[1], G. Lagravinese[2,3], E. Pelosin[2,3], G. Bonassi[4], M. Putzolu[2], C. Cosentino[2], C. Ponte[2], S. Mezzarobba[2], L. Avanzino[1,3]

[1]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[3]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[4]S.C. Medicina Fisica e Riabilitazione Ospedaliera, ASL4, Azienda Sanitaria Locale Chiavarese, Chiavari, Italy

Introduction: Emotional processing has been shown to be able to influence motor behaviour in healthy and in pathological population [1–3]. In Parkinson's disease (PD) emotional processing is thought to be potentially impaired, particularly toward negative emotions [4].

Objective: The aim of this behavioural study was to test whether motor response in PD is mainly driven by the emotional content of a picture or if it is influenced by motor resonance by using different sets of emotional pictures representing emotional body language [5] (EBL), emotional scenes [6] (IAPS) and facial expressions [7] (FACS).

Methods: 24 PD patients (H&Y: 1.91 ± 0.47) and 14 age matched healthy subjects (HS) were enrolled for the experiment. All participants were asked to complete a two-alternative forced choice discrimination task in which they had to press as fast as possible the key corresponding to the emotional (fearful/ happy) visual stimulus respect to the non-emotional (neutral), in order to estimate
response times (RTs).

Results: Results showed increased RTs in PD with respect to HS for fearful IAPS pictures but not for EBL and FACS. Happy stimuli showed significant longer RTs for PD compared to HS in all emotional stimuli. Fearful EBL showed reduced RTs for both PD and HS compared to happy stimuli, while the opposite was found for IAPS pictures. No significant differences in PD's RTs were found
for fearful FACS, but higher RTs were retrieved for fear in HS compared to happy.

Conclusion: These preliminary results show that emotional processing of aversive information conveyed by human bodies acts similarly in PDs and healthy controls, while more complex visual stimuli, such as IAPS, shows a different behaviour. Furthermore, fearful EBL showed to be more easily processed compared to happy stimuli in both groups, but the opposite was observed in IAPS stimuli for all participants and in FACS only for HSs.

References

[1] A Botta, G Lagravinese, M Bove, A Avenanti, L Avanzino. Modulation of Response Times During Processing of Emotional Body Language. *Front. Psychol.* 12, 1–11 (2021).
[2] EMJ Huis In't Veld, GJMvan Boxtel, B de Gelder. The body action coding system II: Muscle activations during the perception and expression of emotion. *Front. Behav. Neurosci.* 8, (2014).

[3] L. Avanzino, G Lagravinese, G Abbruzzese, E Pelosin. Relationships between gait and emotion in Parkinson's disease: A narrative review. *Gait and Posture* vol. 65 57–64 (2018).
[4] J Péron, T Dondaine, F Le Jeune, D. Grandjean, M. Vérin. Emotional processing in parkinson's disease: A systematic review. *Mov. Disord.* 27, 186–199 (2012).
[5] S Borgomaneri, V Gazzola, A Avenanti. Motor mapping of implied actions during perception of emotional body language. *Brain Stimul.* 5, 70– 76 (2012).
[6] MM Lang Bradley, BN Cuthbert. International affective picture system (IAPS): Affective ratings of pictures and instruction manual. (2008).
[7] P Ekman, E Rosenberg. *What the face reveals. What the Face Reveals* (2005).

P81

Feasibility, safety and efficacy of telerehabilitation in mild-to-moderate Parkinson's disease patients: an open label, pilot study

Edoardo Bianchini[1], C. Onelli[1], M. Alborghetti[1,2], M. Sforza[1], D. Rinaldi[1], S. Galli[1], C. Morabito[1], M. Giovannelli[1], F.E. Pontieri[1,2]

[1]Dipartimento NESMOS, Sapienza Università di Roma, Roma, Italy
[2]Fondazione Santa Lucia IRCCS, Roma, Italy

Introduction: Besides pharmacological treatment, Parkinson's disease (PD) patients frequently engage rehabilitation for management of motor and nonmotor symptoms [1]. During Covid-19 pandemic, access to outpatient and inward rehabilitation programs has been markedly limited, consequently telerehabilitation gained popularity [2-3].

Objective: To evaluate the feasibility, safety and efficacy of telerehabilitation in mild-to-moderate PD patients.

Methods: Sixteen PD patients, aged 64±10 years with H&Y score <3 and without gait disturbances, referring to our Movement Disorders Centre were recruited for a 5-week telerehabilitation program, consisting of 1 remote visit with a therapist and a minimum of 2 sessions of at least 30-min of self-conducted exercises per week. Patients received video tutorials of the exercises and were asked to keep a diary of sessions. At baseline (T0) and after the intervention (T1) patients were remotely assessed by means of the MDS-UPDRS part I-III, PDQ-39, FIM and FAB scales. Acceptable compliance to the program was defined as at least 60% matching of frequency and duration of self-conducted sessions, whereas optimal compliance was set at >80% matching. Wilcoxon test was used to assess change from baseline for clinical and functional scores.

Results: Of 310 overall rehabilitation sessions, 257 matched duration criteria (82.9%) and 81% of weekly sessions matched frequency criteria. When considering single patients, 11 patients (68.8%) reached optimal cut-off and 13 (81.3%) reached acceptability. Two patients experienced a mild self-limiting adverse event during a single supervised session and no adverse events were reported during self-conducted sessions. Wilcoxon test showed a significant reduction of MDS-UPDRS total score ($p=0.001$) and MDS-UPDRS-III score ($p=0.003$) with a mean decrease of 5.47±4.94 and 3.65±3.44, respectively. No significant difference were found between T0 and T1 for the other clinical scores.

Conclusions: Our study demonstrates that telerehabilitation is a feasible, safe and effective instrument for management of PD in mild-to moderate stage.

References

[1] SH Fox, R Katzenschlager, SY Lim, B Barton, RMA de Bie, K Seppi, M Coelho, C Sampaio. Movement Disorder Society Evidence-Based Medicine Committee. International Parkinson and movement disorder society evidencebased medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord. 2018 Aug;33(8):1248-1266. doi: 10.1002/mds.27372.

[2] A Langer, L Gassner, A Flotz, S Hasenauer, J Gruber, L Wizany, R Pokan, W Maetzler, H Zach. How Covid-19 will boost remote exercise-based treatment in Parkinson's disease: a narrative review. NPJ Parkinsons Dis. 2021 Mar 8;7(1):25. doi: 10.1038/s41531-021-00160-3.
[3] TD Ellis, GM Earhart. Digital Therapeutics in Parkinson's Disease: Practical Applications and Future Potential. J Parkinsons Dis. 2021 Feb 23. doi: 10.3233/JPD-202407.

P82

Facial emotion expressivity in Parkinson's and Alzheimer's diseases

Antonio Cannavacciuolo[1], D. Colella[1], M. Salzillo[1], A. De Biase[1], G. Paparella[2], M. Canevelli[1], G. Bruno[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: Among motor symptoms, one of the most prominent features in Parkinson's disease (PD) is reduced facial expressivity, e.g., hypomimia. Although parkinsonian signs and symptoms are relatively common in Alzheimer's disease (AD), no study has specifically assessed the possible occurrence of reduced facial expressivity in these patients [1-2].

Objective: We here aimed to comprehensively investigate facial emotion expressivity in PD and AD patients compared to healthy controls (HCs).

Methods: Twenty-four PD patients (17 M, mean age ± standard deviation: 73.83±4.2 years), 24 AD patients (9 M, 77.79±7.8 years), and 24 HCs (13 M, 72.96±7.1 years) were video-recorded while posing facial expressions of six primary emotions (anger, disgust, fear, happiness, sadness, surprise) and neutral expressions. Ten neurologists were screened for the ability to recognize facial expressions during an Emotion Recognition Task (ERT) and then asked to identify the emotion of the participants' pictures in a seven-forced choice response format (Emotion Expressivity Task - EET). Accuracy of responses, reaction times, and confidence levels in the response were considered in the analysis.

Results: The overall ERT score was higher than 80% (range: 72-93%). In the EET, raters identified a lower number of correct responses in PD and in AD than in HCs (37%, 36%, and 52% respectively, $p<0.01$) with no differences between PD and AD ($p=0.61$). We also found longer reaction times for the evaluation of patients' compared to HCs' pictures ($p<0.05$). Finally, the pattern of reduced facial emotion expressivity between PD and AD was similar.

Conclusions: Along with the confirmation of reduced facial expressivity in PD, the study provides evidence of a similar motor abnormality in AD. The facial expressivity deficit in PD and AD may result from common pathophysiology or a manifestation of distinct mechanisms. Further studies should better delineate the clinical relevance of reduced facial expressivity in AD.

References

[1] Ricciardi L, Visco-Comandini F, Erro R, Morgante F, Bologna M, Fasano A, Ricciardi D, Edwards MJ, Kilner J. Facial Emotion Recognition and Expression in Parkinson's Disease: An Emotional Mirror Mechanism? PLoS One. 2017 Jan 9;12(1):e0169110. doi: 10.1371/journal.pone.0169110. PMID: 28068393; PMCID: PMC5221788.
[2] Bologna M, Merola A, Ricciardi L. Behavioral and Emotional Dysfunction in Parkinson's Disease. Parkinsons Dis. 2019 Jun 18;2019:1749525. doi: 10.1155/2019/1749525. PMID: 31316745; PMCID: PMC6604351.

P83

Evaluation of the psychometric properties of the Health Assessment Questionnaire in patients with Parkinson's disease

Giovanni Galeoto[1,2], A. Berardi[1], M. Tofani[3], F. Panuccio[4], G. Fabbrini[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCSS Neuromed, Pozzilli, (IS), Italy
[3]Department of Public Health and Infection Disease, Sapienza University of Rome, Rome, Italy
4Department of Anatomical and Histological Sciences, Legal Medicine and Orthopedics, Sapienza University of Rome, Rome, Italy

Objective: People living and aging with Parkinson's disease (PD) experience increasing daily life challenges due to the progressive nature of the disease [1]. Dysfunctions related to PD lead to difficulties in activities of daily living (ADL) [2-3], with loss of independence and poor quality of life (QoL). This study aims to evaluate the psychometric properties of Health Assessment Questionnaire (HAQ) in a population of individuals with PD.

Methods: This study was conducted on 34 patients diagnosed with PD from February to October 2020 in the Department of Human Neurosciences, Sapienza University of Rome. The evaluation tools administered were the Parkinson's Disease Questionnaire (PDQ-39) to evaluate the quality of life of
the patients and the Health Assessment Questionnaire (HAQ), to evaluate the limitations of the ADL due to the disease.

Results: Of the 34 patients 11 were women (32.4%) and 23 men (67.6%) with a mean age of 68 years. The internal consistency of the HAQ assessed by the Cronbach's alpha was equal to 0.93. The study revealed significant correlations between the dimensions of the PDQ-39 and the subcategories of the HAQ using the Pearson Index. Significant correlations also emerged between the demographic and clinical characteristics of patients and the subcategories of HAQ.

Conclusions: The HAQ is a valid tool to assess the impact of PD on the patient's functioning and well-being and may provide the healthcare and rehabilitation sector with an additional evaluation tool.

References

[1] G Gefenaite, J Björk, S Iwarsson, B Slaug, S M Schmidt, M H Nilssonn (2020*); Longitudinal association between housing accessibility and activities of daily living: the role of self-efficacy and control in people ageing with Parkinson's disease; in* "BMC Geriatrics".
[2] M Tofani, A Ranieri, G Fabbrini, A Berardi, E Pelosin, D Valente, A Fabbrini, M Costanzo, G Galeoto (2020); *Efficacy of Occupational Therapy Interventions on Quality of Life in Patients with Parkinson's Disease: A Systematic Review and Meta-Analysi; in* "Movement Disorders".
[3] F Wolfe, K Michaud, T Pincus. Development and validation of the Health Assessment Questionnaire II: A revised version of the Health Assessment Questionnaire. Arthritis and Rheumatism. 2004.

P84

Impact of Covid-19 on Parkinson's disease: experience of an Italian centre

Sandy Maria Cartella, S. Bertino, F. Cucinotta, C. Terranova, A. Quartarone, P. Girlanda

Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

Background: Covid-19 had a negative impact on motor [2-3] and non-motor [1-4-5] aspects of movement disorders.

Objective: To assess the impact of Covid-19 on Parkinson's disease patients, with regard on non-motor symptoms, social aspects and everyday life.

Methods: Self-administered survey, based on Hamilton Depression and Anxiety Rating Scale, UPDRS, Hospital Anxiety and Depression Scale. Motor evaluation (UPDRS III) before and after lockdown.

Results: We analysed 33 patients. 50% of them felt more depressed and anxious than before lockdown. Sleep quality decreased for 38% of patients. These features are related between them and with the patients' level of education. For 5 patients hallucinations got worse, while four experienced worsened binge-eating disorder, one had ICDs and DDS for the first time. 43% of patients felt more fatigued, 58% of them felt more slowness of movements. 37% of patients felt their FOG worsened, 44% felt their posture did and 29% got worse motor fluctuations. UPDRS III worsened in 38% of patients. Only 5 patients had difficulty in finding their doctors, none of them in finding their drugs. 6 patients knew what telemedicine is, and 4 of them used it. 29% of patients said their health and quality of life decreased. For 51% of patients the most important problem was the impossibility to practice physiotherapy. Most people emailed our centre to postpone appointments or to seek medical advice, only 1% asked for Covid-19 related issues and telemedicine consultations.

Conclusions: Covid-19 had a negative impact on motor and non-motor symptoms of PD, with quality of life repercussions.

References

[1] G. Palermo, L. Tommasini, F. Baldacci, E. Del Prete, G. Siciliano, R. Ceravolo. Impact of Coronavirus Disease 2019 Pandemic on Cognition in Parkinson's Disease. Vol. 35, Movement Disorders. John Wiley and Sons Inc; 2020. p. 1717–8.
[2] E. Cubo, A. Hassan, B.R. Bloem, Z. Mari. Implementation of Telemedicine for Urgent and Ongoing Healthcare for Patients with Parkinson's Disease during the Covid-19 Pandemic: New Expectations for the Future. Vol. 10, Journal of Parkinson's Disease. IOS Press; 2020. p. 911–3.
[3] T. Schirinzi, G. Di Lazzaro, C. Salimei, R. Cerroni, C. Liguori, S. Scalise et al. Physical Activity Changes and Correlate Effects in Patients with Parkinson's Disease during Covid-19 Lockdown. Mov Disord Clin Pract. 2020 Oct 1;7(7):797–802.
[4] T. Schirinzi, R. Cerroni, G. Di Lazzaro, C. Liguori, S. Scalise, R. Bovenzi et al. Self-reported needs of patients with Parkinson's disease during Covid-19 emergency in Italy. Neurol Sci. 2020 Jun 1;41(6):1373–5.
[5] I. Subramanian. Virtual Parkinson's Disease Support Groups in the Covid-19 Era: Social Connection in the Time of Social Distancing. Vol. 7, Movement Disorders Clinical Practice. Wiley-Blackwell; 2020. p. 739–40.

P85

A longitudinal study on the impact of non-motor symptoms on quality of life of patients with Parkinson's disease before and during the Covid-19 pandemic

Alfonsina D'Iorio[1], C. Baiano[1], G. Maraucci[1], C. Vitale[2,3], M. Amboni[3,4], G. Santangelo[1]

[1]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Department of Motor Sciences and Wellness, University "Parthenope", Naples, Italy
[3]Institute of Diagnosis and Care (IDC), Hermitage-Capodimonte, Naples, Italy
[4]Department of Medicine, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Salerno, Italy

Introduction: The coronavirus disease 2019 (Covid-19) caused severe psychological consequences on people's mental health, representing a condition of increased vulnerability for the weakest sections of population, including elderly patients with Parkinson's disease (PD).

Objectives: This longitudinal study aimed at exploring the putative impact of the most frequent non-motor symptoms and their contribute to poor health related quality of life (HRQoL) of PD patients after the Covid-19 outbreak, in comparison with the pre-pandemic status.

Methods: Forty-three non-demented PD patients were enrolled. They underwent the first assessment between December 2018 and January 2020 (T0), before the Covid-19 outbreak. Then, between March and May 2021 (T1), they were contacted again and asked to complete the second assessment. The Montreal Cognitive Assessment assessing global functioning and several questionnaires assessing depression (by the Beck Depression Inventory-II, BDI-II), apathy (by the Dimensional Apathy Scale, DAS), anxiety (by the Parkinson Anxiety Scale, PAS), anhedonia (by the Temporal Experience of Pleasure Scale, TEPS) and health-related quality of life (by the Parkinson's Disease Quality of Life Questionnaire, PDQ-8) were administered.

Results: Results of the MANOVA showed that BDI-II, TEPS and PDQ-8 scores did not change between T0 and T1. At T1, PD patients scored lower on the emotional subscale of the DAS, $F = 7.66$ (1, 40); $p = 0.007$, and on PAS total score, $F = 4.09$ (1,40); $p = 0.047$.

Conclusions: In the present study no worsening of depression and anhedonia was found in PD patients. Contrariwise, an improvement of emotional apathy and anxious symptoms were reported. These evidences seem to suggest that restrictive measures such as self-isolation at home might lead to a reduction of apathy and anxiety in PD due to the increase in social support provided by PD patients families during Covid-19 restrictions. This evidence suggest the need of a consistent and persistent social support which might be represented by caregivers or/and social assistive robotics.

P86

Diagnosis and monitoring of Parkinson's disease (PD) looking in the patients' eyes

Susanne Buechner[1], D. De Blasio[2]

[1]Department of Neurology, General Hospital of Bolzano, Bolzano, Italy
[2]Orthoptic Service, General Hospital of Bolzano, Bolzano, Italy

*Introduction***:** Parkinson's disease (PD) can be divided into preclinical, prodromal, and clinical PD. Although disease-modifying treatments are still lacking, early diagnosis of PD has become of huge interest and several prodromal markers have been identified. Retinal abnormalities are seen in many PD patients, therefore some authors propose the retina as a biomarker for diagnosis and monitoring of PD. The human retinal structure can be assessed non-invasively by optical coherence tomography (OCT).

Objectives: OCT studies in PD patients reported in literature have provided conflicting results, therefore we wanted to investigate retinal morphology in some PD patients by ourselves.

Methods: 20 subjects diagnosed with PD, subdivided in 2 groups (A and B) according to their Hoehn and Yahr (H&Y) stage (I and II) and 10 age-matched control subjects underwent OCT, assessing the
thickness of retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), internal plexiform layer (IPL) and inner nuclear layer (INL).

Results: RNFL around the optic nerve showed an increased thickness in several quadrants in PD patients in comparison with the healthy controls, especially in the group A. Also the macular thickness
resulted thicker in PD patients as well as the thickness of some singularly layers.

Conclusions: While many studies have documented thinning of the various retinal layers (RNFL, GCL, IPL, and INL) in PD patients when comparing with healthy subjects, our study has demonstrated mostly increased thickness profiles. The small group of subjects is surely a limitation of our study, however, the discrepancy between previously published data and our findings underlines the need for further studies if the retina might be considered as a biomarker in PD. Those studies should be characterized by standardized OCT techniques, include PD patients of all H&Y stages, and consider additional ophthalmological investigations.

P87

Relationship between oligomeric α-synuclein/SNARE complex proteins and cerebral blood flow alteration in Parkinson's disease

Mario Meloni[1], L. Pelizzari[1], C. Agliardi[1], F.R. Guerini[1], F.L. Saibene[1], A.V. Milner[1], J. Navarro[1], M. Clerici[1,2], F. Baglio[1]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Introduction: Together with neuronal degeneration, perfusion parameters may also be altered in Parkinson's disease (PD) due to neurovascular unit function changes. Despite the consistent evidence of these perfusional alterations [1], it remains unclear the relationship between synucleinopathy and abnormal cerebral blood flow (CBF) in PD. Within pathological biomarker in PD, neural derived extravesicles (NDEs) measurements of oligomeric α-Synuclein and presynaptic SNARE complex proteins are widely recognized to play a crucial role [2].

Objective: The aim of this study was to pilot testing in a cohort of mild PD the relationship between disruption of Arterial Spin Labeling (ALS)-measured CBF brain networks and NDEs levels of pathogenic oligomeric α-Synuclein and SNARE complex proteins (STX-1A, VAMP-2 and SNAP-25).

Methods: Twenty-five subjects with a diagnosis of PD according to the Movement Disorder Society Clinical Diagnostic Criteria were enrolled. The MRI acquisition protocol (3T Siemens Prisma scanner) included a T1-3D high-resolution sequence and a multi-delay pseudo-continuous ASL (pCASL) sequence to derive CBF maps. pCASL images processing was conducted according to [3] and CBF values within functional networks were obtained. NDEs were isolated from peripheral serum samples by immunocapture with L1CAM antibody. Oligomeric α-Syn and SNARE complex proteins levels were measured in NDEs extracts by sandwich ELISA.
The relationship between NDEs levels and CBF values was tested with partial Spearman's correlation analysis, controlling for age.

Results: Positive significant correlations were observed between CBF and STX-1A within several networks (i.e. dorsolateral-rho 0.51, *p*.005 and frontoparietal networks-rho 0.55, *p*.003). No significant negative correlations were found.

Conclusions: Our results suggest that a relationship between low levels of STX-1A and low CBF values in the cortical frontoparietal brain networks may be present. A combination of structural imaging and measurement of serum NDEs biomarkers can provide new insights into the relationship between synucleinopathy and CBF changes in PD.

References

[1] Arslan DB et al. J Neural Transm (Vienna). 2020 Sep;127(9):1285-1294.
[2] Agliardi C et al. Neurobiol Dis. 2021 Jan;148:105185.
[3] Pelizzari et al. Front Neurol. 2020; 11: 562. [5] Mancini et al. Front Neurol. 2019 Jan 7;9:1149.

P88

Anodal cerebellar tDCS can reduce sleep onset latency in Parkinson's disease patients

Michelangelo Dini[1], M. Vergari[2], F. Ruggiero[2], M. Nigro[2], F. Cortese[3], M.R. Reitano[4], M. Guidetti[1], N. Maiorana[1], A. Averna[1], T. Bocci[1,4], A. Priori[1,4], R. Ferrucci[1,4]

[1]Department of Health Science, "Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[2]Neurophysiology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Neurology Unit, San Filippo Neri Hospital, Rome, Italy
[4]III Neurology Clinic, ASST Santi Paolo e Carlo, Milan, Italy

Introduction: Sleep problems are frequent in Parkinson's disease (PD), and influence the quality of life of patients [1]. Studies have shown that transcranial direct current stimulation (tDCS) can improve sleep quality in both healthy people [2] and PD patients [3].

Objective: To assess the effect of 1-week anodal cerebellar tDCS on sleep quality in PD patients.

Methods: We assessed sleep quality in 9 patients with PD (aged 42-77, 4 females) using the Pittsburgh Sleep Quality Index (PSQI) questionnaire, which assesses subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleeping disturbances, use of sleeping medication, and daytime dysfunction (higher scores indicate greater dysfunction). Patients were assessed before and after completing a cycle of cerebellar tDCS sessions (2 mA for 20 minutes, twice-daily, anode over the cerebellum midline, cathode over the right deltoid muscle). All patients received sham and anodal stimulations in a randomised balanced order. Analyses were conducted using Wilcoxon signedrank tests (α=.05).

Results: Following anodal tDCS, we observed improvements in sleep latency (baseline vs. post-tDCS; median [1st-3rd quartiles]= 1 [0-1] vs. 0 [0-0]; p=.046) and PSQI total score (6 [4-9] vs. 5 [4-7]; p=.034), while there were no differences after sham tDCS. Baseline PSQI scores were not significantly different between anodal and sham conditions.

Conclusions: Cerebellar tDCS may prove to be an effective option for PD patients who experience sleep difficulties, and in particular for those who have problems falling asleep. Larger studies are needed in order to substantiate our preliminary results, which nevertheless suggest an involvement of the cerebellum in the top-down regulation of sleep.

References

[1] M Menza, RD Dobkin, H Marin, K Bienfait. Sleep disturbances in Parkinson's disease. Mov Disord[Internet] 2010 [cited 2019 Aug 18];25 Suppl 1(Suppl 1):S117-22.
[2] J Charest, A Marois, CH Bastien. Can a tDCS treatment enhance subjective and objective sleep among student-athletes? J Am Coll Heal 2019.
[3] H Hadoush, A Al-Sharman, H Khalil, SA Banihani, M Al-Jarrah. Sleep Quality, Depression, and Quality of Life After Bilateral Anodal Transcranial Direct Current Stimulation in Patients with Parkinson's Disease. Med Sci Monit Basic Res 2018;24:198–205.

P89

The effect of music-induced emotion on visuospatial learning in people with Parkinson's disease

Giovanna Lagravinese[1,2], T. Lencioni[1,3], M. Putzolu[1], C. Ponte[1], C. Cosentino[1], L. Avanzino[2,4], G. Bonassi[5], S. Mezzarobba[1], E. Pelosin[1,2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[2]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[3]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[4]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[5]ASL4, Chiavarese, S.C. Physical Medicine and Rehabilitation, Rapallo/ Sestri Levante, Italy

Background: Emotional states influence cognitive processes including visuospatial learning. Parkinson's disease (PD), besides manifesting with the cardinal motor symptoms, presents cognitive dysfunctions, including impairment in visuospatial abilities, and affective disturbances. It has been demonstrated that visuospatial learning and movement preparation might share similar attentional and working memory resources in PD.

Aim: To investigate whether manipulation of the emotional state by means of music was able to influence the performance in a visuospatial learning task in PD patients.

Methods: 10 PD patients and 11 healthy elderly (ELD) performed a visuospatial learning task while listening two musical pieces evoking neutral or fearful emotions. Targets were presented on a screen in a preset order over four session blocks and subjects were asked to learn the sequence order by attending to the display. At the end of each block, participants were asked to verbally recall the sequence and a score was assigned (Verbal Score, VS).

Results: Statistical analysis showed that in both groups VS improved significantly after two blocks, but at the end of the task ELD reached a significantly higher VS compared to PD ($p=0.001$). Regarding the effect of music, listening to the Neutral music piece improved VS already after the first
block, whereas listening to the Fear music piece delayed the learning of VS (improvement after the second block), with no differences between PD and ELD.

Discussion: Fearful music exerted the same influence on visuospatial learning in elderly and in PD, despite differences in cognitive abilities between groups. Our hypothesis is that the fearful music influenced the fronto-parietal network, involved in visuospatial learning, and particularly the dorsolateral prefrontal cortex (DLPFC), traditionally considered involved in cognition, but also in emotional processes.

Conclusions: The induced fear state exerts its effect on cognitive circuits underpinning visuospatial ability making less prominent the contribution of individual cognitive and affective characteristics.

P90

Pilot study on the effect of combined treatment with safinamide and opicapone in fluctuating PD patients

Michela Sforza[1], E. Bianchini[1], M. Alborghetti[1,2], D. Rinaldi[1], L. De Carolis[1], F.E. Pontieri[1,2]

[1]Dipartimento di Neuroscienze, Salute Mentale e Organi di Senso (NESMOS), Sapienza Università di Roma, Roma, Italy
[2]Fondazione Santa Lucia, IRCCS, Roma, Italy

Introduction: Fluctuations and dyskinesia are frequent complications in Parkinson's disease (PD) patients treated with levodopa. Monoamine-oxidase-B (MAO-B) and catechol-O-methyl-transferase (COMT) inhibitors increase levodopa and dopamine availability through different mechanisms, and display therapeutic efficacy on fluctuations in PD patients, as well as similar side-effects. Based on the different mechanism of action of these drugs, the question raises of whether combining MAO-B and COMT inhibition may provide further benefit to fluctuating PD patients.

Objective: Here we preliminarily investigated the tolerability, safety and efficacy of add-on with safinamide 100 mg (SF) and opicapone 50 mg (OPC) in fluctuating PD subjects.

Methods: Seven PD patients displaying re-occurrence of fluctuations while under add-on therapy with either SF or OPC underwent combined treatment with the two drugs. SF was administered in the morning and OPC in the evening. The remaining antiparkinsonian therapy was unmodified. Outcome measures included MDS-UPDRS-III, NMSS and WOK-19 scores.

Results: After 4 months of add-on with SF+OPC, there was marked reduction of WOK-19 score, together with significant improvements of both MDS-UPDRS-III at the end of levodopa dose and NMSS score. Sleep was the most significantly improved non motor domain. Patients did not report clinically relevant side effects, in particular there was no evidence of development/worsening of dyskinesia.

Conclusions: These preliminary results show the tolerability, safety and efficacy of combining SF and OPC in fluctuating PD patients. The effects on sleep pattern and quality suggest that such potentiation of dopamine replacement therapy may provide particular benefit during night-time and akinesia at awakening. Furthermore, the antiglutamatergic mechanism of high dose SF may be useful for anti-dyskinetic effects. If confirmed on larger studies, add-on with SF+OPC may provide a convenient strategy for second line treatment of motor and nonmotor complications of PD.

P91

Application of the mPSPRS to the Salerno cohort and a comparison between PSP-RS and vPSP

Filomena Abate, M.F. Tepedino, P. Barone, M. Picillo

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Salerno, Italy

Introduction: Recently, a new evaluation scale for progressive supranuclear palsy (PSP) has been proposed (modified PSP-rating scale - mPSPRS) [1]. In this version, some items from the PSPRS have been condensed or eliminated in order to focus on meaningful disease milestones.

Objective: To apply the mPSPRS to the Salerno PSP cohort and investigate its sensitivity to change in patients with Richardson syndrome (PSP-RS) and the other variants (vPSP).

Methods: PSP diagnosis and phenotype attribution were determined according with the Movement Disorder Society criteria [2-3]. The mPSPRS was computed for 36 patients (29 PSP-RS and 7 vPSP) and assessed at least twice (mean±standard deviation follow-up: 15.33±9.78 months). Power calculations were used to estimate the sample size required to detect 20% and 50% change from baseline in PSP-RS and vPSP for the mPSPRS and PSPRS.

Results: Our data confirm that for the whole PSP cohort the mPSPRS has a slight lower sensitivity compared to its original version to detect a 50% change over follow up. Sample sizes for power calculations in our cohort are in general smaller than those reported by Grötsch et al. [1], possibly due to the longer follow up (15 vs 12 months). When considering PSP phenotypes, the mPSPRS presented higher sensitivity for PSP-RS than vPSP. In keeping with the slower disease progression in vPSP, effect sizes are smaller, thus larger samples would be needed to detect significant changes over time [1].

Conclusions: Our data further support the use of the proposed mPSPRS in the clinical practice when considering all the disease phenotypes. However, we also highlight that more work needs to be done to improve sensitivity to change of rating scales and sample size calculations for vPSP. Given the heterogeneous forms of disease included in the vPSP category, a revision rather than a simple compression of the original PSPRS would be advisable.

References

[1] Grötsch MT, Respondek G, Colosimo C, et al. A Modified Progressive Supranuclear Palsy Rating Scale. Mov Disord 2021 online ahead of print.
[2] Höglinger GU, Respondek G, Stamelou M, et al. Clinical diagnosis of progressive supranuclear palsy: the movement disorder society criteria. Mov Disord 2017;32(6):853–864.
[3] Grimm MJ, Respondek G, Stamelou M, et al. How to Apply the Movement Disorder Society Criteria for Diagnosis of Progressive Supranuclear Palsy. Mov Disord. 2019 Aug; 34(8):1228–1232.

P92

Psychometric properties of the Beck Depression Inventory-II in progressive supranuclear palsy

Sofia Cuoco[1], A. Cappiello[1], F. Abate[1], M.F. Tepedino[1], R. Erro[1], G. Volpe[2], M.T Pellecchia[1], P. Barone[1], M. Picillo[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience Section, University of Salerno, Salerno, Italy
[2]Neurology Unit, AOU S. Giovanni di Dio e Ruggi D'Aragona, Salerno, Italy

Objectives: Depression is one of the most common neuropsychiatric symptoms in progressive supranuclear palsy (PSP) [1]. Yet few studies have examined the ability of available instruments to detect depressive symptoms in PSP. Aims of the present study were to: (I) report psychometric properties of the Beck Depression Inventory, Second Edition (BDI-II) in PSP, (II) establish the BDI-II cutoff indicating the presence of depression in PSP, (III) describe clinical correlates as well as correlation with quality of life of depressive symptoms in PSP.

Design, Setting, Participants: At the Center for Neurodegenerative Diseases of the University of Salerno, Salerno (Italy) the BDI-II was validated in 62 PSP patients diagnosed according to the Movement Disorder Society criteria. Patients underwent a clinical interview, a motor evaluation, extensive cognitive and behavioral testing.

Results: The mean BDI-II total score was 15.92 ± 10.31. The internal consistency was high (Cronbach's alpha = 0.868); corrected item-total correlation was > 0.40 for the majority of items. The significant and moderate correlation of the BDI-II with other tools evaluating depressive symptoms indicated adequate convergent validity of the scale. The satisfactory cut-off to identify patients with clinically significant depression was > 14.5. We also showed a correlations between higher scores on BDI-II and lower quality of life, irrespective of motor and cognitive burden.

*Conclusions***:** In conclusion, the BDI-II is a reliable and valid tool for assessment of depression symptoms in PSP. Such data are useful to standardize studies of depression in PSP and to quantify the effectiveness of any interventions on this disabling symptom [2-3].

References

[1] A Gerstenecker, K Duff, B Mast, I Litvan. and ENGENE-PSP Study Group (2013). Behavioral abnormalities in progressive supranuclear palsy. Psychiatry research, 210 (3), 1205–1210. https://doi.org/10.1016/j.psychres.2013.08.045.
[2] B Uttl, P Santacruz, I Litvan and J Grafman (1998). Caregiving in progressive supranuclear palsy. *Neurology*, *51*(5), 1303– 1309. https://doi.org/10.1212/wnl.51.5.1303.
[3] M Picillo et al. (2019). Validation of the Italian version of carers' quality-of-life questionnaire for parkinsonism (PQoL Carer) in progressive supranuclear palsy. *Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *40*(10), 2163–2169. https://doi.org/10.1007/s10072-019-03944-x.

P93

Energy expenditure, body composition and dietary habits in progressive supranuclear palsy: a case-control study

Maria Francesca Tepedino, M.C. Russillo, F. Abate, M. Savastano, A. De Simone, R. Erro, M.T. Pellecchia, P. Barone, M. Picillo

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy

Introduction: Recent evidence suggests that neurodegenerative diseases are associated with a wide spectrum of metabolic changes [1-3]. However, the nature of these metabolic changes and how they can affect disease progression are largely unknown.

Objective: Goals of the present study were to (1) investigate whether progressive supranuclear palsy (PSP) at early stages is associated with changes in energy expenditure, body composition and dietary intake compared with PD patients and healthy controls (HC); (2) assess the accuracy of the equation of Harris-Benedict, constructed to estimate rest energy expenditure (eREE) in healthy individuals, to predict measured REE (mREE) in PSP; (3) verify differences in the above-mentioned variables according to pre-specified categories in the PSP cohort4 (phenotypes, disease severity and presence of clinically significant dysphagia).

Methods: Twenty-one PSP, 41 PD and 9 HC were included. REE was assessed with indirect calorimeter, body composition with biompedance analysis and physical activity and dietary intake were estimated with a validated frequency questionnaire. Parametric testing was used to analyze differemces between group.

Results: On a group-level, PSP showed reduced total daily energy expenditure (TDEE) and physical activity compared to both PD and HC ($p<0.001$) and a tendency towards lower fat free mass compared to PD ($p>0.05$). Limited accuracy was shown for the Harris-Benedict equation (accurate prediction
frequency<60%). PSP with greater disease severity presented lower REE ($p=0.030$), fat free mass ($p=0.026$) and muscle mass ($p=0.029$).

Conclusions: PSP present lower TDEE possibly linked to reduced mobility compared with PD and HC. Greater disease severity is associated with a reduction in REE possibly due to the reduction in lean mass and muscle mass. Such data may pave the way to clinical trials evaluating the efficacy of muscletargeted nutritional support and physical therapy in preserving muscle mass and improving motor performances in PSP at early stages.

References

[1] M Barichella, E Cereda, E Cassani, et al. Dietary habits and neurological features of Parkinson's disease patients: implications for practice. Clinical nutrition 2017;36(4):1054-61.
[2] M Barichella, G Pinelli, L Iorio et al. Sarcopenia and dynapenia in patients with Parkinson's disease. J Am Med Dir Assoc 2016;17(7):640-46.
[3] M Barichella, E Cereda, SA Faierman et al. Resting energy expenditure in Parkinson's disease patients under dopaminergic treat ment. Nutr Neurosci 2020;7:1-10.
[4] GH Hoglinger, G Respondek, M Stamelou et al. Clinical Diagnosis of Progressive Supranuclear Palsy: The Movement Disorder Society Criteria. Mov Disord 2017;32:853–864.

P94

Relationship between orthostatic hypotension and cognitive functions in multiple system atrophy: a longitudinal study

Immacolata Carotenuto, S. Cuoco, A. Cappiello, S. Scannapieco, M.C. Russillo, V. Andreozzi, L. Forino, M. Amboni, M. Picillo, R. Erro, P. Barone, M.T. Pellecchia

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience Section, University of Salerno, Salerno, Italy

Introduction: The aim of this study is to investigate the impact of orthostatic hypotension (OH) on cognitive functions in patients with multiple system atrophy (MSA) [1] followed over time.

Methods: Thirty-two patients were enrolled and underwent a comprehensive neuropsychological battery [2]; at baseline (T0) 15 out of 32 patients presented OH, assessed by means of orthostatic standing test. All patients underwent a follow-up (T1) evaluation 12 months after baseline. Thirteen out of 32 patients underwent a second follow-up (T2) evaluation at 24 months. Changes over time on different neuropsychological tasks were compared between patients with and without OH by means of Mann-Whitney's U test. Moreover, clinical categories of normal cognition, mild cognitive impairment and dementia[3] were determined and changes at T1 and T2 in global cognitive status were compared between patients with and without OH.

Results: At T0, patients with OH had better performance on words/non-words repetition task ($p=.02$) compared to patients without OH. Compared to patients without OH, patients with OH performed worse on semantic association task ($p< .01$) at T1 and on Stroop test-error effect ($p= .04$) at T2. The percentage of patients with worsened cognitive status at T1 was higher among patients with OH than among patients without OH (93% vs 59%, $p=.03$). OH ($\beta= -4.67$, $p=.01$), education ($\beta=.45$, $p=.02$), age ($\beta=.19$, $p=.03$) and MOCA score at T0 ($\beta= -.26$, $p=.04$) were significant predictors of global cognitive status worsening at T1.

Discussion: We found that global cognitive status worsened at one-year followup in 93% of patients with OH and OH, along with age, education, and MOCA score predicted cognitive worsening over time. To clarify the relationship between OH and cognitive dysfunction in MSA, we suggest the use of clinical categories of normal cognition, mild cognitive impairment and dementia in further longitudinal studies on MSA patients with and without OH.

References

[1] S Gilman, GK Wenning, PA Low, DJ Brooks, CJ Mathias, JQ Trojanowski et al., Second consensus statement on the diagnosis of multiple system atrophy. Neurology. (2008) Aug 26;71(9):670-6.
[2] R Iseli, VTV Nguyen, S Sharmin, EM Reijnierse, WK Lim, AB Maier. Orthostatic hypotension and cognition in the elderly: a systematic review and a metaanalysis. Exp Gerontol. (2019) Jun; 120: 40-49. Doi: 10.1016 / j.exger.2019.02.017. Epub 2019 Feb 28. PMID: 30825549.
[3] I Litvan, JG Goldman, AI Tröster, BA Schmand, D Weintraub, RC Petersen et al., Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord. (2012). Mar;27(3):349-56. doi: 10.1002/mds.24893.

P95

The ScanMove instrument as predictive of degenerative parkinsonism in bipolar disorder

Annamaria Landolfi[1], G. D'Agostino[1], M. Picillo[1], C. Vitale[2], M.T. Pellecchia[1], P. Monteleone[1], P. Barone[1], R. Erro[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Baronissi, Italy
[2]Department of Motor Sciences and Wellness, University Parthenope, Naples, Italy

Introduction: Recent evidence suggests that up to 20% of patients with Bipolar Disorder (BD) and extrapyramidal symptoms might have an underlying degenerative parkinsonism [1]. Moreover, neuroleptic exposure does constitute an independent risk factor for developing parkinsonian symptoms in these patients. Clinical phenotype, as it is characterized and quantified by the MDS-UPDRSIII scale, is usually not predictive for the signs and symptoms' etiology (i.e. degenerative vs. iatrogenic).

Objective: The aim of our work is to evaluate the predictive power of the ScanMove Instrument, which is a 31-item scale originally designed for the screening of antipsychotic-associated movement disorders for use by mental health nurses, for degenerative parkinsonism in bipolar patients.

Materials and Methods: We applied the ScanMove Instrument [2] to a population of patients affected by BD and presenting extrapyramidal signs, who underwent ^{123}I-ioflupane dopamine transporter single-photon emission computer tomography (SPECT). The ScanMove items were grouped into the following categories: "bradykinesia-rigidity" (items 1-2-3-25-26-27-28-33), "tremor-myoclonus" (items 7-9-15-17-22-36-38), "dystonia" (items 4-5-13-20-34), "facial movement disorders" (items 6-14-21-29-35), "voice-sialorrhea" (items 31-32), "dyskinesia-akathisia" (items 10-11-18-24).

Results: Thirty-one patients affected by BD were evaluated. Five of them (19%) had abnormal scans, defined as a striatal binding ratio z-score of <-2. The two groups did not differ in terms of age, motor symptom duration, MDS-UPDRSIII scores, and antipsychotic treatment in terms of chlorpromazine equivalents. Mean scores obtained for the "dystonia" category were significantly higher in patients with dopaminergic denervation compared to patient with normal dopaminergic imaging (2 vs 0.38, respectively; p: 0,03). Anterior stooped posture (camptocormia) and neck antero-lateral dystonic deviation were the main findings in the group of patients affected by neurodegenerative parkinsonism.

Conclusions: Our preliminary findings suggest that the Scan Move Instrument might be a useful screening tool for clinical signs that may be suspect for underlying neurodegeneration in bipolar patients with parkinsonian symptoms. A larger sample is needed to validate results.

References

[1] R. Erro, A. Landolfi, G. D'Agostino, L. Pace, M. Picillo, M. Scarano, A. Cuocolo, S. Pappatá, C. Vitale, M.T. Pellecchia, P. Monteleone, P. Barone, (2021). Bipolar Disorder and Parkinson's Disease: A ^{123}I-Ioflupane Dopamine Transporter SPECT Study. *Frontiers in neurology*, *12*, 652375. https://doi.org/10.3389/fneur.2021.652375.
[2] B. Balint, H. Killaspy, L. Marston, T. Barne, A. Latorre, E. Joyce, C.S. Clarke, R. De Micco, M.J. Edwards, R. Erro, T. Foltynie, R.M. Hunter, F. Nolan, A. Schrag, N. Freemantle, Y.

Foreshaw,N. Green, K.P. Bhatia, D. Martino. Development and clinimetric assessment of a nurse-administered screening tool for movement disorders in psychosis. BJPsych Open. 2018 Sep 27;4(5):404-410. doi: 10.1192/bjo.2018.55. PMID: 30294450; PMCID: PMC6171333.

P96

Gait analysis in normal pressure hydrocephalus: a meta-analysis

Massimiliano Passaretti[3*], A. Maranzano[1,2*], B. Bluett[4,5], A. Fasano[6]
** These authors share co-first authorship*

[1]Department of Neurology-Stroke Unit and Laboratory of Neuroscience, Istituto Auxologico Italiano IRCCS, Department of Pathophysiology and Transplantation, "Dino Ferrari" Center, Università degli Studi di Milano, Milan, Italy
[2]Neurology Residency Program, Università degli Studi di Milano, Milan, Italy
[3]Departement of Human Neurosciences, Sapienza University of Rome, Rome Italy
[4]Stanford University School of Medicine, Movement Disorders Program, Palo Alto, CA, USA
[5]Dignity Health, Pacific Central Coast Health Center, Arroyo Grande, CA, USA
[6] Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, UHN; Krembil Brain Institute; Division of Neurology, University of Toronto, Toronto, Ontario, Canada

Background and aims: Gait analysis is a useful instrument to assess gait impairment in Normal Pressure Hydrocephalus (NPH) patients. This is the first meta-analysis to summarize quantitative gait data in NPH. Specifically, we investigated which gait parameters are more likely to improve after tap-test (TT) and CSF shunt surgery (CSS), and differentiate responders (R) from non-responders (NR).

Methods: A literature review was conducted by accessing PubMed. Papers were selected using search criteria of idiopathic NPH with at least one instrumented measure of gait. We defined three time points of gait assessment: baseline (PRE), after TT (POST-TT) and after CSS (POST-CSS). Five gait metrics were consistently reported and taken into account for the meta-analysis: gait velocity, cadence, step length, stride length, and double limb support time (DLS). Findings were categorized as iNPH (total sample), NPH-NC, not classified according to diversion procedures responsiveness, R (TT-R and CSS-R), and NR (TT-NR and CCS-NR). Healthy controls (HC) were included when reported.

Results: Twenty studies met the inclusion criteria. TT-R patients improve significantly POST-TT and POST-CSS in each meta-analyzable gait metric. NPH-NC improved in gait velocity, stride length and DLS POST-TT, whereas only in gait velocity POST-CSS. Several gait parameters consistently discriminated R from NR and HC.

Conclusions: This meta-analysis demonstrates gait analysis is a reproducible quantitative instrument to assess gait in NPH, and is useful in selecting responders to shunt placement. Specific parameters seem to delineate the gait pattern of TT-R, providing a critical opportunity to select patients that will respond to CSS.

P97

Sexual dysfunction in female patients with multiple system atrophy

Cecilia Raccagni[1,2], E. Indelicato[1,3], V. Sidoroff[1], M. Daniaux[4], A. Bader[5], B. Toth[6], L.A. Jelisejevas[7], A. Fanciulli[1], F. Leys[1], S. Eschlboeck[1], C. Kaindlstorfer[1], S. Boesch[1,3], G.K. Wenning[1]

[1]Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria
[2]Department of Neurology, Regional General Hospital, Bolzano, Italy
[3]Center for Rare Movement Disorders Innsbruck, Medical University of Innsbruck, Innsbruck, Austria
[4]Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria
[5]Women´s Health Care Centre, Medical University of Innsbruck, Innsbruck, Austria
[6]Department of Gynecological Endocrinology and Reproductive Medicine, Medical University of Innsbruck, Innsbruck, Austria
[7] Department of Urology, Medical University of Innsbruck, Innsbruck, Austria

Objective: To characterize sexual dysfunction in female patients with Multiple System Atrophy (MSA).

Background: The diagnosis of probable MSA relies on the presence of parkinsonian and/or cerebellar signs along with a severe cardiovascular or urogenital dysautonomia. Erectile dysfunction is required to fulfil the urogenital dysautonomia criterion in males, whereas no correlating item has been established for females. Up to date, the characterization of sexual disturbances in female patients with MSA has been neglected.

Methods: We administered a standardized questionnaire, the Female Sexual Function Index (FSFI) and investigated the effect of mood and concomitant gynecological comorbidities in female patients with MSA and in age-matched controls. We additionally interviewed patients and controls about presence of "genital hyposensitivity" [1].

Results: We recruited 25 MSA female patients (12 of cerebellar type) and 42 female controls. FSFI scores in MSA females were significantly lower as compared to controls (16,2(8,7;20,1) versus 28,4(21,3;30), p=0,001). The largest difference concerned the items desire (p=0,007), arousal (p=0,01) and lubrication (p=0,02). Genital hyposensitivity was reported by 14 MSA (56%) and 4 controls (9%, p<0,0001).

Conclusions: Sexual dysfunction is highly prevalent in MSA female patients. Screening for disturbances of specific sexual domains should be implemented in the clinical evaluation of female patients with suggestive motor symptoms.

References

[1] W. Oertel, T Wächter, NP Quinn, G Ulm, D Brandstädter, Reduced genital sensitivity in female patients with multiple system atrophy of parkinsonian type, Mov. Disord. 18 (2003) 430–432. https://doi.org/10.1002/mds.10384.

P98

Impact of safinamide on central fatigue in Parkinson's disease: preliminary data

Caterina Pauletti, N. Locuratolo, D. Mannarelli, A. Maffucci, A. Petritis, F. Fattapposta

Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy

Introduction: Central fatigue has been reported to be a common and disabling symptom in Parkinson's disease (PD), affecting up to 58% of PD patients [1-2]. Safinamide is an orally administered alfa-aminoamide derivative that selectively and reversibly inhibits MAOB and blocks/modulates voltage-dependent sodium and calcium channels, as well as glutamate release, targeting both dopaminergic and glutamatergic systems. Many studies demonstrated its effectiveness in improving motor functions and fluctuations, and also in reducing non-motor symptoms, such as mood fluctuations and chronic pain, in fluctuating PD [3].

Objective: The aim of the present study was to evaluate whether safinamide could represent an effective treatment to reduce central fatigue in PD patients, given safinamide's dual mechanism of action.

Methods: 28 non-demented mid- to late-stage fluctuating PD patients with central fatigue received safinamide 100 mg as add-on therapy to a stable antiparkinsonian treatment. Before and after 6 months of treatment, patients underwent an assessment of central fatigue, as well as secondary variables such as depression, quality of life, motor and non-motor symptoms, utilizing a battery of validated scales.

Results: Central fatigue significantly improved after 24 weeks of treatment (FSS p=0.04; PFS16 p=0.05). An improvement bordering on significance was observed also in the domain 3 (mood/cognition) of the NMSS (p=0.08). On the contrary no significant variation in UPDRS-III was found.

Conclusions: Our data seem to confirm that central fatigue is a symptom intrinsic to the pathological substrates associated with PD, rather than secondary to the motor impairment. Moreover safinamide seems to ameliorate central fatigue in fluctuating PD patients after 6 months of treatment. As for many non-motor symptoms, the pathophysiology of central fatigue appears to be complex and multifactorial and a dysfunction of both dopaminergic and non-dopaminergic systems may contribute to its development. Drugs that interact with several neurotransmission systems, such as safinamide, seem to be helpful in reducing this symptom in PD patients in later stages of the disease.

References

[1] A. Chaudhuri, P.O. Behan. Fatigue and basal ganglia. J Neurol Sci. 2000 Oct 1;179(S 1-2):34-42. doi: 10.1016/s0022-510x(00)00411-1. PMID: 11054483.
[2] J.H. Friedman, R.G. Brown, C. Comella, C.E. Garber, L.B. Krupp, J.S. Lou et al. Fatigue in Parkinson's disease: a review. Mov Disord 2007;22:297–308. https://doi.org/10.1002/mds.21240
[3] E. Peña, C. Borrué, M. Mata, J.C. Martínez-Castrillo, A. Alonso-Canovas, J.L.Chico, L. López-Manzanares, M. Llanero, J. Herreros-Rodríguez, A. Esquivel, T. Maycas-Cepeda, C. Ruíz-Huete. Impact of Safinamide on Depressive Symptoms in Parkinson's Disease Patients (SADness-PD Study): A Multicenter Retrospective Study. Brain Sci. 2021 Feb 13;11(2):232. doi: 10.3390/brainsci11020232.

P99

Neuropsycological assessment in patients undergoing Magnetic Resonance Imaging-guided Focused Ultrasound (MRgFUS) thalamotomy

Gennaro Saporito[1], P. Sucapane[2], C. Marini[2,3], D. Cerone[2], T. Russo[2], S. Sacco[1], 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

Introduction: Unilateral magnetic resonance imaging-guided focused ultrasound (MRgFUS) ventral intermediate nucleus (Vim) thalamotomy is a well-established treatment for medically resistant Essential Tremor (ET) and Parkinson Disease (PD) related tremor. Data about the possible correlation between cognitive changes and the MRgFUS treatment are inconsistent. More evidence about this issue may be of help also in evaluating the safety of potential future bilateral treatments.

Objective: The aim of the present study was to assess the presence of any cognitive changes three months after the MRgFUS-Vim thalamotomy.

Methods: Thirty-five patients (mean age±SD 68.8±11.7, mean disease duration±SD 9.8±5.5, mean education±SD 10.7±4.0) with a diagnosis of medically resistant Essential Tremor (n=20) or Parkinson disease related tremor (n=15) were included in the study. Cognitive domains were evaluated by a complete neuropsychological battery [(Montreal Cognitive Assesment, Frontal Assesment Battery (MOCA), Verbal and Semantic Fluency Test, Mini-mental State Examination (MMSE), Rey Auditory Verbal Learning Test (RAVLT), Raven's progressive Matrices, Beck Depression Inventory (BDI-II), Hamilton Anxiety Rating Scale (HAM-A) and the Quality of Life in Essential Tremor Questionnaire (QUEST)] before (T0) and three months after the treatment (T1) to investigate the presence of any post-treatment impairment. Data were analyzed through the SPSS software using a paired T-Test. The level of significance was fixed at 0.05.

Results: Our data showed that BDI-II (p=0,003), HAM-A (p=0.011) and QUEST (p=0.000) scores significantly improved at the 3-month evaluation. No significant differences have been detected in the other cognitive domains.

Discussion: Our findings show that unilateral MRgFUS-Vim thalamotomy is a safe treatment not associated with cognitive changes in the short-term. In our sample, an improvement of feelings of anxiety and depression, together with a general improvement in quality of life, have been observed.

Conclusions: Future studies are necessary to assess potential cognitive and behavioral changes in the long-term.

P100

Does deep brain stimulation lead to personality change? A pilot study in Parkinson's disease

F. Ruggiero[1], R. Ferrucci[2], S. Marceglia[3], M. Prenassi[3], L. Borellini[1], F. Cogiamanian[1], *Eleonora Zirone*[1], B. Capetti[1], D. Mellace[1], M. Dini[2], M. Vergari[1], E. Pirola[1], M. Locatelli[1], A. Priori[2], S. Barbieri[1], F. Mameli[1]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2]Department of Health Science, "Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[3]University of Trieste, Trieste, Italy

Introduction: Deep brain stimulation (DBS) has emerged as one of the most effective treatment modalities for Parkinson disease (PD). There is, however, increasing evidence that subthalamic nucleus-DBS (STN-DBS) may be associated with a higher incidence of adverse changes in behavior when compared to other stimulation sites [1].

Objective: To date, no study has investigated the effect of the amount of total electrical energy delivered (TEED) on behavioral adverse changes. To characterize this issue, we assessed personality traits correlated with TEED in twenty PD patients.

Methods: 20 PD patients (12 women, mean [±SD] age 57.6±7.6 years) with advanced L-dopa responsive PD were included in this study. We tested psychological issues before and 12 months after bilateral DBS-STN. To assess personality we used MMPI-2 according to CAPSIT-PD procedure [2].

Results: After 12 months of DBS, patients showed significant changes in some MMPI-2 scales. Specifically, we observed higher scores in the D scale ($p = 0.015$), DEP scale ($p = 0.009$), LSE scale ($p = 0.023$) and WRK scale ($p = 0.002$). We found a correlation between the changes in MMPI-2 subscale D and TEED on the right hemisphere (Spearman's rho = -0.68, $p = 0.007$) after 12 months.

Conclusions: Different influences of multiple factors contribute to impact the personality traits such as TEED, intra/postsurgical coping mechanisms and outcome expectations. Our study encourages broader research programs focused on increasing our knowledge of the TEED effect on mood and personality traits. Further studies should be designed based on longer follow-up, in order to clarify the duration of the potential stimulation effects on patients' mood and personality traits.

References

[1] Hannah et al. Neuropsychol Rev 2015;25(4):439-54.
[2] Defer et al. J Mov Disord 1999;14(4):572-84.

P101

Comparison study of advanced therapies on sleep disorders in Parkinson's disease

Gabriele Imbalzano, E. Montanaro, A.F. Olivetti, A. Romagnolo, C.A. Artusi, M.G. Rizzone, M. Zibetti, L. Lopiano

Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy

*Introduction***:** Sleep disorders are a very common non-motor symptom in advanced Parkinson's disease (PD), with significant negative impact on patients and caregivers' quality of life [1]. Advanced Stage Therapies (AST) for PD could have beneficial effects on sleep disorders [2, 3]. However, the impact of AST on sleep disorders is still matter of debate, especially considering a long-term follow-up.

*Objective***:** To evaluate long-term impact of AST for PD on sleep disorders and daytime sleepiness.

*Methods***:** Sixty-six PD patients at the time of evaluation for AST (T0) underwent an extensive neurological and neuropsychological assessment, including subjective evaluation of sleep nocturnal symptoms and daytime sleepiness through the Parkinson's Disease Sleep Scale (PDSS-2) and the Epworth Sleepiness Scale (ESS). After the assessment, twenty-four patients underwent Deep Brain Stimulation (DBS), twenty-six Levodopa-Carbidopa intestinal gel (LCIG) infusion, and sixteen continued Best Medical Treatment (BMT). Sleep assessment was repeated at 36 months (T1) for all patients.

*Results***:** A significant reduction in the PDSS-2 and ESS scores was observed at T1 in the DBS group (PDSS-2: 24.13±10.69 vs 18.37±9.85; p=0.034; ESS: 9.38±4.30 vs 6.58±3.83; p<0.001), and for the ESS score in the LCIG group (9.08±5.29 vs 6.38±5.00; p=0.046). No significant differences were observed for BMT group in both PDSS-2 and ESS scores. After correction for multiple comparisons, the PDSS-2 score significantly improved in the DBS group compared to BMT (p=0.049); better scores were found for LCIG group compared to BMT, albeit without reaching the statistical significance (p=0.109). No significant differences were observed between DBS and LCIG groups for both questionnaires.

*Conclusions***:** Our study supports previous findings on efficacy of AST on sleep disturbances in PD [2,3]. In particular, the efficacy of LCIG on daytime sleepiness was outlined. Moreover, the beneficial impact of DBS on sleep quality was confirmed, even after 36 months from surgery.

References

[1] Chahine et al., 2017. Sleep Med Rev: 35: 33-50.
[2] Jost et al., 2021. J Parkinsons Dis: 11 (1): 323-335.
[3] Zibetti et al., 2017. J Neurol: 264 (6): 1085-1090.

P102

Optimizing deep brain stimulation for essential tremor: comparison of different targets stimulation

Simone Malaspina[1], B. Minafra[2], R. Zangaglia[2], M. Todisco[1,2], F. Valentino[2], A. Picchiecchio[1,3], D. Servello[4], C. Pacchetti[2]

[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]Neuroradiology Department, IRCCS Mondino Foundation, Pavia, Italy
[4]Department of Neurosurgery, Galeazzi Research and Clinical Hospital, Milan, Italy

Introduction: Essential Tremor (ET) is the most common movement disorder and an important cause of disability and social distress for patients. Deep brain stimulation (DBS) is an effective treatment of drug-refractory cases of ET, but the outcomes can vary. DBS has proven to induce an improvement both in performances and activity of daily living (ADL). The optimal DBS target is still debated and different nuclei are currently implanted, namely the ventralintermediate nucleus of the thalamus (VIM), the subthalamic nucleus (STN), the zona incerta and the subthalamic area (STA).

Objective: The aim of this study was to compare different DBS targets (VIM, STN and STA) and their efficacy in the treatment of ET and to understand the functional and structural determinants of the DBS clinical outcome.

Methods: From January 2018 to January 2020, we enrolled seven consecutive ET patients who underwent DBS: 2 VIM-DBS, 3 STN-DBS and 2 STA-DBS. All the patients were evaluated pre- (T0) and post-op (T1 six months after surgery), using TETRAS for clinical assessment and QUEST for quality of life. At T1 presurgical MRI acquisition and post-surgical CT images were used to reconstruct the VTA, axonal tracts and target in order to optimize stimulation and to reduce side effects.

Results: We observed an improvement of TETRAS of 46.5% in VIM-DBS, 55.4% in STN-DBS, and 60.7% in STA-DBS. QUEST mean improvement was 77.7%, 96.7% and 92.0% in VIM-DBS, STN-DBS and STA-DBS respectively.

Conclusions: Our data suggest that STA-DBS better controls the tremor in ET patients. Quality of life improvement was similar in STA-DBS and STN-DBS patients (better in STN-DBS). Perhaps the clinical outcome was correlated to the distance of active electrode contacts to the dentato-rubro-thalamic tract. In VIMDBS, quality of life could be poorer because of adverse effects, more frequent in the stimulation of this target.

P103

Short and long-term motor outcome of STN-DBS in Parkinson's disease: focus on sex differences

Nico Golfrè Andreasi[1], L.M. Romito[1], R. Telese[1], R. Cilia[1], A.E. Elia[1], A. Novelli[1], G. Tringali[2], G. Messina[2], V. Levi[2], G. Devigili[1], S. Rinaldo[1], A. Amato Franzini[2], R. Eleopra

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milano, Italy
[2]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neurosurgery Department, Functional Neurosurgery Unit, Milano, Italy

Introduction: Deep Brain Stimulation of the Subthalamic Nucleus (STN-DBS) is an established treatment for Parkinson's disease (PD) with motor fluctuations and dyskinesias but studies on the long-term outcome are still scarce [1]. Moreover, the possible effect of sex in determining STN-DBS outcome is not well known [2].

Objective: In this study we describe the long-term motor outcome of STN-DBS in a cohort of PD patients consecutively treated in our center, with a focus on the possible differences associated with sex.

Methods: We reviewed all patient charts from our electronic database and retrospectively collected demographical and clinical data at baseline and at three follow-up visits: 1 year (±2 months), 5 years (±12 months), 10 years (±24 months).

Results: 107 patients (71 men) were included in the study. We found a longlasting effect of DBS on motor complications despite a progressive worsening of motor performances in the ON medication condition. Women showed a trend towards worsening in bradykinesia already at 1-year follow-up and possible poorer scores in non-dopaminergic features at 10-years follow-up. Levodopa Equivalent Daily Dose (LEDD) was significantly reduced after surgery however, while in men remained significantly lower than baseline, in women LEDD returned at baseline values at 10-years follow-up. Men showed a sustained effect on dyskinesias but this benefit was less clear in women and the total electrical energy delivered by STN-DBS was consistently lower in women compared to men. The profile of adverse events did not appear to be influenced by sex.

Conclusions: Our data suggest that there are no major differences on the motor effect of STN-DBS between men and women. However, there may be some slight differences that should be specifically investigated in the future and may influence therapeutic decisions.

References

[1] Limousin P, Foltynie T (2019) Long-term outcomes of deep brain stimulation in Parkinson disease. Nat Rev Neurol 15:234–242. https://doi.org/10.1038/s41582-019-0145-9.
[2] Meoni S, Macerollo A, Moro E (2020) Sex differences in movement disorders. Nat Rev Neurol 16:84–96. https://doi.org/10.1038/s41582-019-0294-x.

P104

Deep brain stimulation in Huntington's disease

Roberta Bonomo[1,2], A.E. Elia[1], G. Bonomo[3], L.M. Romito[1], C. Mariotti[4], G. Devigili[1], R. Cilia[1], R. Giossi[5,6], R. Eleopra[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[2]Experimental Neurology Unit, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy
[3]Neurosurgery Department, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Unit of Medical Genetics, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[5]Neuroimmunology and Neuromuscular Diseases Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[6]Department of Oncology and Onco-hematology, Postgraduate School of Clinical Pharmacology and Toxicology, University of Milan, Milan, Italy

Introduction: Huntington's disease (HD) is an inherited neurodegenerative disorder clinically characterized by involuntary movements, cognitive decline, and behavioral changes. The complex constellation of clinical symptoms still makes the therapeutic management challenging. In the new era of functional neurosurgery, deep brain stimulation (DBS) may represent a promising therapeutic approach in selected HD patients.

Objective: We evaluated the effects of DBS on patients affected by HD, providing a critical outlook on the achieved results and the possible developments.

Methods: Articles describing the effect of DBS in patients affected by HD were selected from Medline and PubMed by the association of text words with MeSH terms as follows: "Deep brain stimulation", "DBS", and "HD", "Huntington's disease", "Huntington". Details on repeat expansion, age at operation, target of operation, duration of follow-up, stimulation parameters, adverse events, and outcome measures were collected.

Results: Twenty eligible studies, assessing 42 patients with HD, were identified. The effect of GPi-DBS on Unified Huntington's Disease Rating Scale (UHDRS) total score revealed in 10 studies an improvement of total score from 5.4% to 34.5%, and in 4 studies an increase of motor score from 3.8% to 97.8%. Bilateral GPi-DBS was reported to be effective in reduction of Chorea subscore in all studies, with a mean percentage reduction of 21.4% to 73.6%.

Conclusions: HD patients with predominant choreic symptoms may be the best candidates for surgery, but the role of other clinical features and of disease progression should be elucidated. For this reason, there is a need for more reliable criteria that may guide the selection of HD patients suitable for DBS. Accordingly, further studies including functional outcomes as primary endpoint are needed.

P105

Levodopa/carbidopa intestinal gel for managing pain related to levodopa-induced dystonia in advanced Parkinson's disease

Domiziana Rinaldi[1], M. Sforza[1], E. Bianchini[1], M. Alborghetti[1,2], F. Ceriello[1], F.E. Pontieri[1,2]

[1]Department of Neuroscience, Mental Health and Sensory Organs, Sapienza University of Rome, Rome, Italy
[2]Department of Clinical and Behavioral Neurology, Fondazione Santa Lucia, IRCCS, Rome, Italy

Introduction: Pain is a frequent and disabling nonmotor symptom of Parkinson's disease (PD). In advanced PD, pain frequently occurs or worsens during "off" state and responds to antiparkinsonian therapy. Other patients experience pain exacerbation during dyskinesia/dystonia in "on" state. Levodopa/carbidopa intestinal gel (LCIG) may help optimizing the risk/benefit ratio of treatment and ameliorate quality of life.

Objective: We report the case of a PD patient presenting with disabling levodopa induced right-limb dystonia, who experienced significant reduction of pain and disability and improvement of autonomy with LCIG.

Methods: A 77-year-old female, with 13 years of PD history, presented with peak-dose dystonia (VAS score 8), severe "off" state at the end of each levodopa dose, and overnight muscle cramps. To limit dystonia and pain, she was treated with levodopa/benserazide 50/12.5 mg six daily doses (3 h interval) and opicapone 50 mg/day (LEDD=450 mg). At admission, her MDS-UPDRS-III score in "off" was 77, H&Y score 5, PDSS-2 score 37. After PEG-J placement, she was discharged under 24-h LCIG treatment with infusion rate 1.4 ml/h (28 mg/h), with reduction of pain severity (VAS score 4). Based on lack of dystonia, infusion rate was progressively increased to 2.0 ml/h (40 mg/h) (LEDD 960 mg). At follow-up visit after 2 months with such dosage, the patient was able to walk with assistance for short tracks (H&Y 4), her VAS score lowered to 3, her PDSS- 2 score lowered to 16. She reported moderate limb dystonia, lasting 20-30 min, occurring after tube cleansing (approximately once every 2 days), and mild "off" symptoms lasting 1 h in the afternoon and 2-3 h along night-time.

Results and Conclusions: Severe peak-dose dystonia may benefit from switching to LCIG. This case strengthens the need for optimizing DRT in advanced PD patients with the aim reducing disability and ameliorating quality of life and autonomy.

P106

Cognitive and behavioral effects of deep brain stimulation in patients with Parkinson's disease: results from clinical experience

Ilaria Cani[1], G. Giannini[1,2], L. Sambati[2], S.A. Nassetti[2], C. Ferrari[1], M. De Matteis[2], P. Cortelli[1,2], G. Calandra-Buonaura[1,2]

[1]Department of Biomedical and NeuroMotor Sciences (DIBINEM), Alma Mater Studiorum, University of Bologna, Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Introduction: Cognitive and behavioral effects of deep brain stimulation (DBS) in Parkinson's disease (PD) are not clearly defined, although some evidences suggest a negative impact of DBS on non-motor symptoms [1]. Dementia is a welldefined exclusion criterion for surgery, whereas indication for patients with mild cognitive impairment (MCI) are missing [2].

Objective: To investigate the effect of DBS on cognitive-behavioral functions and their predictive features.

Methods: PD patients are prospectively evaluated before and 12-months after subthalamic nucleus (STN)-DBS surgery, by mean of a comprehensive neuropsychological evaluation (NPS) and specific questionnaires.

Results: Twenty-one patients underwent STN-DBS surgery (mean age 57,29±8,34 years; disease duration 11,29±3,87 years). At pre-operative NPS, 18 patients (78%) had a normal cognition (NC) while 3 patients (22%) displayed a multidomain-MCI (md-MCI). Thirteen patients underwent post-operative NPS which recorded stable NC in 8 patients, progression to md-MCI in 2 previous NC patients and development of dementia in the 3 patients with md-MCI at baseline.
Comparison between pre and post-operative NPS scores documented an overall worsening on attentive functions (p=0,005), phonemic verbal fluency (p=0,046) and global cognition (p=0,005). None of clinical or demographic features resulted predictive of cognition worsening after DBS.
Baseline behavioral assessment performed in 15 patients detected: depression in 3 patients (20%), anxiety disorders in 9 (60%) and impulse-control disorder in 4 (27%).
Post-operative evaluation did not show significant differences compared to baseline confirming an overall prevalence of anxiety disorder.

Conclusions: None of the patient with normal cognition developed a dementia after surgery, suggesting that a careful selection of patients eligible for STN-DBS would reduce the incidence of dementia. Conversely, attention must be paid in patients with multidomain-MCI before surgery where an in-deep characterization is advisable. Recommendation for patients with isolated executive dysfunction should be further discussed. DBS effects on behavior are influenced by post-operative changes in dopaminergic treatment, a cautious decrease of dopaminergic drugs would prevent the occurrence of behavior disorders.

References

[1] Parsons TD, Rogers SA, Braaten AJ, Woods SP, Tröster AI. Cognitive sequelae of subthalamic nucleus deep brain stimulation in Parkinson's disease: a meta-analysis. *Lancet Neurol* 2006; 5: 578–88.
[2] Artusi C A, Lopiano L, Morgante F, Deep Brain Stimulation Selection Criteria for Parkinson's Disease: Time to Go beyond CAPSIT-PD. *J Clin Med* 2020; 9: 3931.

P107

The impact of deep brain stimulation on social and occupational functioning in people with Parkinson disease

Elisa Montanaro, C.A. Artusi, M. Giacchero, G. Imbalzano, A. Romagnolo, M.G. Rizzone, M. Zibetti, L. Lopiano

Neurology 2 Unit, A.O.U. Città della Salute e della Scienza di Torino, Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy

Introduction: Deep brain stimulation of the subthalamic nucleus (STN-DBS) is an established treatment for motor symptoms of advanced Parkinson disease (PD). Nevertheless, the effects of STN-DBS on social/occupational functioning and patients' satisfaction for the procedure are still matter of debate. Therefore, the selection and follow-up of patients are still challenging.

Objective: Our primary aim was to explore STN-DBS impact on social/occupational functioning of PD patients. The secondary aim was to evaluate the relationship between patients' social/occupational
functioning and specific clinical and psychological variables.

Methods: Twelve advanced PD patients (mean age: 59.3 ± 9.8 years) treated with STN-DBS were submitted to an extensive neurological and neuropsychological assessment before (V0) and approximately one year after neurosurgery (V1; mean follow-up duration: 20.3 ± 6.5 months). We administered the "Questionario del Funzionamento Sociale" (QFS), concerning the social functioning, and a semistructured interview aimed to investigate satisfaction for STN-DBS, social and familiar relationship, hobbies and occupational status. Descriptive statistics and Spearman correlations were employed.

Results: Our patients showed a good social functioning (QFS-G V0: 61.92 ± 7.62; V1: 61.58 ± 6.81; range: 16-80; p= 0.84). Patients' satisfaction about STN-DBS was highlighted (8.67 ± 0.98; range: 0- 10). Satisfaction for occupational status and familiar relationship was high (7.50 ± 2.35 and 7.83 ± 1.27 respectively; range 0-10). A significant inverse correlation was found between satisfaction for
STN-DBS (Item 1 of the interview) and UPDRS III score ($r= -0.605$; $p<0.05$). Satisfaction for hobbies (Item 6 of the interview) and domestic activities (Item 8 of the interview) were significantly and inversely correlated with apathy score at v2 ($r= -0.652$ and -0.603 respectively; $p<0.05$).

Conclusions: Our pilot study showed a good level of satisfaction and social/occupational functioning in PD patients who underwent STN-DBS in a short term follow-up, pending confirmation in other cohorts with larger sample size.

INDICE AUTORI

Per visualizzare i contributi
cliccare sui codici alfa-numerici

(A – B – C – D – E – F – G – H – I – J – K – L – M – N – O – P – R – S – T – U – V – W – Y – Z)

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

V

W

Z