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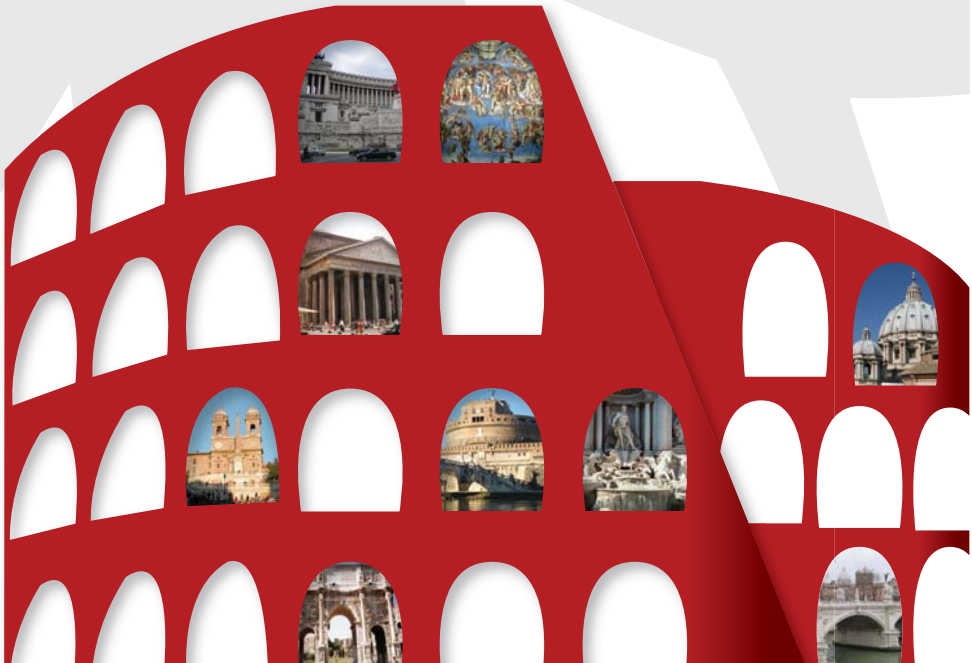

ABSTRACTS

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COMUNICAZIONI ORALI

C1

Brain functional connectomics in early Parkinson's disease

Massimo Filippi[1,2], *F. Agosta*[1], *S. Galantucci*[1], *I. Stankovic*[3], *A. Meani*[1], *P. Valsasina*[1], *I. Petrovic*[3], *G. Comi*[2], *V.S. Kostic*[3]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[3]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: Brain connectomics are promising in the study of neurodegenerative diseases. The analysis of brain networks in Parkinson's disease (PD) could improve the disease understanding.

Objective: To examine the integrity of the functional brain connectome in early PD.

Methods: We enrolled 44 early (Hoehn and Yahr=1.2) PD patients and 27 controls. Graph analysis was applied to resting state functional MRI data from both groups. Functional connectivity between 90 cortical and subcortical brain regions was estimated using bivariate correlation analysis and thresholded to construct a set of undirected graphs. Measures of global and regional network properties were obtained.

Results: Functional brain networks in PD patients did not show loss of small-worldness and differences in global network measurements. Bilateral middle and superior temporal, superior frontal, postcentral, right middle frontal and inferior temporal gyri, left middle occipital gyrus and precuneus were hubs in both groups. Right superior temporal pole was hub only in controls. Right calcarine cortex, cuneus, middle occipital gyrus, precuneus, anterior and middle cingulum, superior-medial frontal gyrus, and left inferior parietal and lingual gyri were hubs only in patients. The analysis of regional nodal characteristics in PD showed decreased nodal degree in supplementary motor area, middle temporal gyrus and superior temporal pole bilaterally, and decreased betweeness centrality in left Heschl's gyrus and rolandic operculum and right angular gyrus.

Conclusion: Graph analysis showed that global structure of brain networks in early PD is preserved. However, the analysis of regional nodal characteristics showed that network changes are detectable in early PD in key areas for the disease. Connectomics in PD may add new light to the understanding of the pathophysiology of the disease and of the mechanisms underlying the development of symptoms and response to treatment.

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C2

Late-onset parkinsonism in NF-kB/c-Rel-deficient mice: insights into novel drugable targets

Marina Pizzi[1,2], *C. Baiguera*[1], *M. Alghisi*[1], *A. Pinna*[3], *A. Bellucci*[1], *M.A. De Luca*[3], *L. Frau*[3], *M. Morelli*[3], *R. Ingrassia*[1], *M. Benarese*[1], *V. Porrini*[1,2], *M. Pillitteri*[4], *G. Bertini*[4], *P. Fabene*[4], *S. Sigala*[1], *M.G. Spillantini*[5], *H.-C. Liou*[6], *P.F. Spano*[1,2]

[1]University of Brescia and National Institute of Neuroscience, Brescia
[2]IRCCS San Camillo Hospital, Venezia
[3]University of Cagliari and National Institute of Neuroscience, Cagliari
[4]University of Verona, Verona
[5]University of Cambridge, Cambridge, UK
[6]Weill Medical College of Cornell University, New York, NY, USA

Nigrostriatal dopamine (DA) neuron degeneration, synaptic dysfunctions and neuroinflammation are among the key pathological features of Parkinson's disease (PD). NF-kB factors are considered cardinal players in the progression of the neurodegenerative process, with dual effect on inflammation and apoptosis. While NF-kB/RelA factor acetylated on the lysine 310 residue is responsible for the commencement of apoptotic gene expression, NF-kB/c-Rel factor promotes transcription of anti-apototic genes, MnSOD, Bcl-xL and UCP4.

Aim: To investigated possible age-associated neurodegeneration in c-Rel-/- mice.

Methods: WT and c-Rel-/- mice were analyzed at 2, 12 and 18 months of age for their motor behaviour and brain neurochemistry and pathology.

Results: At 18 months of age, c-Rel-/- mice exhibited a significant loss of dopaminergic neurons in the substantia nigra pars compacta (SNc), as assessed by TH IHC and Nissl staining. SNc degeneration was accompanied by a significant loss of DA terminals and a significant reduction of DA and HVA levels in the striatum. Mice deficient of the c-Rel factor exhibited a marked immunoreactivity for fibrillary a-synuclein in the SNc, increased level of DMT1 and iron. Aged c-Rel-/- brain showed increased microglial reactivity, but no astrocytic reaction. In addition, c-Rel-/- mice displayed age-dependent deficits in locomotor activity and various gait-related deficits associated with bradykinesia and muscle rigidity. The motor deficits recovered after treatment with L-DOPA. Latest data show that as observed by functional imaging in premotor PD, at an asymptomatic age c-Rel-/- mice display early loss of DAT in the caudatum putamen.

Conclusion: c-Rel factor is a regulator of SNc resilience to aging. It discloses a new therapeutic target deserving further investigation in PD patients. c-Rel-/-mice represent an innovative animal tool to study pathological progression of PD and also model PD preclinical phase of dopamine deficiency [1].

References

[1] Baiguera C, Alghisi M, Pinna A, Bellucci A, De Luca MA, Frau L, Morelli M, Ingrassia R, Benarese M, Porrini V, Pellitteri M, Bertini G, Fabene PF, Sigala S, Spillantini MG, Liou HC, Spano PF, Pizzi M. Late-onset Parkinsonism in NFκB/c-Rel-deficient mice. Brain. 2012 Sep;135(Pt 9):2750-65

C3

Default-mode network changes in Huntington's disease

Elena Salvatore[1], *M. Quarantelli*[2], *C.V. Russo*[1], *S.M.D.A. Giorgio*[3], *A. Cervo*[3], *S. Cocozza*[3], *L. Di Maio*[1], *A. Brunetti*[3], *A. Filla*[1], *G. De Michele*[1]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, University Federico II, Naples
[2]Biostructure and Bioimaging Institute, National Research Council, Naples
[3]Department of Advanced Biomedical Sciences, University Federico II, Naples

Background: Huntington's disease (HD) is associated to prominent atrophy in the striatum, a key component of several basal ganglia-thalamo-cortical networks. Functional MRI allows to assess the integrity of these networks even without relying on task-related activations (Resting-State fMRI - RS-fMRI). Among these, the so-called Default-Mode Network (DMN) appears to play a central role in the coordination of sensori-motor and cognitive goal-directed activities.

Aim: This study aim at evaluates DMN in HD patients and to correlate them to clinical data.

Methods: 26 patients seen at our HD Clinics, and 21 age- and sex-matched controls (NV) were scanned by a 3D-T1w volume and a set of T2*w volumes for RS-fMRI analysis, on a 3-Tesla MRI. Correlation analysis between clinical and MRI data was carried out using AnCova ($p<0.05$).

Results: HD showed decreased connectivity with the PCC in five clusters, with reduced correlation at the level of the caudate nuclei, of the ventral medial prefrontal cortex (VMPFC), the right medial superior prefrontal cortex, the right inferior parietal cortex mainly at the angular gyrus (rANG), and decreased anti-correlation involving the supramarginal gyrus on the left.
The ventromedial prefrontal cortex (VMPFC) cluster showed a significant positive correlation ($p=0.004$) with the cognitive subset of the UHDRS, demonstrating reduced connectivity in more compromised patients, while the rANG cluster showed a significant inverse correlation ($p=0.008$), with relatively spared connectivity in more compromised patients.

Conclusion: DMN dysfunction is present in symptomatic HD patients and correlates to cognitive disturbances. This dysfunction is not directly related to the atrophy of the involved cortical nodes, suggesting a possible role of the striatum in regulating a subset of the DMN in the normal brain and/or the effect of the extensive cortical neuronal loss which occurs in HD.
Further studies are needed to clarify the mechanisms underlying these alterations.

C4

Four-year follow up outcome of Deferiprone for Pantothenate kinase-associated neurodegeneration (PKAN) and Neurodegeneration with brain iron accumulation (NBIA)

Daniela Murgia[1] *G. Cossu*[1], *G. L. Forni*[3], *G. Matta*[2], *R. Galanello*[6], *S. Barella*[6], *M. Balocco*[3], *R. Marchese*[4], *U. Ruffiengo*[5], *U. Bonucelli*[7], *M. Melis*[1], *G. Abbruzzese*[4]

[1]Dipartimento di Neurologia Ospedale G.Brotzu, Cagliari
[2]Dipartimento di Radiologia Ospedale G.Brotzu, Cagliari
[3]Centro della Microcitemia ed Anemie Congenite, Dipartimento di Ematologia, Ospedale Galliera, Genova
[4]Dipartimento di Neuroscienze Università di Genova, Genova
[5]Unità di Neuroradiologia Ospedale Galliera, Genova
[6]Ospedale Regionale Microcitemia, Università di Cagliari, Cagliari
[7]Dipartimento di Neuroscienze, Università di Pisa, Pisa

Deferiprone (D) is an oral active iron chelator, able to cross the blood-brain barrier and effective in the lowering of intracellular iron. NBIA (Neurodegeneration with Brain Iron Accumulation) is a class of neurodegenerative diseases that feature a prominent extrapyramidal movement disorder along with iron deposition in the basal ganglia. The most common form of NBIA is PKAN (NBIA subtype 1) which accounts for about two-thirds of all the cases of NBIA.
The results of our previous one-year-treatment study (*Clinicaltrials.gov Identifier: NTC00907283*) suggested that D might be effective in reverse brain iron deposition and improve neurological manifestations in patients with NBIA. Due to these encouraging results we extended the treatment period and 5 out of 6 pts completed a 4 year-follow-up (only in one case, the time of observation was 36 months).
In all the patients, D was well tolerated and safe (without any serious hematologic or neurologic adverse even), brain MRI demonstrate a persistent mitigation of the pallidal iron accumulation in 5 out of 6 cases which correlate with a persistent motor improvement (in 1 case) or a clinical stabilization (in 4 cases). Furthermore, in two of these patients, clinical data are available since 4 years before the treatment onset and in both cases D seemed to slow disease progression providing a a further suggestion of the drug effectiveness.
The data from our study underline the long-term safety and tolerability of D as a chelator agent for intra- and extraneuronal iron accumulation. The relief or the enduring stabilization of symptoms observed in the large majority of our cohort over a prolonged observation period, together with the MRI data, suggest that treatment with D may be effective in the treatment of neurological manifestations linked with iron accumulation.

C5

Wearing off (WO) detection in the clinical practice. The work-PD study (Wearing off real practice key in Parkinson's disease)

Antonella Peppe[1], *L. Brusa*[2], *E. Cassetta*[3], *A. Denaro*[4], *F. Viselli*[5], *M.C. Altavista*[6]

[1]IRCCS Fondazione Santa Lucia, Roma
[2]Ospedale S.Eugenio, Roma
[3]Ospedale San Giovanni Calibita Fatebenefratelli, Roma
[4]ICOT, Latina
[5]Ospedale San Giovanni Battista, Roma
[6]ACO San Filippo Neri, Roma

Wearing-off (WO) is defined as a generally predictable recurrence of motor and non-motor symptoms before doses of anti-parkinsonian medication which usually improves after the dose. WO questionnaire with 19 items (WOQ19) was previously identified as a recommended tool to early detect WO and ameliorate the diagnosis.

Objective: Evaluating the impact and practicability in real practice of WOQ19 and its capacity to ameliorate clinical detection of WO.

Methods: As a multicenter naturalistic observational study patients were recruited in 6 Lazio hospital centers specialized in Parkinson's disease. Any treatment was allowed while patients with cognitive impairment were excluded. WOQ19 was administered to the patients before the visit. During the visit a data collection scorecard was filled with patients clinical characteristics, WOQ 19 comprehensibility and usability and physicians' evaluation about capability to change the diagnosis and modify the visit.

Results: 533 patients were included, with a mean age of 72.08, a mean disease duration of 7.7 ±4.6 years and a mean l-dopa treatment duration of 5.61 ± 3.8 years; 50.2% of the studied populations was in stage 3 of the H Y scale, 33.6% was in the stage 2. 68.7% (n=352) patients were affected by WO in almost 2 symptoms, with a significant correlation between disease severity and duration, patients age, sex female and l-dopa assumption. WO did not correlated with patients educational degree. Isolated non motor WO strictly correlated with l-dopa intake. WOQ 19 was considered useful in 50% of the patients and diagnosis and visit were modified in almost 15% of the cases.

Conclusion: As previous studies our data revealed that WO detected with WOQ19 correlates with disease severity and duration, female sex and l-dopa intake. The questionnaire appeared a comprehensive tool for its lack of correlation with patients educational degree. We suggest its use in clinical practice.

C6

Identification of two heterozigous mutations in NPC1 gene in patients affected by late onset neurodegenerative dementing disorders

Chiara Cupidi[1], *L. Bernardi*[1], *A. Clodomiro*[1], *F. Frangipane*[1], *R. Colao*[1], *G. Puccio*[1], *M. Anfossi*[1], *M.E. Conidi*[1], *M. Gallo*[1], *S.A.M. Curcio*[1], *M. Mirabelli*[1], *N. Smirne*[1], *R. Di Lorenzo*[1], *A. Dardis*[2], *S. Zampieri*[2], *R. Maletta*[1], *A.C. Bruni*[1]

[1]Regional Neurogenetic Center, ASP CZ, Lamezia Terme
[2]Regional Coordinator Centre for Rare Diseases, University Hospital "Santa Maria della Misericordia", Udine

Background: Niemann-Pick type C (NPC) disease is a lysosomal lipid storage disorder caused by mutations in NPC1 and NPC2 genes. Onset varies from infancy to adults and a broad clinical presentation, such as parkinsonism or behavioural disturbances, makes hard the diagnosis in adults. Although NPC is an autosomal recessive disorder, clinical report and studies on transgenic mice suggest that heterozygous NPC1 mutations could cause neurodegeneration.

Aim: We describe two known NPC1 heterozygous mutations in two patients affected by neurological diseases resembling progressive sopranuclear palsy (PSP) and frontotemporal dementia (FTD).

Patients and Methods: Patient 1 was a 66-years-old woman affected by a parkinsonism resembling PSP, with limitation of vertical gaze, dysphagia and dysarthria, gait apraxia; mild mental retardation was present from birth. Patient 2 was a 56-years old woman affected by behavioural variant of FTD. Infantile epileptic seizures and a severe depression were reported; at 43 years she presented psychogenic seizures, apathy, emotional lability and impairment of recent memory; frontal dementia associated to left hemidystonia and dysphagia were recognized at 56 years. Brain MRI showed midbrain atrophy in patient 1 and mild frontal atrophy in patient 2. NPC1 and NPC2 genes were analysed from genomic DNA; filipin staining was performed.

Results: Patient 1 carries a known heterozygous deletion (F284LfsX26), patient 2 bears a previously reported heterozygous missense mutation (N222S). Filipin staining showed variant biochemical subtype in patient carrying the deletion.

Conclusion: The diagnosis of NPC is plausible for the patient bearing the deletion, since she exhibited a clinical picture suggestive for adult NPC and the Filipin staining was positive, whereas it remains doubtful for the second patient carrying the missense mutation. We speculate that heterozygous mutations in NPC1 gene could cause the neurological disorders in our patients and could explain the late onset and the slow progression of disease.

C7

Supine hypertension in Parkinson's disease and Multiple System Atrophy revisited: a treatable complication of cardiovascular autonomic failure

Alessandra Fanciulli[1,2], *J.P. Ndaysaba*[2], *R. Granata*[2], *S. Dürr*[2], *S. Strano*[3], *C. Colosimo*[4], *W. Poewe*[5], *F.E. Pontieri*[1], *G.K. Wenning*[2]

[1]Department of Neuroscience, Mental Health and Sensory Organs – "Sapienza" University of Rome, Rome
[2]Division of Neurobiology, Department of Neurology – Innsbruck Medical University, Innsbruck, Austria
[3]Department of Cardiovascular, Respiratory, Nephrologic and Geriatric Sciences - "Sapienza" University of Rome, Rome
[4]Department of Neurology and Psychiatry – "Sapienza" University of Rome, Rome
[5]Department of Neurology – Innsbruck Medical University, Innsbruck, Austria

Introduction: Cardiovascular autonomic failure is a frequent non-motor feature of Parkinson's disease (PD) and Multiple System Atrophy (MSA). Beyond orthostatic hypotension (OH), a paradoxical supine hypertension (SH) may develop. Although asymptomatic, SH could exert a major role on survival, cerebrovascular and cognitive outcome in parkinsonian syndromes [1].

Objective: To investigate the prevalence and severity of SH in PD and MSA and to assess its clinical and tilt test correlates.

Methods: 178 PD and 70 MSA patients were included in the present cross-sectional study. Cardiovascular autonomic function was evaluated in a standardized setting by means of continuous ECG and non-invasive beat-to beat blood pressure (BP) monitoring (Finapres, Task Force™ Monitor, CNSystems). Supine BP was evaluated after 10 minutes in the lying position and orthostatic BP changes were evaluated for 10 minutes after 60° passive head-up tilting.

Results: SH (› 140 mmHg systolic, › 90 mmHg diastolic) was observed in 35% and 36% of PD and MSA patients, respectively. In PD, SH was mild in 69% of cases, moderate in 29% and severe in 2%, while in MSA SH was mild in 48 % of patients, moderate in 20% and severe in 32% (p=0.002). No association was observed between SH and sex, age, disease duration or H&Y stage either in PD or in MSA, but with the presence of cardiovascular comorbidities (p=0.001) and use of anti-hypertensive medications (p=0.03) in PD and use of ant-hypotensive medication (p=0.02) and lower daily dopaminergic intake (p=0.001) in MSA. Amplitude of both systolic (r:-0,292; p=0.000) and diastolic (r:-0,368; p=0,000) BP fall upon tilting significantly correlated with degree of SH severity in PD and MSA.

Conclusion: Our results show that one third of PD and MSA patients may suffer from mild to severe SH, independently from age, disease duration or severity. In recent epidemiological and preclinical studies, potential neuroprotective effects from Calcium antagonists of the dihydropyridine class have been reported in PD [2, 3]. If replicated in future studies, administration of short-acting Calcium antagonists may represent promising therapeutic candidates to achieve anti-hypertensive effects in parkinsonian syndromes.

References

[1] Fanciulli et al., 2013. E J Neurol; 20 (2): 231-235
[2] Ritz et al., 2010. Ann Neurol; 67 (5): 600-606
[3] Chan et al., 2007. Nature; 447 (7148): 1081-1086

C8

External Globus Pallidus and pontine nuclei are involved in RSBD in Dementia with Lewy bodies: a DAT/SERT statistical parametric mapping ^{123}I-FP-CIT-SPECT study

Daniele Liuzzi, P. Taurisano, F. Roselli, M. Pennelli, B. Tartaglione, M.F. De Caro, A. Bertolino, P. Livrea, A. Niccoli-Asabella, G. Rubini, G. Defazio

Dipartimento di Scienze Mediche di Base, Neuroscienze ed Organi di Senso, Università degli Studi di Bari, Bari

Background: REM sleep behavior disorder (RBD) is a prominent feature of synucleinopathies and a major diagnostic item for Dementia with Lewy Bodies (DLB). In Parkinson's disease and in DLB, the presence of RBD is thought to highlight a distinct subgroup of patients. However, the differences and the markers between patients with or without RBD are poorly investigated. Furthermore, the neurochemistry of the circuitry responsible for RSBD has not fully elucidated.

Methods: Twenty-one DLB patients (8 with RBD, 13 without RBD) underwent brain SPECT with the DAT and SERT specific radiotracer ^{123} I-FP-CIT.
The scans of the two groups were contrasted with Statistical Parametric Mapping to study DAT and SERT-rich brain structures.

Results: DLB patients with RBD displayed decreased DAT levels in external part of Globus Pallidus (GPe k=81, Z=3.93, p=0.027 FWE corrected; x -20, y -10, z 4); among SERT-rich structures, DLB patients with RBD displayed reduced uptake in a large cluster located in the pons (k=156, Z=2.59, p=0.005; x 8 y -24 z -40) and in a smaller cluster in the right anterior thalamus (k=10, Z=3.93, p=0.005 FWE corrected; x -19 y -14 z 1).

Conclusion: Our data support the identification of DLB with RSBD as a possible DLB subgroup with a distinct patter of degeneration of dopaminergic fibers and more severe degeneration of serotoninergic neurons; our findings provide a tentative in vivo marker for the subgroups and provide evidence for the involvement of dopaminergic and serotoninergic inputs in the onset of RBD.

C9

Role of the polymyography versus a standardized treatment algorithm for management of cervical dystonia with botulinum toxin type A

Roberto Erro[1,2], *K.P. Bhatia*[1], *C. Cordivari*[2]

[1]Sobell Department of Motor Neuroscience and Movement Disorders, University College London (UCL) Institute of Neurology, London, United Kingdom
[2]Department of Clinical Neurophysiology, National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom

Background: Botulinum toxin (BoNT) injections are the first line option for the treatment of cervical dystonia (CD), however there is no consensus or guidelines guiding the muscles selection. Clinical features such as main vector of the abnormal posture and presence of muscular hypertrophy correctly drive the selection of muscles to be injected with BoNT in the majority of cases. However, a significant minority of patients, ranging between 15% and 25%,
have suboptimal or no response to BoNT injections. To investigate the value of polymyography (pEMG) in comparison to a recently proposed standardized algorithm for management of CD, we performed a retrospective analysis of CD patients with an unsatisfactory response to BoNT treatment referred to our service for a pEMG.

Methods: Thirty-eight consecutive patients with idiopathic CD referred to our service because of unsatisfactory response to BoNT were included in the current study. All patients underwent a video-multichannel EMG recording at least 4 months after their last treatment with BoNT.
Video were recollected and severity of symptoms assessed using the Tsui scale during the rest condition. This allowed to identify the muscles to inject according to the treatment algorithm and these sets of suggested injections were compared to those driven by the pEMG findings.

Results: Following the standardized algorithm, none of our patients would have been properly injected. In fact, at least one muscle would have been wrongly injected in all patients and at least one muscle would have been missed in 63.6% of our patient. All of our patients had a positive response to the BoNT injections driven by the pEMG findings.

Conclusion: Here we show that pEMG can lead to a significant change of muscular targets to inject with BoNT compared to a standardized protocol for management of CD patients. This may have a beneficial effect on treatment response in CD patients who are apparently unresponsive to BoNT injections. Inadequate muscle selection is probably the most common cause for treatment failure and we recommend the use of pEMG to improve BoNT response in such CD cases.

C10

Substantia nigra hyperechogenicity in essential tremor: a possible link with Parkinson's disease

Francesco Ripandelli, G. Cardaioli, N. Tambasco, E. Luchetti, E. Marsili, E. Sacchini, A. Gallina, S. Simoni, E. Brahimi, P. Nigro, A. Rossi, P. Calabresi

Clinica Neurologica, Facoltà di Medicina e Chirurgia, Università degli Studi di Perugia - Azienda Ospedaliera di Perugia, Ospedale S. Maria della Misericordia, S. Andrea delle Fratte, Perugia

Introduction: Lack of specific diagnostic markers makes uneasy and uncertain the distinction between ET and PD. The two disorders several times overlap in their clinical expression, with ET preceding PD onset [1]. Transcranial Sonography (TCS) has been shown as a valid, non-invasive, widely available, real-time dynamic and high-resolution diagnostic tool to identify early an idiopathic PD [2].

Objective: We aimed to investigate the prospective meaning of hyperechogenicity of Substantia Nigra (SN) in ET patients.

Methods: 138 patients (79 PD, 59 ET) and 50 matched controls underwent TCS examination. All patients were followed in a prospective longitudinal assessment for at least three years. The sonographer and the clinicians were blinded to the results of each other.

Results: 10 subjects were excluded from the analysis due to the bilateral absence of temporal acoustic window. In PD group, SN echogenicity mean values at TCS examination showed no correlation with disease duration, H&Y and UPDRS III score (Spearman, $p>0,05$). During the follow-up period 21 out of 59 ET patients revealed new onset parkinsonian symptoms or signs. This subgroup of ET patients (ET-PD) showed mean TCS values significantly different from the rest part of ET group without parkinsonian features (post-hoc analysis, p0,05).

Conclusion: ET and SN hyperechogenicity, especially when present together, seem to increase the risk of developing PD later.

References

[1] Berg D et al. Transcranial Sonography in Movement Disorders. International Review of Neurobiology 2010
[2] Fekete R & Jankovic J Revisiting the Relationship Between Essential Tremor and Parkinson's Disease. Movement Disorders 2011

C11

Pisa syndrome in Parkinson's disease: demographic and clinical correlations in a multicenter italian study

M. Tinazzi[1], *Ina Juergenson*[1], *F. Bombieri*[2], *F. Schena*[2], *S. Ottaviani*[3], *T. Bovi*[3], *G. Bisoffi*[4], *C. Uniati*[4], *M. Canesi*[5], *G. Pezzoli*[5], *R. Ceravolo*[6], *D. Frosini*[6], *S. Rossi*[7], *M. Ulivelli*[7], *A. Thomas*[8], *R. Di Giacomo*[8] , *G. Fabbrini*[9], *M. Sarchioto*[9], *A.R. Bentivoglio*[10], *F. Bove*[10], *F. Tamma*[11], *V. Lucchese*[11], *G. Cossu*[12], *F. Di Stefano*[13], *A. Pisani*[14], *G. Amadeo*[14], *N. Modugno*[15], *F. Lena*[15], *M. Zappia*[16], *L. Raciti*[16], *A. Nicoletti*[16], *M.A. Volonté*[17], *F. Spagnolo*[17], *C. Dallocchio*[18], *M. Sciarretta*[18], *T. Altavilla*[19], *G. Abbruzzese*[20], *C. Cordano*[20], *C. Pacchetti*[21], *N.G. Pozzi*[21], *R. Marconi*[22], *S. Gallerini*[22], *A. Mignarri*[22], *R. Allocca*[23], *G. Defazio*[24], *F. Morgante*[25], *L. Ricciardi*[25], *A. Cannas*[26], *P. Solla*[26], *C. Vitale*[27], *A. Fasano*[28], *P. Barone*[29]

[1]Department of Neurological, Neuropsychological, Morphological and Motor Sciences, University of Verona,Verona
[2]Department of Neuroscience and Kinesiology, University of Verona,Verona
[3]Department of Neurology, Azienda Ospedaliera Universitaria Integrata,Verona
[4]Ufficio Supporto alla Ricerca e Biostatistica, Azienda Ospedaliera Universitaria Integrata,Verona
[5]Centro Parkinson e disordini movimento, UVA CTO Milano, Milano
[6]Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa
[7]Policlinico le Scotte, University of Siena, Siena
[8]Università Chieti-Pescara, University Foundation Aging Research Center Behavioural Neurology and Movement Disorders Unit, Chieti
[9]Dipartimento di Neurologia e Psichiatria, Sapienza Università di Roma, Roma
[10]Istituto di Neurologia, Università Cattolica del Sacro Cuore, Roma
[11]UOC Neurologia, Ospedale Generale Regionale "F. Miulli", Acquaviva delle Fonti (BA)
[12]Dept of Neurology AOB Brotzu, Cagliari
[13]Dept of Neurology University of Cagliari, Cagliari
[14]Clinica Neurologica, Dipartimento di Medicina dei sistemi, Università di Roma Tor Vergata, Roma
[15]IRCCS INM NEUROMED, Pozzilli (IS)
[16]Dipartimento di Neurologia, Università di Catania, Catania
[17]Dipartimento di Neurologia e Clinica Neurofisiologica, IRCCS Ospedale San Raffaele, Milano
[18]U.O. Neurologia , Ospedale Civile, A.O. Pavia, Voghera
[19]Servizio di Neurologia e Neurofisiologia, Istituto Clinico Beato Matteo, Vigevano
[20]Clinica Neurologica 2, Università di Genova, Genova
[21]Unità Operativa Parkinson e Disordini del Movimento, Fondazione Istituto Neurologico Nazionale "C. Mondino", IRCCS, Pavia
[22]UO Neurologia, Ospedale Misericordia, Grosseto
[23]Università degli Studi di Napoli Federico II, Napoli
[24]Dipartimento di Scienze Mediche di Base, Neuroscienze e Organi di Senso, Università di Bari, Bari
[25]Dipartimento di Neuroscienze, Università di Messina, Messina
[26]Clinica Neurologica, AOU Cagliari, Cagliari
[27]Università degli Studi di Napoli Parthenope, Idc Hermitage Capodimonte, Napoli
[28]Division of Neurology, Movement Disorders Center, TWH, UHN, University of Toronto, Toronto, Canada
[29]Centro per le Malattie Neurodegenerative, Università degli Studi di Salerno, Salerno

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C11 (*segue*)

Idiopathic (i.e. not induced by neuroleptics) Pisa syndrome (PS) in Parkinson's disease (PD) is a rare and controversial entity with only sporadic single case descriptions and only one case series [1]. Therefore, its pathophysiology has been poorly investigated [2, 3] .
We performed this multicenter cross-sectional study with the aims to estimate the proportion of patients developing PS in a large cohort of patients with PD and to assess relationships between PS and demographic/clinical variables. Patients with PD were selected from consecutive outpatients attending the participating centres. Patients treated with dopamine receptor blocking agents 6 months before the recruitment and patients with diseases of the vertebral column were excluded from the study.
Age, sex, age at PD onset, UPDRS III and IV, PDQ8, antiparkinsonian therapy and any information on any lateral trunk flexion present at the time of the study were recorded.
A total of 1123 patients (F:M = 503:620) with PD met the eligibility criteria and were entered into the study. Mean age and mean duration of parkinsonian motor symptoms were 69.2 (SD 9.4) and 8.1 (SD 5.2) years, respectively. Mean UPDRS III score was 21.9 (SD 10.9), Hoen and Yahr (H-Y) was 2.2 (0.7) and PDQ 8 was 7.5 (5.4). PS was detected in 103 out of 1123 patients (9.2%). The mean degree of lateral flexion of the trunk was 15.6 (SD 7.8). Lateral flexion of the trunk was towards the right and the left side in 70 and 33 patients, respectively.
The leaning side was contralateral to the side of PD onset in 40 of the 85 cases with identifiable motor asymmetry at onset. Concomitant camptocormia was detected in 63 out of 103 patients with PS while antecollis in 27.
Patients with PS were significantly older, had longer duration of disease and of treatment with antiparkinsonian drugs than patients without PS; the UPDRS III and IV, H-Y were significantly higher in patients with PS.
These preliminary results suggest that PS is a relatively frequent and often disabling complication in PD especially in the middle and advanced phase of disease.

References

[1] Bonnani L., Thomas A., Varanese S. et al. Botulinum toxin treatment of lateral axial dystonia in Parkinsonism. Mov. Disorders 2007; 31; 22: 2097-2103.
[2] Di Matteo A., Fasano A., Squintani G. et al. Lateral trunk flexion in Parkinson's disease: EMG features disclose two different underlying pathophysiological mechanism. J Neurol 2011; 258:740–745.
[3] Tinazzi M., Juergenson I., Vattemi G. et al. Pisa Syndrome in Parkinson's disease: an elctrophysiological and imaging study. J Neurol 2013

C12

Cerebellar cTBS induced-effects on STDT in Parkinson's disease

Francesca Di Biasio[1], *A. Conte*[1,2], *M. Bologna*[1], *E. Iezzi*[1], *G. Fabbrini*[1,2], *P. Li Voti*[1], *L. Rocchi*[2], *N. Modugno*[1], *A. Berardelli*[1,2]

[1]IRCCS Neuromed Institute, Pozzilli (IS)
[2]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome

Objective: To investigate whether cerebellar continuous theta burst stimulation (cTBS) induces changes on the somatosensory temporal discrimination threshold (STDT) in patients with Parkinson's disease (PD).

Background: STDT measures the ability to perceive two stimuli as being sequential. In healthy subjects STDT is under the control of parietal cortex and basal ganglia and altered STDT values have been reported in PD. Given the possible role of cerebellum in the pathophysiology of PD, cerebellum may also play a role in the pathophysiology of STDT abnormalities in PD.

Methods: STDT was investigated in fourteen PD patients. All patients underwent two randomized and counterbalanced sessions: real and sham cerebellar cTBS. STDT was measured on both hands before and after applying cerebellar cTBS. STDT was studied by delivering paired electrical stimuli starting with an interstimulus interval (ISI) of 0 msec (simultaneous pair), and progressively increasing the ISIs in 10 steps. Since it is known that the Purkinje cells activity exerts an inhibitory effect over M1, we controlled the efficacy of the stimulating protocol by monitoring M1 excitability after cerebellar cTBS. STDT and motor evoked potential (MEPs) amplitudes were collected at the baseline (Time =), and 5 minutes (Time1) and 25 minutes (Time 2) after real and sham cerebellar cTBS.

Results: We first confirmed that STDT values are increased in PD patients (119±7 ms) in comparison to healthy subjects (61±2 ms). We now found that real but not sham cerebellar cTBS significantly reduced abnormal STDT values, only on the hand ipsilateral to the stimulated cerebellar hemisphere (p=0.04). Cerebellar cTBS also decreased MEP size in the contralateral M1 area (0.008).

Conclusion: Cerebellar cTBS improved STDT values in PD patients (although the values were not normalized) possibly modulating Purkinje cells activity.

VIDEO

V1

The girgenti family

Marina Picillo[1], *M. Fang*[2], *M. Quadri*[3], *S. Olgiati*[3], *G.J. Breedveld*[3], *J. Graafland*[3], *B. Wu*[2], *F. Xu*[2], *R. Erro*[1], *M. Amboni*[4], *S. Pappatà*[1], *M. Quarantelli*[1], *G. Annesi*[5], *A. Quattrone*[6], *H.F. Chien*[7], *E.R. Barbosa*[7], *The International Parkinsonism Genetics Network*, *B.A. Oostra*[3], *P. Barone*[4], *J. Wang*[2], *V. Bonifati*[3]

[1]Department of Neurological Sciences, University of Naples "Federico II", Naples
[2]BGI-Shenzhen, Shenzhen, China
[3]Department of Clinical Genetics, Erasmus MC, Rotterdam, The Netherlands
[4]Department of Medicine and Surgery, CEMAND, University of Salerno, Salerno
[5]Institute of Neurological Science, National Research Council, Cosenza
[6]Institute of Neurology, University Magna Græcia, Catanzaro
[7]Department of Neurology, University of São Paulo, Brazil

Two healthy first cousins from a small Sicilian village had four offspring, two of whom developed a progressive neurological disease.
The first patient is a 47-year-old man with an uneventful birth and normal development until adulthood. At 22-years old he developed rapidly progressive slowness of movements, fatigue, leg stiffness, gait impairment. Within a few months he was unable to work. Cognitive decline and severe dysarthria also developed, progressing to an anarthric state.
On our first examination, twenty-five years after the onset of the disease, he presented with a stooped posture, and a severely disturbed, short-stepped, shuffling gait. There was severe axial and four-limb rigidity. The postural reflexes were also impaired. Dystonic postures were present in both hands (left>right). Irregular, wide-amplitude jerky movements emerged during action in the upper limbs. His face was markedly staring. There was eyelid apraxia, and a clear supranuclear vertical gaze limitation (downward more than upward). There was also mild dysphagia, allowing feeding with semiliquid food.
The second patient is a 31-year-old woman with normal birth and developmental milestones. At 28 years-old she developed slowness of movements, speech and gait difficulties, and jerky involuntary movements in the right arm.
On our first examination, three years after the onset of symptoms, she presented with a stooped posture, and a short-stepped, shuffling gait. Postural reflexes were markedly impaired. Her face was markedly staring and there was a moderate supranuclear vertical gaze limitation. Almost continuous, irregular, small-amplitude jerky movements were present in the lips and tongue. There was moderate axial and four-limb rigidity and dystonic postures were present in the hands and feet. She also presented marked dysarthria, hypophonia, and mild dysphagia. She was fed with a semiliquid diet.

V2

A complicated myopathy

Rosa Iodice, L. Ruggiero, R. Dubbioso, F. Manganelli, M. Esposito, A. Topa, S. Tozza, L. Santoro

Università degli Studi di Napoli "Federico II", Napoli

Background: Mutations in valosin-containing protein (VCP) cause inclusion body myopathy (IBM) associated with Paget's disease of the bone (PDB) and fronto-temporal dementia (FTD) or IBMPFD. However only a small percentage of patients show a full phenotype.

Case Report: A 54 years old man was referred to our clinic for a severe progressive lower limb weakness, needing walking support. Over about two years he developed a language difficulties with non fluent speech and parafasic errors, behavioral alterations such as personal/social unawareness, perseveration and abulia with relative preservation of memory, orientation and praxis. Electromyography revealed a myophatic pattern and muscle biopsy of quadriceps muscle showed groups of small and rounded muscle fibers, mildly increased endomysial connective tissue and rimmed vacuoles. Nerve conduction study and CK levels were normal.
Serum alkaline phosphatase level was high and, because of our patient complained of low back pain, he underwent to lumbar X-ray that showed hypertrophic trabeculae giving an image similar to that of a "frame picture". FDG-PET brain images revelead hypometabolism in left frontal and temporal areas, cyingulate gyri, uncus and insula. As regards family history, his sister had received a diagnosis of Alzheimer disease and his father died with no better explained ambulation difficulties. Our patient underwent to a molecular analysis that showed a new mutation in VCP gene (IVS 12-35 a>g).

Conclusion: We report clinical and laboratory findings of an Italian patient with a novel mutation in VCP gene. IBMPFD is a heterogenous disorder and patients need not manifest all three phenotypic features. Clinicians evaluating a patient with myopathy, either sporadic or familial, must ask about other symptoms such as cognitive impairment and bone pain. In addition, a careful family history should be taken not just for a history of myopathy but also for a history of dementia and bone disorders . These challenges make IBMPFD an under diagnosed and likely under recognized clinical syndrome.

V3

PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections): a case report

Roberto Allocca[1], *M. Moccia*[1], *M. Picillo*[1], *R. Erro*[1], *K. Longo*[1], *M. Amboni*[1], *C. Vitale*[1], *P. Barone*[2]

[1]Dipartimento di Neuroscienze, Scienze Odontostomatologiche e Riproduttive, Università degli Studi di Napoli Federico II, Napoli
[2]Centro Malattie Neuro Degenerative (CEMAND), Dipartimento di Medicina e Chirurgia, Università di Salerno, Salerno

Introduction: PANDAS is a rare clinical syndrome characterized by the presence of tics, Tourettism, obsessive–compulsive disorder, or chorea in the context of an immediately precedent streptococcal infection. We describe a case of a 9 years - old boy, with acute onset of tic disorder (vocalisations, cough, laughter), following streptococcal infection.

Methods: The patient underwent neurological evaluation, oculistic examination, neuropsychiatric visit, research for acanthocytes, Anti Streptolisin O Antibodies, serum copper and ceruloplasmine, throat swab, whole brain MRI, chest X-ray.

Results: Although previously diagnosed as affected by Tourette syndrome, our patient fulfilled the diagnostic criteria for PANDAS: (1) presence of tic disorder; (2) prepubertal onset; (3) episodic course characterized by acute, severe onset and dramatic symptom exacerbations; (4) adventitious movements present during the symptom exacerbation; (5) temporal association between group A ?-hemolytic streptococcal infection (GAS) and onset or exacerbation of symptoms.

Conclusion: PANDAS is a strictly defined but uncommon clinical disorder characterized by the presence of tics, Tourette syndrome, obsessive–compulsive disorder, or chorea in the context of an immediately precedent streptococcal infection. Therapy for PANDAS includes immunosuppressive agents in the acute stages, while neurological symptoms have been treated with compounds such as tetrabenazine, haloperidol, clonidine, and serotonin reuptake inhibitors. Prompt recognition and treatment of GAS infections is effective in preventing neuropsychiatric sequelae and misdiagnosis.

V4

Insulinoma presenting as choreo-dystonic parossistic attacks and motor assonal neuropathy

Nicolò Gabriele Pozzi[1,2], *B. Minafra*[1,2], *R. De Marzi*[1,2], *R. Zangaglia*[1,2], *C. Pacchetti*[1,2]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia
[2]Interdepartmental Research Center for Neurodegenerative Disease, National Institute of Neurology Foundation "C. Mondino", Pavia

Insulinoma is the most common neuroendocrine pancreatic tumor with an annual incidence of four in every 1 million persons [1]. Usually symptoms of inappropriately elevated insulin level have been classified into two major categories: neuroglycopenic and catecholamine response. Prominent symptoms are diplopia, blurred vision, altered mental status, abnormal behavior, coma and seizures. Symptoms caused by catecholamine response include sweating, anxiety, palpitations, nausea or hunger [2].
In June 2010, a 29-year-old caucasian men, with no anamnestic data developed: 1) parossistic choreo-dystonic movements, 2) episodes of alteration of consciousness with dystonic tremor and 3) myoclonic tremor during sleep (early hours of the day) (Video 1). The symptomatology worsened in time, for duration and frequency of the episodes; any trigger was detachable. During intercritical periods any symptoms or neurological signs were present. A first, ambulatory evaluation, by a neurologist done in 2010 didn't find any clinical manifestation and after a serial of normal NMR images (November and March/11; November/12) diagnosis of functional disorder was made. During winter of 2012 he reported a weight gain, with reduction of the episodes. In February 2013 he was admitted to our clinic. During first hospitalization day, laboratory investigation showed severe level of hypoglycaemia (minimum value 27 mg/dl), relative iperinsulinaemia (insulin 13,6 mU/ml, C-peptide 4,9 ng/ml) without any clinical manifestations. Hematological and biochemical tests including blood count; liver, thyroid, and kidney function tests; immunological tests ; and serum vitamin B12 and folate levels were normal. Computerized tomography (CT) of the abdomen was done, and a tumor (2 cm in diameter) in the toe of the pancreas was identified. Surgery revealed a well-encapsulated tumor (2,5 × 1.5 cm in size) which was histologically a benign islet cell adenoma. Before chirurgic excision EEG, needle EMG and neuropsychological battery tests were done, as report in literature [3]. EEG and neuropsychological examination was normal. Needle electromyography revealed fibrillation potentials, poliplette and positive sharp waves in the right first dorsal interosseous. Signs of chronic neurogenic changes were present in the motor unit potentials of first right dorsal interosseus and right bicipites muscles and in the interference patterns were incomplete. These findings accorded with an axonal motor polyneuropathy of the upper limbs.
After excision glycaemic level and insulinaemia were restored and any neurological manifestation occur in one year follow up period. This case put attention on complication in insulinoma, that can give diagnostic trouble and lead to delay of potentially curative intervention.

References

[1] Service FJ, McMahon MM, O'Brien PC, Ballard DJ. Functioning insulinoma – incidence, recurrence, and long-term survival of patients: a 60-year study. Mayo Clin Proc. 1991; 66:711– 719
[2] Service FJ. Hypoglycemic disorders. N Engl J Med. 1995; 332:1144–1152
[3] Josef G. Heckmann et al. Hypoglycemic sensorimotor polyneuropathy associated with insulinoma. Muscle Nerve 2000; 23: 1891–1894

V5

Unusual monolateral hyperkinetic movement disorder associated with Fahr's disease

Miryam Carecchio[1], *C. Varrasi*[1], *A. Cerino*[1], *A. Stecco*[2], *C. Barzaghi*[3], *B. Garavaglia*[3], *C. Comi*[1], *R. Cantello*[1]

[1]Department of Neurology, Amedeo Avogadro University, Novara
[2]Department of Radiology, Amedeo Avogadro University, Novara
[3]Molecular Neurogenetics Unit, IRCCS C. Besta, Milan

Fahr's disease is a rare neurodegenerative disorder characterized by bilateral striopallidodentate calcification. Classical clinical manifestations include parkinsonism, progressive cognitive decline and psychiatric disturbances. The disorder can be primary or secondary to altered calcium metabolism and is genetically heterogeneous. Familial autosomal dominant cases have been associated with mutations in SLC20A2 and PDGFBR genes and an additional locus has been mapped to chromosome 2q37.
We report on a 64-year old man suffering from diabetes and blood hypertension who came to our attention due to an ischemic left frontal stroke causing acute onset right upper limb paresis and dysarhtria. There was no family history of any neurological disorder. He showed continuous choreic movements in the left hand that had been present for the past 10 years; onset was slowly progressive and he could only partially suppress them. CT scan revealed extensive basal ganglia and dentate nuclei calcification; calcium and parathyroid hormone levels resulted normal on blood tests; brain MRI confirmed the presence of a left frontal ischemic lesion consistent with the acute neurological symptoms. SLC20A2 genetic analysis is in progress.
Hyperkinetic movements have only rarely been described in association with Fahr's disease and the presence of unilateral movement disorder despite extensive bilateral basal ganglia involvement could make this diagnosis even more challenging for clinicians.

POSTER

P1

Midbrain tumor presenting as dopa-responsive Parkisonism

Valentina Fioravanti, F. Cavallieri, A. Chiari, L. Vandelli, S. Contardi, M. Tondelli, S. Meletti, F. Valzania

Dipartimento di Neuroscienze, Università di Modena e Reggio Emilia, Nuovo Ospedale Civile S. Agostino-Estense, Modena

Introduction: Mass lesions of the brainstem or within the posterior fossa underlying parkinsonism are extremely rare. Furthermore, the usual presentation of parkinsonism associated with tumor is a rigid-akinetic syndrome not responsive to dopaminergic treatment. We report a case of levodopa-responsive parkinsonism due to a midbrain low-grade glioma.

Case report: A previously healty 53-year-old man was admitted to our hospital for the progressive onset of resting tremor associated with rigidity involving the left arm. Neurological examination revealed slowed facial expressions and eye-blinking, moderate-severe left-dominant akineto-rigid and tremulous parkinsonism, left mild hemiparesis associated with left-sided hyperreflexia, balance and gait disturbance and dystonic hand movements of the left hand. Brain MRI scan revealed a lesion involving the right mesencephalic region, compatible with a low-grade glioma. A brain biopsy confirmed the diagnosis of low-grade glial neoplasia. Positive response to acute levodopa test was observed, with an improvement of 46% of the motor examination part of the UPDRS. A levodopa/carbidopa therapy was started with a significantly improvement in his resting tremor, bradikinesia and rigidity. A mild further improvement was observed after introduction of ropinirole. Six months after hospital discharge the patient developed fluctuations in motor responses resolved by association of entacapone.

Discussion: Parkinsonian syndromes associated with mesencephalic lesions are very unusual and the physiopathological mechanisms are still not clear.
Anamnestic and physical profile of our patient simulate an idiopathic form of Parkinson disease, whereas the occurrence of mild piramidal signs could suggest an atypical parkinsonism like MSA. It is interesting to notice that, in our patient, the presence of a lesion in the midbrain is matched with a pharmacological good response, suggesting a presynaptic mechanism. We hypothesize that the progressive infiltration of the substantia nigra due to a low-grade neoplasm leads to a progressive reduction of dopamine production, mimicking the degenerative form of Parkinson’s disease.

P2

Cortical action myoclonus due to cortical laminar necrosis: a case report

Francesco Cavallieri, V. Fioravanti, S. Contardi, L. Codeluppi, S. Meletti, F. Valzania

Dipartimento di Neuroscienze, Università di Modena e Reggio Emilia, Nuovo Ospedale Civile S. Agostino-Estense, Modena

Introduction: Cortical myoclonus is the most common form of myoclonus, mainly affecting distal upper limbs and typically occurring during voluntary task. Focal cortical myoclonus could be secondary to focal lesion which affects the sensorimotor cortex, resulting in hyperexcitability. Cortical laminar necrosis (CLN) is defined as hyperintense cortical lesion on MRI T1-weighted imaging involving specific cortical laminae observed after a subacute or chronic brain damage Different etiologies are described, the commonest being infarctions and hypoxia. We report a case of cortical myoclonus due to CLN.

Case Report: A 61-year-old woman had a 7-year history of tremor-like involuntary jerks of the right arm during antigravity postures and voluntary movement. This movement disorder started subacutely and presented a very slow progression over time. 3 Tesla brain MRI disclosed a layer of increased signal in left fronto-parietal cortex in correspondence of the central sulcus in Sagittal T1-weighted images. This hyperintense band was associated with hypointensity of the underlying subcortical white matter; these findings were considered consistent with CLN. Surface EMG recording showed the presence of middle frequency (7-8 Htz) arrhythmic myoclonic jerks.

Discussion: Neurophysiological studies suggest the cortical origin of myoclonus; indeed paired TMS at short ISIs shows loss of ICI.The ICI tested by paired TMS is likely due to the activity of GABA cortical interneurons that are distributed across layers II-VI of the motor cortex. On the basis of the neuropathological data, layers III and VI, having the highest concentration of large somata GABAergic neurons, are most vulnerable to ischemia and hypoxic damage.
In our case, focal hypoxia or incomplete infarction could have led to a CLN with selective damage of GABAergic neurons, inducing a loss of cortical inhibitory processes responsible for myoclonic jerks.

P3

Gender differences in non-motor symptoms in early, drug naïve Parkinson's disease

Marcello Moccia[1], *M. Picillo*[1], *M. Amboni*[2], *R. Erro*[1], *K. Longo*[2], *C. Vitale*[2,3], *R. Allocca*[1], *A. De Rosa*[1], *G. De Michele*[1], *L. Santoro*[1], *G. Orefice*[1], *M. T. Pellecchia*[4], *P. Barone*[4]

[1]Department of Neurosciences, University "Federico II", Naples
[2]IDC "Hermitage Capodimonte", Naples
[3]University "Parthenope", Naples
[4]Center for Neurodegenerative Diseases, University of Salerno, Salerno

Objective: Gender differences in brain structure and function may lead to differences in the clinical expression of neurological diseases, including Parkinson's disease (PD). Few studies reported gender-related differences in the burden of non-motor symptoms (NMS) in treated PD patients, and this matter has not been previously explored in drug-naïve patients. In consideration of this, we assessed gender differences in NMS frequency in a large sample of early, drug-naïve PD patients compared with age-matched healthy controls.

Methods: Two hundred early, drug-naïve PD patients and sixty age-matched healthy controls were included in the study. Frequency of NMS was evaluated by means of NMS Questionnaire. The difference in gender distribution of NMS was evaluated with the X2 exact test; multiple comparisons were corrected with Benjamini-Hockberg method.

Results: Male PD patients complained of problems having sex and taste/smelling difficulties significantly more frequently than female PD patients.
Furthermore, men with PD complained more frequently of dribbling, sadness/blues, loss of interest, anxiety, acting during dreams, and taste/smelling difficulties as compared to healthy control men, while female PD patients reported more frequently loss of interest and anxiety as compared with healthy control women.

Discussion: This study shows specific sex-related patterns of NMS in drug-naïve PD. In contrast with previous data, female PD patients did not present higher prevalence of mood symptoms as compared to male PD patients. Comparison with healthy controls showed that some NMS classically present in premotor and early stage of disease (i.e. acting during dreams, taste/smelling difficulties) are more frequent in male than in female patients.

P4

Prevalence and features of peripheral neuropathy in Parkinson's disease

Francesca Mancini[1], *C. Comi*[2], *D. Calandrella*[1], *C. Pacchetti*[3], *G. D. Oggioni*[2], *G. Riboldazzi*[4], *M. Coletti Moja*[5], *M. Dal Fante*[6], *L. Manfredi*[1], *M. Lacerenza*[1], *A. Antonini*[7]

[1]Parkinson's Disease and Movement Disorders Centre, Neurology Unit, San Pio X Clinic, Fondazione Opera San Camillo, Milan
[2]Parkinson's Disease and Movement Disorders Centre, Department of Neurology, University of Eastern Piedmont "Amedeo Avogadro", Novara
[3]Parkinson's Disease and Movement Disorders Centre, Neurological Institute IRCCS "C. Mondino", Pavia
[4]Parkinson's Disease and Movement Disorders Centre, University of Insubria, Varese
[5]Department of Neurology, Mauriziano Umberto I Hospital, Turin
[6]Endoscopy Unit San Pio X Clinic, Fondazione Opera San Camillo, Milan
[7]Department for Parkinson Disease, IRCCS San Camillo, Venice

Introduction: Increased frequency of peripheral neuropathy (PN) in Parkinson's disease (PD) patients on levodopa compared to age matched controls was recently described. Moreover, several reports described the occurrence of PN in patients undergoing continuous levodopa delivery by intestinal infusion (CLDII).

Objective: The aim of this study was to compare frequency, clinical features, and outcome of PN in PD patients undergoing different medication regimens.

Methods: We compared three groups of consecutive PD patients: group 1: 50 patients on CLDII; Group 2: 50 patients on oral levodopa; Group 3: 50 patients on dopamine agonists and/or MAO-B inhibitors.

Results: Frequency of PN was 28% in Group 1, 20% in Group 2, and 6% in Group 3 patients. Regarding clinical features, 71% of Group 1 patients and all Groups 2 and 3 PN patients displayed a subacute sensory PN. On the contrary, 29% of Group 1 patients displayed acute motor PN. Levodopa daily dose, vitamin B12 (VB12) and homocysteine (hcy) levels differed significantly in patients with PN compared to patients without PN.

Conclusion: Our findings supported the relationship between levodopa and PN and confirmed that an imbalance in VB12/hcy metabolism may be a key pathogenic factor. Moreover, we suggested two different but possibly overlapping mechanisms of PN in patients on CDLII: axonal degeneration due to vitamin deficiency and inflammatory damage. Whether inflammatory damage is triggered by vitamin deficiency and/or by modifications in the intestinal micro-environment should be further explored. Proper vitamin supplementation may prevent peripheral damage in most cases.

P5

Sleep complains and persistence of dystonia during sleep in patients with idiopathic focal dystonia

Elena Antelmi, F. Provini, C.L. Scaglione, M. Fabbri, P. Martinelli, R. Liguori

IRCCS Institute of Neurological Sciences and Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna

Background: Among the non-motor symptoms of dystonia, sleep characteristics have been poorly investigated and very few polisomnographic (PSG) studies have been conducted, reporting contrasting finding.

Objective: To investigate sleep quality and the pattern (amplitude and persistence) of cervical muscles activity during wake and sleep stages in patients with idiopathic cervical dystonia.

Methods: Ten patients (6 females and 4 males) with a mean age of 51± 8 years and mean disease duration of 10± 6 affected by idiopathic cervical dystonia were recruited among those attending the Botulinum Toxin Units of the University of Bologna. All the patients underwent a video-polygraphic recording, scheduled from 8 pm to 8 am, included EEG, ECG, EOG, thoraco-abdominal respiration and surface bilateral EMG of submental, orbicularis oris, stemocleidomastoideus, splenius capitis, trapezius, brachial biceps, pectoralis and tibialis anterior. Examinations were performed three months after the last botulinum toxin. Patients were also examined by means of questionnaires in order to assess subjective quality of sleep (i.e Pittsburgh Sleep Quality Index) and subjective daytime sleepiness (i.e Epworth Sleepiness Scale). PSG was scored according to standard method. Coupled EEG and EMG patterns were automatically analyzed offline by means of HypnoLab software.

Results: Macrostructural analysis showed normal sleep architecture and organization except for sleep fragmentation, impaired sleep efficiency and decreased REM and stage 3 NREM sleep. EMG activity on dystonic muscles progressively reduced in amplitude and persistence through the night, even if phasic contractions of small amplitude tended to persist during sleep on muscles affected by dystonia, especially during sleep lightening . Sleep analysis showed that EMG activity sometimes preceded EEG arousal. Finally, subjective sleep perception was impaired, however patients did not report excessive daytime sleepiness.

Conclusion: Dystonia tended to persist during sleep impairing sleep quality. Moreover, sleep could represent an important window into the pathophysiology of dystonia.

P6

Rest tremor as very early presenting symptom of sepiapterin reductase deficiency (SRD)

Vincenzo Leuzzi[1], *Cl. Carducci*[2], *M.T. Giannini*[1], *M. Tolve*[2], *C. Pignattoni*[2], *A. Pasquali*[2], *M. Mastrangelo*[1], *R. Danti*[1], *Ca. Carducci*[2]

[1]Dipartimento di Pediatria e Neuropsichiatria Infantile, Sapienza Università di Roma, Roma
[2]Dipartimento di Medicina Sperimentale, Sapienza Università di Roma, Roma

SRD is a rare neurotransmitter disorder presenting with early developmental delay and axial hypotonia. We report on the presentation symptoms of SRD in a new case observed since the first months of life. This 7-month-old girl was born at term from healthy nonconsanguineous Italian parents. Occasional jerks of upper left limb were noticed since the first days of life and became continuous and generalised in the following few weeks, associated with irritability and gastro-oesophageal reflux. On examination (5 months) she exhibited: neuromotor delay, extensor stiffening pattern of head and trunk with upward gaze deviation; hypokinesia; limb rigidity; almost continuous oscillatory movements of limb, trunk and head at rest, which could be interrupted by voluntary movements or when the examiner handled her. Social smile ad reactivity were preserved. CSF examination revealed (r.v.): Neopterin 4.52 microg/L (2.30-10.10); Biopterin 21.05 microg/L (2.40-11.80); Sepiapterin 17.5 nmol/L, (< 1); HVA 77 nmol/L (324-1379); 5-HIAA nmol/L 18 (189-1380); 3-MHPG 42 nmol/L (98-168)]. SPR gene sequence (patient and parents) revealed the patient was compound heterozygote for two pathogenetic mutations (p.R150V, p.K251*). Levodopa/Carbidopa plus 5-OH-Triptophan treatment resulted in a prompt clinical improvement.

Conclusion: SRD is one of the few causes of early rest tremor in the infancy.

P7

Validation study of the Italian version of the REM sleep behavior disorder screening questionnaire (RBDSQ)

Alice Manzoni[1], *I. Delrio*[1], *A. Pilotto*[1], *B. Bigni*[1], *M. Bianchi*[1], *E. Cottini*[1], *M.C. Rizzetti*[2], *E. Premi*[1], *B. Borroni*[1], *A. Alberici*[1], *A. Padovani*[1]

[1]Centre for Neurodegenerative Disorders, Neurology Unit, University of Brescia, Brescia
[2]O.U. Rehabilitation Parkinson, S. Isidoro Hospital, FERB Onlus Trescore Balneario, Bergamo

Introduction: The REM Sleep Behavior Disorder (RBD) Screening Questionnaire (RBDSQ) is widely used as screening for RBD.

Objective: Aim of this study was to evaluate the construct validity of Italian version of RBDSQ.

Materials and Methods: The RBDSQ scale was translated from English into Italian language and then back-translated from Italian into English to ensure the fidelity of translation. The back-translation was double checked by a native English speaking assistant and by AA. The questionnaire was administered to a consecutive sample of 123 patients affected by an Extrapyramidal Syndrome (73 Parkinson Disease, 39 Atypical Parkinsonisms, 8 Lewy Body Disease and 3 Multisystemic Atrophy) (mean age: 68.75±10.76; UPDRS-III mean score: 18.35±10.98; MMSE mean score: 27.18±2.84) and 31 sex and age-matched control subjects (mean age: 69.64±10.61). Inter-rater reliability and test-retest were performed in a subset of 32 patients (mean age: 72.45±6.59; UPDRS-III mean score: 19.63±8.59; MMSE mean score: 26.78±4.09). Statistical analysis were performed by using IBM SPSS Statistics 20.

Results: The RBDSQ was found to have high internal consistency, reliability and validity coefficients (Cronbach's alpha coefficient: 0.813; Cohen's kappa coefficient: 0.858; Intraclass correlation coefficient, ICC: 0.948, 95% CI=0.896-0.974). RBDSQ total score differentiated patients affected by an Extrapyramidal Syndrome and controls (RBDSQ total score 4.27±2.98 vs 2.42±2.46, respectively; p=0.0018).

Conclusion: This study demonstrated that the Italian version of the RBDSQ is reliable and could be applied as a useful tool in clinical practice. The use of RBDSQ may be helpful in early diagnosis of Extrapyramidal Syndromes, and further studies will explore its contribution to the differential diagnosis in different forms of neurodegenerative parkinsonism.

P8

Sexual functions in Parkinson's disease

Roberta Ferrucci[1,2], *V. Raoli*[1], *G. Ardolino*[1], *P. Barone*[3], *L. Bertolasi*[4], *M. Ciocca*[2], *F. Cogiamanian*[1], *A. Padovani*[5], *M. Panzeri*[6], *L. Ronconi*[6], *E. Scelzo*[2], *A. Priori*[1,2]

[1]Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano
[2]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano, Milano
[3]Dipartimento di Medicina e Chirurgia, Università degli Studi di Salerno, Salerno
[4]Unità di Neurologia, Azienda Ospedaliera Universitaria Integrata, Verona
[5]Dipartimento di Scienze Mediche e Chirurgiche, Università degli Studi di Brescia, Brescia
[6]Università degli Studi di Padova, Padova

Introduction: Patients with Parkinson's disease (PD) can have impaired sexual function. Although the disease itself likely contribute to sexual dysfunction, antiparkinsonian drugs can also have an effect.

Objective: To assess sexual function in PD.

Methods: 121 PD patients (aged 40-80; 70 males, 51 females) and 123 controls (aged 40-80; 71 males, 52 females) were recruited from four Italian Movement Disorders Clinics. To assess sexual function in PD four different scales were used: the Brief Index of Sexual Functioning (BISF-M for man; BISF-W for woman), the International Index of Erectile Function (IIEF) and the Female Sexual Function Index (FSFI).

Results: PD patients did not differ from controls on total scores of sexual function scales (BISF-M, BISF-W, IIEF, FSFI: $p>0.05$). Only analysis of singular scale domains showed that orgasm was significantly impaired in male patients (BISF-M, D5:$p=0.03$). Regarding the effects of drugs whereas Levodopa had no significant effect, monoamine oxidase B inhibitors (MAOI-B) showed controversial results. In males they improved the IIEF score ($p<0.02$) without any significant effect on BISF-M, while in females they were effective in improving BISF-W ($p<0.05$) and left it unchanged the FSFI score.
Anyway MAOI-B improved receptivity and initiation, erection, desire and satisfaction in males (BISF-M: D4:$p=0.05$; IIEF: D1:$p=0.02$, D3: $p=0.05$, D4:$p=0.02$) and desire, arousal and frequency of sexual activity in females (BISF-W: D1:$p= 0.05$, D2:$p=0.03$, D3:$p=0.01$). Dopamine agonists did not show any effect on scales total scores while they have been demonstrated to significantly improve erection and satisfaction in males compared to Levodopa (IIEF: D1:$p=0.04$; D4:$p=0.04$).

Conclusion: The present study on a relatively large unselected sample of patients reveals a rather preserved sexual function in PD. Additionally, specific antiparkinsonian drug classes positively influence sexuality. The occurrence of sexual dysfunction should therefore not always considered as a "normal" symptom of PD, but should always be carefully considered with sexual medicine specialist to diagnosis possible comorbidities and to provide the appropriate treatment.

P9

Parkinsonism in DOOR syndrome: a possible role of 2-oxoglutarate dehydrogenase complex deficiency

Silvio Peluso[1], *L. Bilo*[1], *A. Antenora*[1], *A. De Rosa*[1], *G. Auletta*[2], *S. Pappatà*[3], *G. De Michele*[1]

[1]Department of Neurological Sciences, Federico II University, Naples
[2]Audiology Unit - Neuroscience Department, Federico II University, Naples
[3]Biostructure and Bioimaging Institute, CNR, Naples

Introduction: DOOR syndrome is a rare autosomal recessive disorder; less than 40 cases have been reported from its first complete description in 1970. Deafness, onychodystrophy, osteodystrophy, and mental retardation represent the pathognomonic features of the syndrome; supplementary findings consist of facial dysmorphisms, dermatoglyphic abnormalities, neurological manifestations, and, less commonly, dental, cardiac and uro-genital abnormalities. In addition to sensorineural deafness and mental retardation, further neurological manifestations have been described, including seizures, optic atrophy, and peripheral polyneuropathy. The pathogenesis of DOOR syndrome is unknown but a metabolic etiology has been supposed. In particular, elevated urinary levels of 2-oxoglutaric acid in DOOR patients have indicated a possible deficit of the 2-oxoglutarate dehydrogenase complex (OGDHC) in the tricarboxylic acid cycle.

Case report: We describe an Italian girl affected by DOOR syndrome with a neurological picture characterized by sensorineural deafness, a poorly controlled generalized epilepsy, and an asymptomatic sensori-motor polyneuropathy. In addition, at the age of 21 years she developed a right-sided hemiparkinsonism with good response to dopamine-agonist drugs. A brain I-Ioflupane-SPECT (DaTSCAN) demonstrated striatal presynaptic dopaminergic degeneration, more evident on the left side. A metabolic evaluation was performed and a qualitative assay of urinary organic acids indicated an increased excretion of 2-oxoglutaric acid and, to a lesser extent, of fumaric acid and lactic acid.

Conclusion: This is the first description of parkinsonism concomitant with DOOR syndrome. The link between DOOR syndrome and parkinsonism is unclear but immunohistochemical studies have demonstrated diminished OGDHC immunoreactivity in the substantia nigra of PD patients. Striatal degeneration could be expression of the same pathological mechanisms responsible for the pathognomonic clinical features of the disease.

P10

Vascular Parkinsonism: motor and non motor symptoms with Rotigotine treatment

Sara Mazza[1,3], *C. Imondi*[1,2], *M. Rao*[1,2], *F. Scrascia*[1,2], *S. Fiore*[3], *F. Stocchi*[4], *M.F. De Pandis*[1,2,4]

[1]Centro Parkinson San Raffaele Cassino, Cassino
[2]UO Riabilitazione Neuromotoria San Raffaele Cassino, Cassino
[3]UO Riabilitazione Semiresidenziale San Raffaele Cassino, Cassino
[4]IRCCS San Raffaele Pisana, Roma

Introduction and Objective: Vascular parkinsonism (VP) is still little differentiated, without clear correlation between clinical presentation, Magnetic Resonance imaging, pre-synaptic dopaminergic function and dopaminergic treatment response. We have reviewed our clinical sample to describe the clinical response of motor and non motor symptoms.

Materials and Methods: We describe eleven patient with VP, with subacute onset after strategic infarcts in thalamocortical drive areas (thalamic or internal capsula), with concomitant detection of white matter encephalopathy. All patients had neuropsychological symptoms such as depression, apathy, attention or memory impairment. All patient underwent UPDRS section I-III; BDI-II, NPI, MMSE, MoDA. Patients was treated with rotigotine patch at 4 mg per day. Two patients drop for skin allergy. The remaining were underwent after six and twelve months to the previous assessment.

Results: The score reveal: in UPDRS I decreasing 2 up to 4 points and in section III 0 up to 9 points; MMSE revealed 0 up to 3 and MODA 0 to 2 increasing score. BDI-II revealed 2 up to 7 decreasing score; in NPI six patients showed decreased score (3 up to 5 points), while three patients showed an increased score.

Discussion: In our clinical sample dopaminergic treatment response reveal great variability above all between on motor and non motor efficacy. Is clear the negative role of cerebrovascular lesion in cognitive impairment in parkinsonism but also the role of the remaining dopaminergic pre-synaptic function in VP patients. In our patients should be relevant distinguish subtypes in which strategic infarts leads to decrease thalamocortical drive and pre synaptic dopaminergic dysfunction using FP-CIT-SPECT, correlating with the motor and non motor dopaminergic response.

Conclusion: Dopaminergic treatment can be actually used with rationale in VP. Reviewed diagnostic criteria, differentiating syndrome by clinical motor and non motor presentation, correlated by morphological and functional subtypes, can leave to a stronger rational dopaminergic treatment.

P11

A clinical study on hemifacial spasm

Marika Falla[1], *M. Diana*[1], *G. Fabbrini*[1,2], *G. Ferrazzano*[1], *A. Berardelli*[1,2]

[1]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome
[2]IRCCS Neuromed Institute, Pozzilli (IS)

Background: In primary hemifacial spasm (HFS) muscle spasms usually start in the upper facial muscles and rarely in the lower facial muscles. Spasms spread in most of the cases to the other ipsilateral muscles of the face, however no studies have evaluated the frequency of spread and whether the frequency of spread is associated with any clinical-demographic features.

Objective: To investigate in a large population of HFS patients the frequency of spread and the clinical-demographic characteristics associated with the presence of spread.

Methods: One hundred and seventy-eight consecutive outpatients with diagnosis of primary HFS were included in the study. We collected data regarding gender, age, family history for HFS, age at HFS onset, symptoms duration, muscles involved by the spasm at time of onset and at the time of examination, spasm severity, spread of the spasm and presence of synkinesis.

Results: Muscle spasms began in the orbicularis oculi in 143 (80%) patients, in the orbicularis oris in 9 (5%) patients and simultaneously in the orbicularis oculi and oris in 26 (15%) patients. Spread of muscle spasms to other ipsilateral facial muscles occurred in 142 of the 152 (91%) patients with single onset site of the spasm. Spread occurred in 133 (93%) of the 143 patients with onset in the orbicularis oculi and in all the 9 patients with onset in the orbicularis oris. The mean latency of spread was 26.9 ± 38.8 months. We observed synkinesis in 104 of the 178 patients studied (58.4%). No differences in clinical-demographic variables emerged between patients with or without spread including the presence or absence of synkinesis.

Conclusion: Spread of muscle spasms was observed clinically in the vast majority of patients suggesting that this is a typical feature of primary HFS. Further studies are needed to clarify the relationship between spread and synkinesis.

P12

The relationship of action tremor in the upper limbs to other motor and non motor symptoms in Parkinson's disease: a cross-sectional study

Angelo Fabio Gigante, M. Superbo, D. Liuzzi, P.V. Mancino, R. Pellicciari, M. Guido, G. Iliceto, G. Defazio

Dipartimento di Scienze Mediche di Base, Neuroscienze e Organi di Senso, Universita' degli Studi "Aldo Moro", Bari

Background: Action tremor is often noted in patients with Parkinson disease (PD), yet the clinical correlates of this type of tremor have been the focus of few studies.

Objective: To assess the relationship between the severity of action tremor in PD and other relevant demographic/clinical (motor and non motor) features.

Methods: Demographic and clinical features were ascertained in 234 patients with PD (mean age, 68 ± 10 years; mean age of Pd onset 61.6 ± 10.8 years; mean duration of PD, 6.4 ± 4.4 years; mean HY staging, 2 ± 0.5) . All patients underwent a neurological examination and Unified Parkinson Disease Rating Scale part III (UPDRS III), scale, Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB) and Non-Motor Symptoms Questionnaire were administered.

Results: Action tremor in the upper limbs was present in 84/234 patients (35.9%) . The action tremor score was not associated with age, sex, age at onset, disease duration and Hoehn and Yahr staging . The action tremor score was associated with UPDRS III total score ($r=0.22$, $p < 0.0001$). Stratifying by UPDRS-III items, yielded a significant correlation of the action tremor score in the upper limbs with rest tremor score in the upper limbs ($r=0.55$, $P < 0.0001$), head tremor ($r=0.22$, $p < 0.001$) and gait ($r=-0.2$, $p=0.007$). On multivariable linear regression analysis, adjusted for age and sex, head tremor and gait lacked significance, whereas the relationship between action tremor and rest tremor remained still significant. No association was observed between action tremor in the upper limbs and MMSE, FAB or sleep, autonomic, psychiatric and sensory disturbances.

Conclusion: Action tremor in the upper limbs was associated with rest tremor but lacked any relationship with other motor and nonmotor manifestations of PD. This suggests that action tremor in PD may represent an underlying pathophysiological process different from these other manifestations.

P13

Do non motor symptoms in Parkinson's disease differ from essential tremor before the initial diagnosis? A clinical and scintigraphic study

Maurizio Giorelli[1], *J. Bagnoli*[2], *L. Consiglio*[2], *M. Lopane*[2], *D. Zizza*[2], *G.B. Zimatore*[1], *P. Difazio*[2]

[1]Operative Unit of Neurology, "Dimiccoli" General Hospital, Barletta
[2]Operative Unit of Nuclear Medicine, "Dimiccoli" General Hospital, Barletta

Aims: Non-motor symptoms (NMS) in Parkinson's disease (PD) have an important negative impact on quality of life. Essential tremor (ET) is affected by non-motor symptoms also and enters into differential diagnosis with PD. DAT scan is a technique used to facilitate differential diagnosis between PD and ET. The aim of this study was to compare non motor symptoms declared by patients still not aware of diagnosis in the moment they undergo to DAT scans, and confirmed thereafter to be affected either by Parkinson's disease or Essential Tremor.

Methods: We evaluated both motor impairment (MDS-UPDRS-III) and non motor symptoms (NMSQuest) in patients who underwent to DAT scan for diagnostic purposes. Both clinicaland scintigraphic data obtained from selected PD (n=31) and ET (n=22) patients were compared.

Results: We did not detect a significant difference in the total number of NMS reported by either PD (10.39 ± 4.9) and ET patients (8.41 ± 3.33). PD patients reported more drooling (29%), hyposmia (32.2%), hallucinations (19.3%), difficulty in concentrating (51.6%), orthostatic dizziness (67.7%), falling (19.3%), vivid dreams (32.2%), REM sleep behavior disorder (58%), and diplopia (22.5%) as compared with ET patients. PD patients complaining drooling, orthostatic dizziness, and diplopia hadgreater ($p < 0.05$) denervation of caudata than PD patients who did not report the same symptoms. The differences observed were not associated with differences in age, sex, UPDRS-III score, and presence / absence of tremor.

Conclusion: The combined presence of hyposmia, drooling, hallucinations, difficulty in concentrating, orthostatic dizziness, vivid dreams, RBD, and diplopia may help to clinically differentiate PD from ET, and may predict striatal denervation on DAT scan. Some, but not all the NMS referred by PD patients prior to diagnosis, are associated with higher striatal dopaminergic denervation. When analyzed early and before receiving a definitive diagnosis, PD patients complain specific symptoms that seem to depend on different pathogenetic mechanisms.

P14

Development and validation of a clinical guideline for diagnosing blepharospasm

Giovanni Defazio[1], *M. Hallett*[2], *H.A. Jinnah*[3], *A. Berardelli*[4]

[1]Department of Basic Medical Sciences, Neurosciences and Sensory Organs, "Aldo Moro" University of Bari, Bari
[2]Human Motor Control Section, NINDS, NIH, Bethesda, Maryland, USA
[3]Departments of Neurology, Human Genetics & Pediatrics, Emory University, Atlanta GA, USA
[4]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome and IRCCS Neuromed Institute, Pozzilli

Background: The lack of validated diagnostic criteria sometimes makes it difficult to distinguish blepharospasm from other conditions of involuntary eyelid closure.

Objective: To design and validate a clinical diagnostic guideline for aiding physicians in confirming or refuting suspected blepharospasm.

Methods: The guideline was developed and validated in a three-step procedure: (i) identification of clinical items related to the phenomenology of blepharospasm, (ii) assessment of the relevance of each item to the diagnosis of blepharospasm, and (iii) evaluation of the reliability and diagnostic sensitivity/specificity of the selected clinical items.

Results: Of 17 clinical items initially identified, 7 were admitted by content validity analysis to further assessment. Both neurologists and ophthalmologists achieved satisfactory interobserver agreement for all 7 items, including "involuntary eyelid narrowing/closure due to orbicularis oculi spasms", "bilateral spasms", synchronous spasms", "stereotyped spasm pattern", "sensory trick", "inability to voluntarily suppress the spasms" and "blink count at rest". Nevertheless, each selected item yielded unsatisfactory accuracy in discriminating patients with blepharospasm from healthy subjects and patients with other eyelid disturbances. Combining the selected items, however, could improve diagnostic sensitivity/specificity. The best combination, yielding 93% sensitivity and 90% specificity, was an algorithm starting with the item "stereotyped, bilateral and synchronous orbicularis oculi spasms inducing eyelid narrowing/closure" and followed by recognition of "sensory trick" or, alternatively, "increased blinking".

Conclusion: This study provides an accurate and valid clinical guideline for diagnosing blepharospasm. Encouraging providers to use this guideline, would make it easier to recognise dystonia in clinical and research settings.

Participants to the content validity analysis and videotape assessment: Giovanni Alessio, Giovanni Abbruzzese, Anna Rita Bentivoglio, Giovanni Cossu, Alfonso Fasano, Gina Ferrazzano, Paolo Girlanda, Rocco Liguori, Antonella Macerollo, Davide Martino, Neil R. Miller, Francesca Morgante.

P15

Lewy body dementia: a three years follow up study

Lorenzo Kiferle, A. Vergallo, G. Palermo, R. Ceravolo, U. Bonuccelli

Unità di Neurologia, Università di Pisa, Pisa

Introduction: Few studies, conducted on small cohort of patients, systematically investigated the relationships between the symptoms and the clinical course of Lewy Body Dementia (DLB) with a long term follow up.
Aim of this study is to analyze a broad pattern of clinical aspects of the disease in a population of DLB patients, with a follow up of at least three years.

Methods: We selected 77 patients with the diagnosis of probable DLB. We retrospectively analyzed the age of onset, the prevalent type of onset (motor, cognitive and mixed type), motor disease severity, the acute and chronic response to levodopa (LD) and the levodopa equivalent daily dose. MMSE, cognitive fluctuations (CFs), visual hallucinations (VHs), therapies with cholinesterase inhibitors or Memantine and neuroleptic treatments. Of these patients, 47 were followed for at least 3 years.

Results: The most common onset type was a mixed phenotype, followed by the motor and cognitive phenotype. The postural instability and gait disorders phenotype (PIGD) was predominant. A positive acute LD response was present in 40.3% of patients. In the three years follow up, all tremor dominant patients converted to PIGD. An earlier onset was associated to a prevalent PIGD phenotype. PIDG phenotype was associated to a higher occurrence of VHs, higher worsening of rigid-akinetic subscores at UPDRS part III and a higher worsening of MMSE during three years. VHs occurred at baseline in 30.4 % and were associated with a more prevalent PIDG phenotype at onset, with a younger disease onset and with a faster MMSE and rigid-akinetic UPDRS subscores decline during the three years follow up. The presence of VHs was associated to CFs.

Discussion: We found significant associations between symptoms in DLB patients and if confirmed by larger studies, some of them could represent possible predictors of the 3 years follow up outcome.

P16

Psychiatric disturbances in PSP patients. A case-control study

Paola Stirpe[1], *I. Berardelli*[1], *V. Roselli*[1], *M. Bloise*[1], *M. Pasquini*[1], *G. Fabbrini*[1,2], *C. Colosimo*[1], *N. Modugno*[1,2], *A. Conte*[1,2], *A. Berardelli*[1,2]

[1]Dipartimento di Scienze Neurologiche e Psichiatriche, Sapienza Università di Roma, Roma
[2]IRCCS Neuromed Institute, Pozzilli

Background: While the motor and cognitive features of PSP patients are well characterized, little is known about the presence of neuropsychiatric symptoms in these patients.

Objective: To investigate the frequency and different types of psychiatric disturbances in PSP patients.

Methods: We enrolled 23 PSP patients according to standard diagnostic criteria. Clinical and demographic information were collected with a face-to-face interview. Disease severity was scored using the PSP rating scale and by the Hoehn and Yahr stage (HY). Patients with MoCa score ‹ 24 were excluded. Results were compared with those of 20 age and gender matched healthy subjects. Psychiatric evaluation was based on the structured clinical interview for DSM-IV criteria using the Structured Clinical Interview (SCID-I) for Axis-I disorders. The Hamilton Anxiety Rating Scale (HAM-A) was administered to evaluate the severity of anxiety symptoms, the Hamilton Depression Rating Scale (HAM-D) to assess the severity of depressive symptom and the Brief Psychiatric Rating Scale (BPRS) for to evaluation of psychotic symptoms.

Results: Age at onset of symptoms was 66.1± 5.9 years, symptoms duration was 3.3 ± 1.7 years. Neurological examination showed that PSPRS was 32.3 ± 13.6 and H&Y was 3.04 ± 1.08. Psychiatric disturbances were more frequently present in PSP patients than in controls (p =0.006, Chi-square). In comparison with normal subjects, depressive disorders were more frequent in PSP patients (p= 0.01), but there was no difference in the frequency of anxiety disorders or obsessive compulsive disorders. PSP patients also show higher scores in all the scales used to evaluate the severity of psychiatric symptoms: BPRS (29.2 ± 4.5 vs 25.7 ± 2.6 p=0.003), HAMA (6.08 ± 4.1 vs 3.05 ± 3.5; p=0.008); HAD (7.6 ± 5.5 vs 3.5 ± 3.8; p=0.009).

Conclusion: Psychiatric disturbances, namely depressive disorders, were more frequent in PSP patients than in controls. A better evaluation of these disorders is important for the treatment of these patients.

P17

Action language processing in Parkinson's patients

Silvia Spadacenta[1,2], *G. Giannini*[2], *N. Modugno*[2], *G. Mirabella*[1,2]

[1]Dept. of Physiology and Pharmacology 'V. Erspamer', University of Rome La Sapienza, Rome
[2]IRCCS Neuromed, Pozzilli (IS)

A few studies have demonstrated that action verbs processing is impaired in Parkinson's disease (PD) patients, suggesting that the integrity of the motor system is needed to properly elaborate action-related verbs.
We thus exploited a go/no-go paradigm where 30 non-demented (15 with right side onset and 15 with left side onset of motor symptoms) idiopathic PD patients were required to perform arm reaching movements toward a target when verbs expressing either hand or foot actions were shown and to refrain from moving when abstract verbs were presented. Patients were tested once on dopaminergic medication (ON-state) and once after a washout period of 12 hours (OFF-state), in two different and counterbalanced across patients experimental sessions.
Results showed that reaction times (RT) increased when the verb involved the same effector used to give the response in both groups. This interference effect was greater in the OFF-state than in the ON-state only in right side onset patients. Furthermore, a control experiment showed that when the color of the printed verb and not its meaning was the cue for movement execution, the differences between RTs disappeared. Thus the interference occurs only when the semantic content of a verb has to be retrieved.
The modulation of arm reaching movements induced by hand-related verbs reveals that when PD patients assume their dopaminergic medication a near normal interplay between action language and motor system still occurs. However, the enhancement of the interference effect in the OFF-state in right side onset patients suggests that PD alters the semantic processing of action-related material, thus indicating that the motor system is likely to play a role in understanding the meaning of action words.

P18

Declarative learning interference and consolidation in Parkinson's disease

Lucio Marinelli[1], *L. Mori*[1], *S. Canneva*[1], *C. Trompetto*[1], *G. Abbruzzese*[1], *M.F. Ghilardi*[2]

[1]Clinica Neurologica, DINOGMI, Università di Genova, Genova
[2]Department of Physiology, Pharmacology & Neuroscience, CUNY Medical School, New York, USA

Introduction: Learning and retention of motor skills are essential for daily activities. While in normal subjects both anterograde and retrograde interference has been demonstrated in learning motor tasks with implicit and declarative attributes [3,2], in Parkinson's disease (PD) the acquisition of declarative components of a motor skills is slower [1], however, retention and interference of such skills have not yet been addressed.

Aims: This work investigates anterograde interference and consolidation of declarative learning in patients with PD.

Methods: In a group of newly diagnosed and untreated PD patients and a group of age-matched controls, we used a motor sequence learning task with a declarative learning component, in which eight radially arrayed targets appeared at a fixed temporal interval in a repeating order [1]; subjects were instructed to reach for the targets, to learn the sequence order and, when known, to anticipate the target appearance. In Day 1, a first sequence (SEQ1) was learned to saturation; the following day (Day 2), first, SEQ1 was performed again to saturation, then a different sequence of comparable difficulty (SEQ2) was learned.

Results: Compared to Day 1, retention of SEQ1 on Day2 was lower in PD patients compared to controls. Moreover, unlike in normal controls, in PD, the learning rate of SEQ2 was comparable to SEQ1, thus reflecting a lack of anterograde interference.

Conclusion: These preliminary findings suggest that short and long-term retention of both declarative and implicit learning are impaired in early PD. If confirmed in PD patients undergoing pharmacologic treatment and with a longer disease duration, these results have important relevance to plan an efficient rehabilitative approach.

References

[1] Ghilardi MF et al. Neurology 2003;60:1313
[2] Ghilardi MF et al. J Neurophysiol 2009;101:2218
[3] Krakauer JW et al. J Neurosci 2005;25:473

P19

The UP-TECH project for studying an integrated social system in Alzheimer's patient and his caregiver in the Marche region. A randomized study protocol and preliminary result

Cristina Paci[1], *F. Masera*[2], *C. Chiatti*[2], *M. Ragno*[1], *R. Gobbato*[1], *S. Sanguigni*[1], *T. Carboni*[1], *F. Di Marzio*[1], *G. D'Andreamatteo*[1], *A. Cinti*[1], *B. Moretti*[1], *F. Bonfranceschi*[2], *J. Rimland*[2], *O. Scarpino*[2], *per conto del Gruppo di ricerca Up-Tech*[3]

[1]Unità Operativa Complessa di Neurologia, Ospedale Civile "Madonna del Soccorso", San Benedetto del Tronto (Ascoli Piceno)
[2]INRCA Istituto Nazionale di Riposo e Cura, Ancona
[3]Azienda Territoriale Sanitaria, ASUR - Regione Marche, Ancona

Alzheimer's disease has an impact on quality of life also on caregivers and families.
The UP-TECH project, funded by Marche Region in collaboration and with the contribution of INRCA, Ancona, through the financing of the "No Self-Sufficiency Fund, 2010" and developed with INRCA-IRCCS and territorial medicine services, distributed in five Areas (Pesaro, Ancona, Macerata, Fermo, S. Benedetto del Tronto), aims to experiment a system of integrated services for patients with Alzheimer's and their family caregivers to improve the health and social care.
Main objectives of the protocol are:
a. reduce the care burden of caregivers;
b. keep patients with Alzheimer's in their own home.
Secondary objectives are:
a. define the overall care profile for patients with Alzheimer's and their caregivers;
b. ensuring continuity of care and integration of care pathways;
c. create an information system-specific management for Alzheimer's disease;
d. evaluate the costs of patients with Alzheimer's disease and measure the cost effectiveness of the intervention.
The duration of the study is 12 months, the total number of patients is 450 pairs formed by patient-caregiver, randomized into three study groups,

1. UP: couples taken over by a case manager and receiving three visits to nursing home care;

2. UP-TECH: couples assisted as in the previous group receiving an intervention and technologic assistance identified by the case manager;

3. Control: couples receiving usual care, receiving only three visits nursing home and brochures on the management of symptoms of Alzheimer's.
The research started on January 2013 and is currently in progress. The 10 case managers and social workers were placed functionally integrated in the five places of study sites. 623 households were called and out of which 405 have already expressed their willingness to participate (about 65%). Our preliminary data will be definitive in 12 months with final results.

P20

REM and NREM parasomnias in Parkinson's disease with Mild Cognitive Impairment

Brigida Minafra[1], *R. Cremascoli*[2], *M. Picascia*[3], *M. Terzaghi*[2], *N.G. Pozzi*[1], *R. Zangaglia*[1], *E. Sinforiani*[3], *R. Manni*[2], *C. Pacchetti*[1]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia
[2]Sleep Medicine, National Institute of Neurology Foundation "C. Mondino", Pavia
[3]Laboratory of Neuropsychology, National Institute of Neurology Foundation "C. Mondino", Pavia

Introduction: Cognitive impairment is common in patients with Parkinson's disease (PD), ranging from mild cognitive impairment (MCI) to dementia. REM sleep Behaviour Disorders (RBD) is frequently associated with PD in every phase of disease. Recent study has established that RBD was associated with increased risk of dementia. However, PD patients, mainly those manifesting dementia, may present abnormal sleep-related motor-behavioural episodes which consist not only in RBD events but also in episodes occurring on arousal from NREM sleep.

Objective: The aim of this study is to clarify the relationship between REM/NREM parasomnias in PD patients with or without MCI.

Methods: We enrolled 116 consecutive PD patients without dementia. All the patients underwent a neuropsychological assessment. Based on that, they have been divided in two groups : group 1 (G1)- PD without cognitive impairment (n 58), and group 2 (G2)- PD with MCI (n 58). All patients underwent to neurological examination, sleep interview and nocturnal video polysomnography (VPSG).

Results: G2 showed longer disease duration, lower education level and greater disease's severity than G1. No difference was found between the two groups as for the prevalence of anamnestic RBD.
VPSG data: we documented paroxysmal motor-behavioural episodes in 21 out of 56 patients in G1 and in 22 out of 41 patients in G2.
In G1, all the patients have RBD.
In G2, 19 patients have RBD, 10 patients have NREM parasomnia (6 pseudo RBD and 4 confusional episodes).

Conclusion: Paroxysmal motor-behavioural episodes were more present in G2; this was especially due a numbers of NREM parasomnias. Based on these results NREM parasomnias could be suggested as a "sleep-markers" of cognitive impairment in PD. To better recognise the relationship between NREM parasomnias and the progression of cognitive impairment in PD we must design a large prospective VPSG studies in these populations.

P21

Follow-up study of Mild Cognitive Impairment in Parkinson's disease: determinants of reversible state

D. Frosini, Eleonora Del Prete, C. Pagni, G. Linsalata, G. Tognoni, R. Ceravolo, U. Bonuccelli

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

Introduction: Mild cognitive impairment (MCI) is a common condition in PD, even in the earliest stages; this condition also correlates with a highly risk of dementia. The identification of MCI in the early stage could be crucial for early intervention.

Objective: To evaluate the pattern of PD-MCI progression in early PD according to neuropsychological pattern.

Methods: 65 non-demented, drug-naive, PD patients were enrolled in the study. Assessment including motor evaluation by UPDRS III and neuropsychological evaluation were performed baseline and after 1 year. MCI diagnosis was made according to MDS criteria. Categorization into single-domain(S), multiple-domain(M), amnestic(A), and non-amnestic(NA) subtypes, based on the results of neuropsychological testing, was made. After baseline, therapy with dopaminergic medication was started.

Results: At baseline 15/62 patients (24%) were MCI: 6/15 showed M-A, 7/15 M-NA, 2/15 S-A deficit. At follow-up 50 patients were evaluated, 6 MCI patients were still cognitively impaired, 5 MCI (31%) reverted to normal cognition (2M-NA, 2M-A, 1S-A); 4 MCI were lost to follow up.
In addition 8 new MCI diagnosis were made and at 1 year there were 14 (28%) MCI patients. 5/14 have M-A pattern, 6/14 M-NA, 1/14 S-A and 2/14 S-NA. Comparing reverter-MCI versus non-reverter MCI, the former at baseline performed significantly better on RAVLT immediately recall (29,8 vs 23,8), CPM47 (28,6 vs 18) and Rey Figure Copy (29 vs 13,4), had lower motor impairment (15 vs 23) and higher educational level (11 years vs 8 years).

Conclusion: Both baseline and follow-up high prevalence of MCI in PD was detected in our study confirming previous evidences. Baseline cognitive pattern might not predict the 1-year prognosis of MCI but higher educational level and lower impairment of verbal learning and visuospatial planning and of motor function characterized patients reverting to normal cognition after dopaminergic treatment.

P22

Professional artists, creative drive and Parkinson's disease: a new insight

Margherita Canesi[1], *M.L. Rusconi*[2], *F. Moroni*[2], *A. Ranghetti*[2], *E. Cereda*[1], *G. Pezzoli*[1]

[1]Centro Parkinson e Disordini del Movimento, Istituti Clinici di Perfezionamento, Milano
[2]Dipartimento di Scienze Umane, Università di Bergamo, Bergamo

Background: Artistic-like production may emerge or change in PD patients on dopaminergic (DA) therapy. Although an increase in artistic-like production has been associated to compulsive and repetitive behaviours, recent data suggest that it could represent the emerging of innate skills. We investigated creativity features in a PD group of professional artists (PD-A) and in non-artist with (PD-C) and without (PD-NC) an emerging artistic-like production.

Patients and Methods: We included 36 PD (12 PD-A, 12 PD-C, 12 PD-NC) and 24 matched HC (12 professional artists (HC-A), 12 non-artists (HC-NC)). Neurological and neuropsychological evaluation was performed, LEDDs was calculated. Creativity features were evaluated through the Abbreviated Torrance Test for Adults (ATTA).

Results: Demographic, clinical and therapeutic data were similar between PD and HC. The ATTA sub-scores for elaboration and originality were significantly higher in PD-A, PD-C and HC-A when compared to PD-NC and HC-NC. Only PD resulted positive to mMIDI. Punding sub-score by mMIDI was negative in all groups.

Discussion: Creative thinking (CT) is not related to DA therapy. This observation is supported by similar ATTA scores between PD-A and HC-A.
The acquired artistic drive (AD) in PD-C is likely triggered by DA therapy as it emerges after the introduction of PD treatment. An enhanced AD has been reported in PD-A but not reported as a novelty as in PD-C.
AD is not secondary to impulse control deficit as impulsive disorders are present in all PD groups but are not significantly higher in PD-C.
The enhanced AD is not due to punding-like activities. ATTA sub-scores for elaboration and originality distinguish the CT in professional artist from non-artist independently of PD.

Conclusion: CT in PD appeared unrelated to DA treatment. AD seemed to be associated with innate skills rather than impulse control disorder or punding.

P23

The cognitive reserve: perspectives in Parkinson's disease - Mild Cognitive Impairment

Cristina Pagni, D. Frosini, R. Ceravolo, G. Palermo, U. Bonuccelli, G. Tognoni

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

Introduction: Cognitive reserve (CR) is an exciting construct that provides an explanation for individual differences in susceptibility to age-related brain changes or neurodegenerative disorders like Alzheimer's disease [1]. Knowledge about cognitive reserve in Parkinson's Disease (PD) is still limited. Preliminary empirical evidence shows that education might exert a protective effect on cognitive decline in PD [2].

Objective: The aim of this study was to evaluate the relation between CR and PD-MCI.

Methods: 23 non-demented, drug-naïve, PD patients (mean age 66 years) were assessed by a neuropsychological battery together with the Cognitive Reserve Index questionnaire (CRIq[3]), that comprehensively assessed CR. The CRIq includes demographic data and items grouped into three part: education, working activity and leisure time, each of which returns a subscore.
CRIq score was divided in medium-low (up to 100) and medium-high (› 101). MCI diagnosis was made according to MDS criteria. Assessment was performed at baseline and after 1 year.

Results: A chi-square test was performed to examine the relation between MCI and CRIq subscore. The relation between MCI and CRIq education, working and leisure activity was not significant at baseline; while at follow-up patients with higher CRIq education score were less likely to present MCI (X^2 = 9.16, p ‹ .005). In particular, none of the MCI subjects had a medium-high CRIq education value.

Conclusion: Our findings confirm that CR may provide an exploratory approach on cognitive dysfunction in PD. Education appeared the factor affecting cognitive evolution, while working and leisure activity did not seem to play a role. We might speculate that cognitive impairment due to dopaminergic dysfunction in de novo PD patients is not modulated by CR and could be restored by therapy. Differently CR may modulate cognitive impairment during the course of the disease, by providing a buffer for cognitive compensation probably through mechanism of cortical reorganization.

References

[1] Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurol. 2012 Nov;11(11):1006-12
[2] Poletti M, Emre M, Bonuccelli U. Mild cognitive impairment and cognitive reserve in Parkinson's disease. Parkinsonism Relat Disord. 2011;17(8):579-86
[3] Nucci M, Mapelli D, Mondini S. Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. Aging Clin Exp Res. 2012 Jun;24(3):218-26

P24

Longitudinal study of cognitive and psychiatric functions in spinocerebellar ataxias type 1 and 2

Roberto Fancellu[1], *D. Paridi*[2], *C. Tomasello*[1], *M. Panzeri*[1], *A. Castaldo*[1], *C. Mariotti*[1], *S. Genitrini*[1], *P. Soliveri*[2], *F. Girotti*[3]

[1]SOSD Genetica delle Malattie Neurodegenerative e Metaboliche, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano
[2]UO Neurologia 1 – Disordini del Movimento, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano
[3]UO Neurologia 4 – Neuropatologia, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano

Introduction and Objective: The role of cerebellum in cognition, both in healthy subjects and in patients with cerebellar diseases, is debated. Neuropsychological studies in patients with spinocerebellar ataxia type 1 (SCA1) and type 2 (SCA2) have demonstrated impairments in executive functions, verbal memory, and visuo-spatial performances, but prospective evaluations still lack. Our aims were to assess longitudinal progression of cognitive and psychiatric functions in patients with SCA1 and SCA2 in a two-year longitudinal study.

Methods: At baseline, 20 patients with SCA1, 22 patients with SCA2 and 17 matched controls were assessed. Two subgroups of patients (9 SCA1, 11 SCA2) were re-evaluated after two years. We tested cognitive functions (Mini Mental State Examination, Digit Span, Corsi Span, Verbal Memory, Attentional Matrices, modified Wisconsin Card Sorting Test, Raven Progressive Matrices, Benton Test, Phonemic and Semantic Fluencies), psychiatric status (Scales for Assessment of Negative and Positive Symptoms, Hamilton Depression and Anxiety Scales), neurological conditions (Scale for Assessment and Rating of Ataxia), and functional abilities (Unified Huntington Disease Rating Scale-part IV).

Results: At baseline, SCA1 and SCA2 patients had significant cognitive deficits compared to controls mainly in executive functions (Phonemic and Semantic Fluencies, Attentional Matrices; $p < 0.001$); SCA2 patients showed further impairment in visuo-spatial and visuo-perceptive tests (Raven Matrices, $p < 0.001$; Benton Test, $p < 0.002$; Corsi Span, $p < 0.0001$). Both SCA groups had higher depression scores ($p < 0.01$) and negative symptoms, particularly apathy ($p < 0.0005$), compared to controls. After two years, motor and functional disability worsened, while only attentive performances deteriorated ($p < 0.05$).

Conclusion: This is the first longitudinal study evaluating cognitive functions in a large series of SCA patients. At follow-up, our data showed that progression of motor disability was not paralleled by a similar progression of cognitive deficits, suggesting that in SCA1 and SCA2 motor and cognitive functions might be involved with different progression rate.

P25

The Parkinson's disease clinic in the Hospital of Rovereto (TN): experience of a multidisciplinary team

Donatella Ottaviani, P. D'Antonio, L. Gallosti, I. Azzolini, A. Simoncelli, M. Fontana, M.P. Maiola, C. Berti, M. Fracchetti, M. Scottini, G. Rossi

U.O. Neurologia, Ospedale Santa Maria del Carmine, Azienda Provinciale per i Servizi Sanitari, Provincia Autonoma di Trento, Rovereto

Introduction: An official resolution by the Autonomous Province of Trento, led to the creation of an integrated Parkinson's Disease (PD) clinic in the hospitals of Trento and Rovereto, as part of a firm commitment to investing in the quality of life of patients with PD and Parkinsonisms.

Aims: We aim to describe our multidisciplinary approach to use the best diagnostic tools and adopt state of the art therapeutic and rehabilitative program in order to minimize the effects of symptoms on quality of life.

Methods: Patients referred to our PD clinic were evaluated a two parts assessment. The first part was conducted by the nurse and the speech therapist. The nurse investigated principal problems and administered part I and part II of the UPDRS and evaluated the presence of orthostatic hypotension. The speech therapist observed the possible presence of speech and swallowing problems and select patients for a speech therapy program. The second part of the evaluation was conducted by the neurologist in the presence of the physiotherapist. The medical history, the UPDRS part III, the Hoehn and Yahr scale and the neurological examination were performed by the neurologist. The physiotherapist examined the major problems of the patients, and following the Dutch guidelines for physioterpy in PD, prescribe a rehabilitation treatment for the patients.

Results: 68 patients (n 36 M; n 32 F) underwent the multidisciplinary evaluation from the beginning of January 2013. UPDRS I mean score was 9.7; UPDRS part II mean score was 17.2; UPDRS part III mean score was 15. Twenty-two percent of patients were enrolled for a rehabilitation training and 10 % started a speech therapy.

Conclusion: The MDT's wide ranging expertise recognize a number of aspects of Parkinson's which specifically effect every patient, from medication and mobility to drooling and diet. The role of the MDT is to treat each symptoms in order to minimize the impact Parkinson's has on daily activities.

P26

Association between extrapyramidal signs, subjective memory complaints and depressive symptoms in nondemented subjects: population-based data from the Zabùt Aging Project

Roberto Monastero, C. Camarda, S. Sutera Sardo, R. Camarda

Dipartimento BioNeC, Università degli Studi di Palermo, Palermo

Objective: Extrapyramidal signs (EPS) have been associated with increased risk of dementia, Parkinson's disease, parkinsonism, and vascular lesions of white matter and are also a significant predictor of mortality. However, little is known about the relationship between EPS, subjective memory complaints (SMC), and depressive symptoms (DS). We examined this putative cross-sectional association using population-based data collected on an italian rural community.

Materials and Methods: Over 1750 nondemented individuals aged 50 years or over from the Zabùt Aging Project - a population-based cross-sectional, epidemiologic study of aging and dementia performed on a rural italian community - were included in the present study. All participants were assessed with standardised instruments for EPS (i.e. resting tremor, rigidity, bradykinesia and gait disturbance), SMC and DS. Multiple regression models were used to examine the associations of EPS with SMC and DS, calculating the odds ratios (ORs) with 95% confidence intervals (CIs).

Results: EPS were more frequent in men than women (54.9% vs 45.1%, p= < .03), and increased with age reaching a maximum prevalence of 14% in subjects aged 80-89 years. Multiple regression analyses, controlled for age, sex, and education, showed that EPS were independently associated with SMC (OR= 1.5, 95% CI= 1.0-2.2) and DS (OR= 1.8, 95% CI= 1.1-2.7). Furthermore, SMC and DS additively interact to increase the association with EPS (OR= 2.5, 95% CI= 1.5-4.0).

Discussion and Conclusion: We demonstrated that EPS correlate with SMC and DS, which together interact to increase the risk of EPS. Ongoing, prospective data on the Zabùt cohort as well as data from other prospective population-based studies are needed to evaluate the prognostic role of EPS in nondemented subjects with SMC and DS.

P27

Relationship between apathy and cognitive dysfunctions in untreated, de novo patients with Parkinson's disease: a prospective longitudinal study

Gabriella Santangelo[1,2], *M. Picillo*[3], *G. Pisano*[1], *M. Moccia*[3], *D. Pezzella*[1], *S. Cuoco*[1], *R. Erro*[3], *K. Longo*[2], *C. Vitale*[2,4], *M.T. Pellecchia*[5], *M. Amboni*[2], *A. De Rosa*[3], *G. De Michele*[3], *P. Barone*[5]

[1]Department of Psychology, Second University of Naples, Caserta
[2]IDC-Hermitage-Capodimonte, Naples
[3]Department of Neurological Sciences, University Federico II, Naples
[4]University Parthenope, Naples
[5]Neurodegenerative Diseases Center, Department of Medicine and Surgery, University of Salerno, Salerno

Introduction: Apathy may be either a psychic symptom of major depression or a behavioral disturbance occurring in concomitance with depression or alone in Parkinson's Disease (PD). The aim of the present study was to determine the progression of cognitive impairment in drug-naive, untreated PD patients with or without clinically significant apathy.

Material and Methods: Sixty-two patients with a disease duration <2 years, and without history of present or past therapy with pro-dopaminergic agents received a diagnosis of PD and were included in the present study. All untreated, de novo PD patients underwent Self-Report Version of Apathy Evaluation Scale (S-AES) and a comprehensive neuropsychological battery to assess memory, frontal functions and visuospatial functions. Two years after the first assessment, all patients were recall and re-evaluated on S-AES and on standardized neuropsychological tests.

Results: According to cut-off value of S-AES, among the 62 PD patients, 9 patients experienced apathy at both baseline and follow-up (A+A+), 8 patients had apathy only at follow-up (A-A+), 37 patients never experienced apathy (A-A-) and 8 patients showed apathy at the baseline only (A+A). Cognitive performance significantly declined in all four groups. After Bonferroni post-hoc test, at both baseline and follow-up A+A+ performed worse than A-A- on visuospatial and frontal tests. Moreover, A-A+ had significantly lower scores than A-A-, but similar to A+A+ on interference task of Stroop test. Regression analysis showed that poor performance on interference task of Stroop Test at baseline (odd ratio= 7.800; 95% CI: 1.344-45.276; Wald=5.241, p=0.022) was the only independent predictor of onset of apathy at follow-up.

Conclusion: The results indicated a relationship between apathy and dysexecutive syndromes in early PD. Moreover, reduced scores on interference task of Stroop Test may predict development of apathy in PD patients.

P28

Movement disorders and deception

Francesca Mameli[1,2], *E. Tomasini*[1,3], *E. Scelzo*[1,3], *M. Fumagalli*[1,2], *R. Ferrucci*[1,2], *F. Cogiamanian*[4], *L. Bertolasi*[5], *A. Priori*[1,2,3]

[1]Centro Clinico per la Neurostimolazione, le Neurotecnologie ed i Disordini del Movimento, Fondazione IRCCS Ca'Granda–Ospedale Maggiore Policlinico, Milano
[2]Servizio di Neuropsicologia e Psicologia Clinica per i Disordini del Movimento, Fondazione IRCCS Ca'Granda–Ospedale Maggiore Policlinico, Milano
[3]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti,Università degli Studi di Milano, Milano
[4]U.O. Neurofisiopatologia, Fondazione IRCCS Ca' Granda–Ospedale Maggiore Policlinico, Milano
[5]Azienda Ospedaliera Universitaria Integrata, Verona

Neuropsychological research challenging the traditional view shows that patients with essential tremor (ET) can have deficits in cognitive and behavioural functioning. The available evidence suggests that this impairment might arise from dysfunction in either the fronto-subcortical or cortico-cerebellar circuits. Although abnormalities in the fronto-subcortical circuits could imply difficulty in lying, no study has investigated deception in patients with ET.
In this study, to investigate whether deceptive responses are impaired in ET, we tested patients with the Guilty Knowledge Task (GKT), a simple, fast, computerized paradigm specifically assessing the ability to lie. We also tested a group of patients with PD, a disease associated with a known difficulty in lie production, and a group of healthy control subjects (HS).
Our results showed that in the GKT for deception, patients with ET responded less accurately than HS ($p=0.014$) but similarly to patients with PD ($p=0.955$). No differences between groups were found in truthful responses ($p=0.488$). Reaction times for both GKT responses tested were significantly longer in patients with ET than in those with PD and healthy subjects (true responses: $p = 0.0001$; lie responses: $p = 0.005$).
Besides confirming impaired deception in patients with PD, our results show a lie production deficit in patients with ET also. These findings suggest that difficulty in lying is an aspecific cognitive feature in movement disorders characterised by fronto-subcortical circuit dysfunction, such as PD and ET. Impairment in the prefrontal executive system can prevent people exhibiting the flexible and goal-directed behaviors that are considered essential human behavioral features. These new insights into the complex cognitive processes in patients with ET and PD could be useful in designing novel specific approaches for cognitive rehabilitation.

P29

Impulse control disorder and related behaviours in Parkinson's disease associated with GBA or PARK2 gene mutations

Paolo Amami[1], *C.F. Bagella*[1], *A.E. Elia*[1], *J. Azzollini*[1], *C. Barzaghi*[1], *M. Carecchio*[1,2], *B. Garavaglia*[1], *A. Albanese*[1,3]

[1]Fondazione Istituto Neurologico Carlo Besta, Milano
[2]Clinica Neurologica Azienda Ospedaliero-Universitaria Maggiore della Carità, Novara
[3]Istituto di Neurologia, Università Cattolica del Sacro Cuore, Milano

Objective: To evaluate whether the presence of GBA gene mutations or PARK2 gene mutations are associated to more severe impulse control disorders and related behaviors (ICD-RB) in Parkinson's disease (PD).

Materials: We enrolled a consecutive series of PD patients according with the following inclusion criteria: 1) diagnosis of PD according to Gelb's criteria; 2) early-onset of PD (< 50 years) or positive family history for PD; 2) disease duration of at least 3 years; 4) genetic assessment available for PARK2 and GBA.

Methods: Patients were classified according to the genotype as 1) carriers of homozygous PARK2 mutations, 2) carriers of heterozygous GBA mutations, 3) non carriers. Each patient was evaluated with a complete neuropsychological assessment, ICD-RB was investigated using "Questionnaire for impulsive-compulsive disorders in Parkinson's disease Rating scale" (QUIP-RS). The levodopa equivalent daily dose (LED, measured in mg) was obtained for each patient. The QUIP-RS total score (0-112) and subscores were expressed as means (±SD) and compared between the three groups by non-parametric statistical analysis.

Results: We enrolled a series of 20 patients. Eight patients (mean age at onset 48.1 ±9.7 years) carried a mutation in the GBA gene, 7 patients (mean age at onset 38.6 ±6.8 years) carried a mutation in the Parkin gene, 5 patients (mean age at onset 40.4 ±2.5 years) were not carriers. There was no significantly difference among groups in age at onset, disease duration or LED. The QUIP-RS total score was significantly higher in the GBA group compared with both Parkin and non carriers (respectively, GBA total score of 17.9 ±17.5, Parkin 1.9 ±3.3, non carriers 4.4 ±6.7; $p<0.05$). Furthermore patients who carried GBA mutation had higher subscores for both impulse control disorders ($p<0.05$) and for compulsive buying ($p<0.01$).

Discussion: We found more severe ICD-RB in PD patients who carry heterozygous GBA gene mutation than in Parkin patients or in non carrier. This findings confirm previous studies which revealed a high frequency of non motor symptoms in GBA carriers, particularly related to neuropsychiatric symptoms [1, 2].

Conclusion: GBA mutation status may be an independent risk factor for impulse control disorder and related behaviours in patients with PD.

References

[1] Alcalay RN et al. Cognitive performance of GBA mutation carriers with early-onset PD: the CORE-PD study. Neurology. 2012 May 1;78(18):1434-40
[2] Brockmann K et al. GBA-associated PD presents with nonmotor characteristics. Neurology. 2011 Jul 19;77(3):276-80

P30

Nigrostriatal correlates of cognitive performances in early, drug-naïve PD patients with Mild Cognitive Impairment: A ^{123}I-FP-CIT-SPECT study

Marina Picillo[1], *M.T. Pellecchia*[2], *M. Amboni*[2], *G. Santangelo*[2], *S. Pappatà*[1], *C. Vitale*[2], *M. Moccia*[1], *K. Longo*[1], *R. Erro*[1], *P. Barone*[2]

[1]Department of Neurological Sciences, University Federico II, Naples
[2]Neurodegenerative Center (CEMAND), University of Salerno, Salerno

Background: Mild cognitive impairment (MCI) is a common finding since the first stages of Parkinson's disease (PD). A role of dopamine nigrostriatal dysfunction in PD-related cognitive deficits has been demonstrated, but no previous study examined nigrostriatal function in patients with MCI as compared with cognitively intact PD patients. We aimed to study the nigrostriatal correlates of cognitive performances in PD patients with MCI and without MCI by means of ^{123}I-FP-CIT-SPECT.

Patients and Methods: A consecutive series of 39 de novo, drug-naïve PD patients were enrolled. They underwent ^{123}I-FP-CIT-SPECT and comprehensive neuropsychological battery. Correlations between neuropsychological measures and DAT availability were assessed by Spearman's rank correlation test. Partial correlations were calculated among significant correlations to control for the effect of age and disease severity.

Results: PD patients with MCI (n=14) and PD patients without MCI (n=25) did not show any significant difference as regards sex, age, age at onset and disease severity. Only in patients with MCI executive and visuospatial functions were significantly correlated to both nigro-caudate and nigro-putaminal dysfunction, irrespective of age and disease severity.

Conclusion: These results suggest that striatal dopamine denervation may be a possible early pathophysiological substrate for MCI in PD patients. Our findings support the hypothesis that, in addition to caudate, also putamen denervation may contribute to frontostriatal cognitive impairment in PD.

P31

Music versus rhythmic stimulation in motor promotion in Parkinson's disease

E. Gastaldo[1], *Marina Padroni*[1], *P. Fazio*[2], *G. Granieri*[1], *G. Brugnoli*[1], *E. Groppo*[1], *I. Casetta*[1], *C. Da Ronch*[1], *E. Granieri*[1]

[1]Section of Neurology, Department of Bio-Medical and Specialized Surgical Sciences, University of Ferrara, Ferrara
[2]Department of Clinical Neuroscience, Centre for Psychiatry Research, Karolinska Institutet, Stockholm, Sweden

Objective: To verify the different impact of a physical activity accompanied by engaging and enjoyable musical stimulation rather than by simple rhythmic cueing, on motor performances and quality of life, in a population of parkinsonian patients.

Material and Methods: This study involved 25 patients with idiopathic Parkinson's disease, with motor disabilities from mild to moderate (2-3 Hoenh and Yahr scale). Mean disease duration was 8 years. All patients were treated with L-Dopa in a good therapeutic compensation.
Physical activity was conducted in small groups in 9 weekly sessions. 14 patients carried out an unguided physical activity, accompanied by exciting music (group 1). 11 patients (group 2) have carried out motor activity through dictated by the trainer and punctuated by a metronome exercises. The patients underwent clinical evaluation through: Unified Parkinson's Disease Rating Scale (UPDRS III), Tapping Test, single finger tapping, and Walking Velocity. Parkinson's Disease Quality of Life Questionnaire (PDQLQ) and Happiness Measure (HM) were also administered.

Results: In both groups there was a reduction of approximately 28% UPDRS III, an increase in walking velocity of 29.4% in group 1 (0.57 m/s to 0.74 m/s) and 20% in group 2 (0.64 m/s to 0.76 m/s). The PDQL improved of 44% in group 1 and 26.4 in group 2. The HM in both groups increased by about 27%. The Tapping test showed no significant changes in the two groups (group 1: 9%, group 2: 1.5%). The single finger tapping demonstrated a reduction of 2.3 s in group 1 while it remained unchanged in group 2.

Conclusion: The results confirm the effectiveness of a training program for motor activity in patients with Parkinson's disease and the usefulness of a concurrent acoustic stimulation. The present study shows that the musical stimulus compared to the rhythmic one has proved to be more effective especially in increasing the speed of the gait and in improving the quality of life.

P32

Changes in motor-cortex excitability after rehabilitation programs in PD patients with freezing of gait

Mauro Catalan[1], *P. Busan*[2], *G. Sgubin*[3], *M. Belfiore*[2], *L. Pellegrini*[3], *A. Gorian*[1], *M. Banica*[1], *A. Cucca*[1], *L. Antonutti*[1], *F. Monti*[1], *G. Pizzolato*[1], *S. Mezzarobba*[3]

[1]Dipartimento Universitario Clinico di Scienze Mediche, Chirurgiche e della Salute. UCO Clinica Neurologica Ospedale di Cattinara, Università degli Studi di Trieste, Trieste
[2]Dipartimento di Scienze della Vita, Università degli Studi di Trieste, Trieste
[3]Corso di Laurea Fisioterapia, Università degli Studi di Trieste, Trieste

Introduction: Freezing of gait (FoG) is a highly disabling symptom of Parkinson's disease (PD) characterized by sudden disruption of gait with absence of forward progression of feet during walking. Pharmacological treatments are generally unsuccessful while rehabilitation is now playing a central role for FoG management.

Objective: Testing the efficacy of two different rehabilitation programs in improving FoG in PD patients and studying the impact of these treatments on cortical excitability.

Materials and methods: 20 PD patients with FoG were enrolled and randomly assigned to treatment groups. Group 1 performed 20 sessions of a Neurocognitive Rehabilitation program based on Motor Imagery (NR-MI), while Group 2 underwent 20 sessions of Treadmill Training (TT). At baseline and at the end of the rehabilitation program (T1), patients were evaluated by assessing: disease stage (H&Y and UPDRS III), FoG (FOGQ), cognitive abilities (e.g. attention, executive functions) and indexes of cortical excitability evaluated registering from lower limbs, by means of single and paired-pulse Transcranial Magnetic Stimulation (TMS).

Results: At baseline, the groups did not differ for any considered variable. After treatment, Group 1 experienced a significant reduction of FoG ($p < 0.001$) while Group 2 did not show any improvement. TMS mainly suggested a tendency toward an increase in the excitability of the motor cortex after both treatments with respect to baseline indexes of motor thresholds and motor evoked potentials recruitment curves, as well as in intracortical inhibition.On the other hand, a tendency toward a prolongation in the duration of the silent period could be observed in both groups, as well as a tendency toward a diminution in intracortical facilitation in the TT group.

Conclusion: Although both rehabilitation programs mainly induced comparable effects on TMS, only NR-MI showed a significant improvement of FoG, suggesting a different mechanisms of intervention between the two treatments.

P33

Is a group-rehabilitation therapy based on action observation effective on reducing freezing of gait in patients with Parkinson's disease?

Giovanna Lagravinese[1], *E. Pelosin*[1], *L. Avanzino*[2], *R. Marchese*[1], *P. Ruggeri*[2] , *G. Abbruzzese*[1]

[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno Infantili (DINOGMI), Università degli Studi di Genova, Genova
[2]Dipartimento di Medicina Sperimentale (DIMES), Istituto di Fisiologia Umana, Università degli Studi di Genova, Genova

Background: Freezing of gait (FOG) is a disabling and frequent symptom in Patients with Parkinson (PwPD). Individual-rehabilitation combined with action observation (AO) seems to have a positive effect on FOG [2]. Moreover, recent studies showed that sensory cues are useful to improve walking performance, reducing FOG [1,3].

Objective: To assess whether a group-rehabilitation based action observation is effective when administered in PwPD and FOG. Secondly, to evaluate if adding an auditory cue to AO may enhance the positive effect of therapy.

Methods: 30 patients (mean age: 68,4 ±7,3) participated in the study. Disease severity was evaluated using UPDRS and Hoen & Yahr scale. Patients were randomly divided into two groups: Group 1 underwent to 10 sessions of physiotherapy (FKT) + AO combined with an acoustic cue (AO+S), while Group 2 received the same treatment without the acoustic cue (AO-S). FOG Questionnaire (FOGQ), diary of FOG episodes, Timed-Up&GO, 10 meter walking test (10MWT), Berg Balance Scale (BBS) have been used to evaluate motor performance. All patients were tested at the beginning (T0), immediately after (T1) and 30 days after (T2) the end of treatment.

Results: Data from walking performances (Timed-Up&GO and 10MWT) and balance (BBS) showed a significant improvement both in Group 1 and Group 2 at T1 and at T2($p < 0.05$).
Regarding FOG, data indicated a significant improvement at T1 in both groups (FOGQ: $p < 0.05$; FOG diary: $p < 0.05$). However, at T2 only Group 2 maintained the improvements obtained (FOGQ and FOG diary T0 vs T2: $p < 0.05$).

Conclusion: Our study demonstrated that AO therapy could be an effective rehabilitative approach also if administered to a group of patients. However, combining action observation with acoustic cue seemed not to promote this kind of learning, probably because the cue constituted a distracting factor.

References

[1] Nieuwboer A., Baker K., Willems A.M., Jones D., Spildooren J., Lim I., Kwakkel G., Van Wegen E., Rochester L., The short-term effects of different cueing modalities on turn speed in people with Parkinson's disease, Neurorehabil Neural Repair. 2009 Oct;23(8):831-6
[2] Pelosin E., Avanzino L., Bove M., Stramesi P., Nieuwboer A., Abbruzzese G., Action observation improves freezing of gait in patients with Parkinson's disease, Neurorehabil Neural Repair. 2010 Oct;24(8):746-52
[3] Velik R., Hoffmann U., Zabaleta H., Marti Masso J.F., Keller T., The effect of visual cues on the number and duration of freezing episodes in Parkinson's patients, Conf Proc IEEE Eng Med Biol Soc. 2012;2012:4656-9

P34

Osteopathic treatment can be significant improvement of walking in patients with advanced Parkinson's disease?

Pietro Marano[1], *M.R. Seminara*[1], *L. Ravidà*[1], *E. Buccheri*[2]

[1]Dept. of Rehabilitation, Villa dei Gerani Clinic, Catania
[2]C.d.S. in Physiotherapy, University of Catania, Catania

Introduction: In our paper we report the observation of a patient diagnosed with Parkinson's disease, admitted to our rehabilitative unit for 30 days about.

Objectives and methods: To ameliorate the gait control, not only with pharmacological therapy but with classic rehabilitative therapy and osteopathic strategies. We have tested a 78 y.o. female with Parkinson's disease at H&Y stage 2.5. The patient showed severe slowdown ideomotoric, cognitive impairment, changes in step with the march and episodes of freezing, starting esitation, instability 'postural propensity to falls forward. Rehabilitation treatment has provided rehabilitation sessions neuromotor, neuropsychological, carried out in the gym every two times a day and lasting approximately 3 hours with repeated intervals between one year and another, with the use of visual cues, auditory and proprioceptive control gait; action obervation, segmental mobilization, psychomotor exercises, maneuvers with the use of osteopathic craniosacral techniques are three times a week were performed. The cognitive dimension was assessed with the Brief Neuropsychological Examination Protocol (ENB), the Montreal Cognitive Assessment (MoCA), the Frontal Assessment Battery (FAB), the Mini Mental State Esamination (MMSE). The scores obtained were indicative of a state of global cognitive impairment (MMSE score = 21) and cognitive deficits that primarily concerned the areas of long-term memory, working memory, selective attention, divided and alternating skills planning and programming and executive functions. The motor side was assessed by Barthel Index, TUG, UPDRS section III, EDF, FOG, TEN METER WALK TEST.

Results and discussion: The patient, however, shows a weak compliance to the rehabilitation treatment presumably determined by the cognitive deficits described above.
It has been noted that alterations in the step were reduced and better controlled by the patient at the end of the sessions conducted with osteopathic techniques. The control post-discharge, made after 20 days, showed that despite the drug treatment had remained unchanged and the patient would not perform any rehabilitative treatment, alterations and pitch gear with episodes of freezing were again present.

P35

Repeated muscle vibration (RMV) as a new therapeutic tool in postural and gait disturbances in Parkinson's disease

Filippo Camerota[1], *C. Celletti*[1], *M. Galli*[2,3], *P. Sale*[3], *G. Albertini*[3], *F. Stocchi*[3], *M.F. De Pandis*[3,4]

[1]Physical Medicine and Rehabilitation Division, Umberto I Hospital, Sapienza University, Rome
[2]Bioengineering Department, Politecnico di Milano, Milan
[3]IRCCS San Raffaele Pisana, Tosinvest Sanità, Rome
[4]IRCCS San Raffaele Cassino, Tosinvest Sanità, Cassino

Introduction: Disturbances of proprioceptive regulation may underlay or contribute to motor deficits in Parkinson's Disease (PD). Increasing evidences demonstrate that pathophysiology of gait and postural problems in PD includes deficits in proprioceptive processing and integration. Muscle vibration provides proprioceptive inflow via primary muscle spindle endings. Vibratory stimulation has been shown to be able to provoke gait and postural changes in PD in different studies and with different modality of applications.

Objective: The aim of this study is to investigate the effects of the repetitive focal muscle vibration (rMV) on posture and kinetic/kinematic gait parameters PD.

Material and Methods: Twenty patients with PD on stable dopamine replacement medication were evaluated with gait analysis before, after treatment, one and 4 week later.
Spatio-temporal parameters and kinematics characteristics were evaluated. Patient were randomized into two groups: treated with rMV (study group SG) and placebo (control group CG). In the SG the rMV was applied simultaneously on the 2 legs close to the quadriceps tendon insertion and after on the paravertebral lumbar spine muscles. Mechanical stimulation was applied over 3 consecutive days and each application lasted 60 minutes. In the CG the vibrator was positioned close to zone but without touching the skin.

Results: The application of rMV shows a positive effect on the gait pattern, as for spatio-temporal parameters (Velocity and step length that were increased after treatment) and kinematics (tendency to normalization of pelvic tilt).

Conclusion: Our results suggest that rMV treatment may improve walking and stability in PD; more larger and controlled studies confirming this preliminary data are needed.

References

[1] De Nunzio A.M., Grasso M., Nardone A., Godi M., Schieppati M.; Alternate rhythmic vibratory stimulation of trunk muscles affects walking cadence and velocity in Parkinson's disease. Clin. Neurophysiol. 2010 Feb;121(2):240-7
[2] De Nunzio A.M., Nardone A., Picco D., Nilsson J., Schieppati M.; Alternate trains of postural muscle vibration promote cyclic body displacement in standing parkinsonian patients. Mov Disord. 2008 Nov 15;23(15):2186-93
[3] Abbruzzese G., Berardelli A.; Sensorimotor integration in movement disorders. Mov. Disord. 2003 Mar;18(3):231-40. Review
[4] Filippi G.M., Brunetti O., Botti F.M., Panichi R., Roscini M., Camerota F., Cesari M., Pettorossi V.E.; Improvement of stance control and muscle performance induced by focal muscle vibration in young-elderly women: a randomized controlled trial. Arch Phys Med Rehabil. 2009;90:2019-25

P36

Laboratorio Espressivo MoviMente (LEMM) as a rehabilitation strategy in Parkinson's disease patient: randomized trial as pilot study

Silvio Ferraiuolo[1], *F. Nardone*[1], *F. Camerota*[2], *F. Stocchi*[3], *P. Sale*[3], *M.F. De Pandis*[1]

[1]San Raffaele Cassino, Tosinvest Sanità, Cassino
[2]Physical Medicine and Rehabilitation Division, Umberto I Hospital, Sapienza University, Rome
[3]IRCCS San Raffaele Pisana, Tosinvest Sanità, Rome

Introduction: In Parkinson Disease (PD) the motor impairment is no more than an integration dysfunction between input, cognitive processing and output. The destruction of the dopamine circuits (those related to the posterior striatum in the first time and then those related to the anterior striatum in the second time) involves, in addition to the well-known "motor-disorders", a perceptual closure and a reduction of mood and motivational aspects, with consequent alteration of the formulation and execution of the motor act itself. The LEMM is a technique of new concept based on the principles of action observation and *mirror neurons* activations and on the own concepts of mimic method by Orazio Costa, theatrical biomechanics by Mejerchol'd and perezivanie by Stanislavskji.

Patients and Methods: For this purpose we ran a randomized, controlled and single-blinded study on 20 subjects affected by a moderate form of idiopathic PD. Ten patients were randomly assigned to LEMM, while the others underwent physiotherapy group, the most common treatment for PD rehabilitation. All patients were evaluated with:UPDRS; FAB; BDI; PDQ-39 administered before(T0) and after 4 weeks of treatment(T1). Both group carried a stable drug therapy and rehabilitation therapy golden-standard.

Results: Univariable analyses showed no significant differences between groups following intervention. However, analyses suggested that patients in the LEMMgroup improved more on mobility, mood and quality of life than patients in the control group. There were no adverse events and a level of adherence to therapy was observed.

Conclusion: These preliminary data suggest the potential usefulness of LEMM to improve motor and non-motor symtomps in PD patients. Further studies in larger sample and with a longer follow-up are needed to confirm our results.

P37

Effects of a short physical therapy program combined with transcranial direct current stimulation (tDCS) on freezing of gait in Parkinson's disease: preliminary data from a randomized, sham-controlled study

Massimo Cincotta[1], *F. Giovannelli*[1], *S. Cozzi*[2], *L. Antoniella*[2], *P. Vanni*[1], *A. Borgheresi*[1], *C. Piccini*[1], *L. Vannucchi*[2], *F. Pasquariello*[2], *G. Zaccara*[1], *S. Bandinelli*[3], *M.P. Viggiano*[4], *M. Baccini*[2]

[1]UO di Neurologia, Azienda Sanitaria di Firenze, Firenze
[2]Lab. Analisi del Movimento, UUOO Riabilitazione Funzionale, Azienda Sanitaria di Firenze, Firenze
[3]UO di Geriatria, Azienda Sanitaria di Firenze, Firenze
[4]Dipartimento di Psicologia, Università di Firenze, Firenze

Objective: The aim of this study was twofold: first, to evaluate the efficacy of a short physical therapy program on freezing of gait (FoG) in Parkinson's disease (PD) and second, to test whether tDCS may potentiate the effect of rehabilitation.

Methods: Nine PD patients with mild FoG attended 5 consecutive daily sessions (45-60 min) of physical therapy focused to learn strategies for overcoming FoG. Patients were randomized to receive sham or real anodal tDCS (2 mA, 20 min) of the leg motor cortex before each session. Kinematic variables were recorded at baseline, one (T1) and six (T2) weeks after intervention.

Results: An overall significant improvement of number of strides and time to turn during a standardized walking test was observed at T1 and T2 compared to the baseline. A trend towards a larger effect on these measures (T1 and T2 vs baseline) was seen in the 4 patients receiving real tDCS compared to the 5 subjects receiving sham stimulation.

Conclusion: Preliminary data may support the efficacy of this short physical therapy intervention in PD patients with mild FOG.
Completion of the study is necessary to interpret the current non-significant trend towards a potentiation of this effect by anodal tDCS.

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Specific physical therapy approach for Parkinson's disease axial deformities: a pilot study with 6 months follow-up

Vincenza Montemurro, E. Sinibaldi, M. Valente, V. De Petris, R. Scatozza, N. Vanacore, G. Monari, G. Meco

Centro Parkinson D.A.I. Neurologia e Psichiatria Policlinico Umberto I, Sapienza Università di Roma, Roma

Background: In advanced PD characteristic symptoms may be associated with postural deformities. Camptocormia and Pisa Syndrome are very disabling and poorly responsive to antiparkinsonian drugs. There are many researches on possible benefits of rehabilitation therapy, but few studies about specific rehabilitation approaches.

Objective: To evaluate the efficacy of a rehabilitation program (Progressive Modular Rebalancing of G. Monari with Proprioceptive Neuromuscolar Facilitation - RMP) on postural alterations and motor performance of Parkinson's Disease (PD) patients.

Matherial and Methods: To examine the effects of RMP program (individual 60-minute-sessions, 2- days-a-week for three months) on postural alterations and mobility of 14 PD patients with Camptocormia, and 4 PD patients with Pisa Syndrome.Patients were evaluated using the Unified Parkinson's Disease Rating Scale Non-motor Experiences and Motor Experiences of Daily Living (UPDRS I-II) and motor subscale (UPDRS-III), Webster Rating Scale (WRS) -Posture, Tinetti-Gait Scale, Protractor for Measuring degrees. Therapy was not changed during the three months of rehabilitation.

Results: After the treatment a significant improvement in motor performance by UPDRS-III (- 6.28 points, p = 0.001) and in Tinetti-Gait scale (-3.22 points, p = 0.001) were observed. A significant decrease in anterior trunk flexion (-18,91°; p=0,001), lateral trunk flexion (-16 °; p=0,001) and knee flexion (-13.8 °, p = 0.05) were also observed. These data confirm the significant improvement of the item 28 of the UPDRS-III (-1.17 points, p = 0.001) and WRS (-3.62 points, p = 0.001). Significant changes were not observed at 6-months follow-up in 14 PD patients, except an improvement in UPDRS I-II (-2,5 points, p = 0,039) and a worsening in TINETTI-gait scale (0 points, p=1,000) and in knee flexion (-5,61 °, p=0,142).

Conclusion: Our data suggest that significant improvements in postural deformities can be obtained through the rehabilitation program described. Further studies with a larger sample are necessary.

P39

Make your Parkinson's disease patients pedalling: effects of a novel forced exercise. A case report

G. Grazzi[1], *E. Bernardi*[1], *S. Uliari*[1], *G. Mazzoni*[1], *F. Leprotti*[2], *E. Groppo*[2], *Mauro Gentile*[2], *E. Cesnik*[2], *I. Casetta*[2], *G. Granieri*[2], *M. Manca*[3], *S. Zanuso*[4], *E. Granieri*[2]

[1]Centro Studi Biomedici Applicati allo Sport,Università di Ferrara, Ferrara
[2]Sezione di Clinica Neurologica, Dipartimento di Discipline Medico-Chirurgiche della Comunicazione e del Comportamento, Università di Ferrara, Ferrara
[3]Laboratorio Analisi del Cammino, UO di Medicina Riabilitativa, Azienda Ospedaliera Universitaria di Ferrara, Ferrara
[4]Technogym Scientific Research Manager

Introduction: Many studies showed beneficial effects of physical activity on brain health.
However the association between chronic neurodegenerative diseases and physical activity is not so well established, particularly for patients with Parkinson's Disease (PD) that often have difficulties managing physical exercise. An active-assisted tandem cycling exercise (Forced Exercise, FE) induced neuroprotective effects and improved motor and central nervous system functions in PD patients. Improvements have been associated with increased cortical/subcortical activation, while imaging data show that symptomatic relief induced by FE utilizes the same pathways of current medications. However, for practical reasons, the use of a tandem cycle is difficultly feasible from a clinical perspective (i.e. accessibility, requirement of a fit exercise partner). Therefore it's currently underway a study to evaluate effects on clinical functions and exercise of active-assisted exercise (AAE) on a new motor-driven cycle-ergometer (AC, Technogym®,Cesena,Italy).

Case description: A 68-year old male patient with a history of mild PD, hypertension, and dyslipidemia, performed a clinical evaluation and a cycle-ergometer cardio-pulmonary incremental test to the limit of tolerance at baseline, in order to assess cardiorespiratory fitness. Balance, mobility and motor control were assessed by the timed-up-and-go, the movement of center-of-gravity and the finger-tapping tests. During all testing and training sessions, patient was receiving habitual therapy as follow: pramipexole 2.1mg, ramipril 5mg, simvastatin 20mg, amlodipin 10mg. Twice a week for eight weeks the patient did one-hour supervised session on the AC. Each session included 3 phases: warm-up (10'), main-phase (40') and cool-down (10'). During the main-phase pedalling cadence was higher than usual (85-to-90 rpm). The degree of assistance on the AC was modulated to ensure an heart rate (HR) within the target range (90-100 bpm, ~70% of maximal, i.e. moderate intensity), and to obtain a work rate of ~60W. At the end of training, peak work rate during incremental exercise improved by 18%, while maximal HR and oxygen consumption remained unchanged.
Ventilatory anaerobic threshold and cycling efficiency improved by 13%, and 35% respectively. Balance, mobility and motor control improved by 36%, 4%, and 25% respectively.

Discussion: This case illustrates the potential benefits of a novel forced exercise as part of mild PD patients management. The association of this kind of treatment with usual care could improve motor and central nervous system functions of PD patients. Non pharmacological therapies for PD appear relevant and effective to improve parkinsonian symptoms and overall quality of life.

P40

Effect of lower limb end-effector robot-assisted therapy with body weight-support vs treadmill gait training in Parkinson patients

Patrizio Sale, D. Galafate, V. Lombardi, M. Casali, F. Stocchi

IRCCS San Raffaele Pisana, Roma

Objective: PD is characterized by a progressive decline of locomotor abilities of lower limb so that gait rehabilitation is an essential, but often frustrated, aim of the treatment. Recent studies demonstrated a major efficacy of physical rehabilitation therapy associated with treadmill training compared with physical therapy alone. The Aim of the study (Randomize Clinical Trial) is to validate the efficacy of a robotic system specific for lower limb (G-EO) compared with training on treadmill.

Setting: Gait analysis evaluation 3D-GA was conducted using the following equipment: a 12-camera optoelectronic system with passive markers (ELITE2002, BTS, Italy), to measure the kinematic of movement; 2 force platforms (Kistler, CH), to obtain the kinetic data of movement (i.e. ground reaction forces); 2 TV camera Video system (BTS,Italy) synchronized with the optoelectronic and force platform systems for videorecording. To evaluate the kinematics of each body segment, markers were positioned as described by Davis et al (Davis, 1991). Subjects were asked to walk barefoot at their own natural pace (self-selected and comfortable speed) along a (10 mlong) walkway where the two force platforms were placed. At least seven trials were collected for each subject in order to ensure the consistency of the data. All graphs obtained from GA were normalized as % of gait cycle and kinetic data were normalized for individual body weight. Using specific software (Smartanalyser, BTS, Italy) from these data some indices (time/distance parameters, angles joint values in specific gait cycle instant, peak values in ankle power graph) were calculated in order to quantify the gait pattern of participants involved in this study.

Participants: Diagnosis of idiopathic PD by UK Brain Bank criteria, with evidence of motor deficit in one lower limb, age between 18 and 79 years.

Interventions: If eligible, the patients were assigned to one of the two study arms (GEO o TREADMILL) by means of a computed randomization. Rehabilitation Treatment: twenty sessions of 45'.
Twenty cognitively intact participants with mild PD and gait disturbance underwent a lower limb rehabilitation consisting of a treatment cycle using the GE-O system device, according to individually tailored exercise scheduling. The practice included an add-on robot-assisted walking therapy at variable speeds for 40 min with a partial body weight support (BWS). All participants started with 30-40% BWS and an initial treadmill speed of1.5 km/hspeed were increased to a range of 2.2 to2.5 km/hbefore BWS were decreased. All the treatment consists of 20 sessions for the lower limbs, each lasting 40 minutes, 5 days a week for 4 weeks.
Ten subject underwent a lower limb rehabilitation consisting of a treatment cycle using the treadmill device according to individually tailored exercise scheduling. The practice included treadmill walking at variable speed for 40 minutes. All participants will start at an initial treadmill speed of1.5 km/h. Speed will be increased to a range of 2.2 to 2.5 km/h."

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P40 (*segue*)

Main Outcome Measures: At the beginning of the treatment and after 20 sessions, opto-cinematic analysis of gait and clinical specific scales (UDPRS, H&Y, Freezing Of Gait Questionnaires, PDQ-39 , The Six-Minute Walk Test e Ten Meter Walk Test) were delivered."

Results: Robot training was feasible, acceptable, safe, and the participants completed 100% of the prescribed training sessions. A statistically significant improvement in gait index was found in favour of the EG (T0 versus T1). In particular, the statistical analysis of primary outcome (gait speed) using the Friedman test showed statistically significant improvements for the EG ($p = 0,0195$). The statistical analysis performed by Friedman test of Step length left ($p = 0,0195$) and right ($p = 0,0195$) and Stride length left ($p = 0,0078$) and right ($p = 0,0195$) showed a significant statistical gain. No statistically significant improvements on the CG were found.

Conclusion: Robot training is a feasible and safe form of rehabilitative exercise for cognitively intact people with mild PD. This original approach can contribute to increase a short time lower limb motor recovery in idiopathic PD patients. The focus on the gait recovery is a further characteristic that makes this research relevant to clinical practice. On the whole, the simplicity of treatment, the lack of side effects, and the positive results from patients support the recommendation to extend the use of this treatment. Further investigation regarding the long-time effectiveness of robot training is warranted.

P41

Effect of lower limb end-effector robot-assisted therapy with body weight-support in progressive supranuclear palsy patients

Fabrizio Stocchi, D. Galafate, V. Lombardi, L. Vacca, P. Sale

IRCCS San Raffaele Pisana, Roma

Objective: Progressive supranuclear palsy (PSP) is a rare neurologic disorder primarily presenting with motor disturbances (e.g., postural instability, parkinsonism, slowing of vertical saccades) and is characterized by a progressive decline of locomotor abilities of lower limb so that gait rehabilitation. The Aim of the study is to validate the efficacy of a robotic system specific for lower limb (G-EO) on gait recovery in this.

Design: Observational study

Participants: Diagnosis of PSP Disease by the clinical criteria of the National Institute of Neurological Disorders and Stroke Society for PSP International Workshop, stable doses of Parkinson's medications for at least 8 weeks prior to study onset, and an endurance sufficient to stand at least 20 minutes.

Inclusion criteria: Evidence of motor deficit in one lower limb, age between 18 and 79 years, capability to walk, unassisted or with minimal assistance, for 25 feet.

Exclusion criteria: Association of neurological, orthopedic or cardiopulmonary pathologies. Psychiatric disorders reducing patient collaboration.

Interventions: If eligible, the patients were assigned to Robot assisted therapy.

Rehabilitation Treatment: Twenty sessions of 45’.

Five subjects underwent a lower limb rehabilitation consisting of a treatment cycle using the GE-O system device, according to individually tailored exercise scheduling. The practice included an add-on robot-assisted walking therapy at variable speeds for 45 min with a partial body weight support (BWS). All participants started with 30-40% BWS and an initial speed of1.5 km/hspeed were increased to a range of 2.2 to2.5 km/hbefore BWS were decreased. All the treatment consists of 20 sessions for the lower limbs, each lasting 45 minutes, 5 days a week for 4 weeks.

Main Outcome Measures: At the beginning of the treatment and after 20 sessions, Timed up and go test, 6 minutes walking test,10 meterswalking test, opto-cinematic analysis of gait and clinical specific scales (PSP rating scales) were delivered.

Results: Five patients (mean age 67,50±9,48 mean) had an H&Y median score of 3,0. The ones treated with G-EO showed a significative changes of Timed Up and Go 40,67±18,55 sec at T0 e 38,83±18,12 sec at T1, 6MWT 177,50±58,61 mat T0 e 181,83±53,21m at T1, 10mWT 0,61±0,22 aT0 e 0,54±0,21 aT1. Also the gait spatio-temporal parameter, the Barthel Index and FIM scores showed an improvement at discharge compared to admittance with an improvement.

Conclusion: Our preliminary results show that G-EO system treatment is well tolerated by all patients with improvements in outcomes measures and performance.

P42

Freezing of gait and theory of mind in Parkinson disease

Alessia Raffo[1], *G. Lagravinese*[1], *L. Avanzino*[2], *E. Pelosin*[1], *R. Marchese*[1], *G. Abbruzzese*[1]

[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno Infantili (DINOGMI), Università degli Studi di Genova, Genova
[2]Dipartimento di Medicina Sperimentale (DIMES), Istituto di Fisiologia Umana, Università degli Studi di Genova, Genova

Background: Theory of Mind (ToM) is the specific cognitive ability to understand other people's mental states. It appears that this ability involves frontal circuits in the brain and indeed ToM deficits are associated with worsening of prefrontal functions [3].
Several studies showed that ToM ability is affected in Parkinson (PD) [4]. Freezing of gait (FOG) is a frequent, disabling symptom of PD. A frontal lobe dysfunction or a disconnection between the frontal lobe and basal ganglia has been implicated in FOG [1].

Objective: To explore whether the ability to attribute a mental state to another person could be influenced by FOG in a group of PD patients.

Methods: 20 PD patients (10 FOG+; 10 FOG-) and 10 healthy age-matched subjects (HS) were enrolled in this study. Disease severity was evaluated with UPDRS III. Subjects were asked to complete the Reading the Mind in the Eyes Test (RMET), that is one of the most popular modality to assess the affective aspects of ToM ability [2]. The task comprised 18 photographs of the eyes region of a Caucasian actor and subjects were required to choose between 4 options, the adjective that better described the eyes expressions. Performance was evaluated by measuring the percentage of correct responses.

Results: On the RMET both PD/FOG+ and PD/FOG- performed significantly worse than HS ($p < 0.05$). Mean value of correct responses was 69%for HS, 37% for PD/FOG+ and 50%for PD/FOG-. Interestingly, PD/FOG+ performed significantly worse than PD/FOG- ($p= 0.03$).

Conclusion: Our preliminary data confirm previous results in the literature on difficulties involving the affective component of ToM in PD. Interestingly, our data suggest that FOG, that is related to frontal dysfunction, seems to affect the ability to attribute a mental state to another person.

References

[1] Amboni M, Cozzolino A, Longo K, Picillo M, Barone P, Freezing of gait and executive functions in patients with Parkinson's disease, Mov Disord. 2008 Feb 15;23(3):395-400
[2] Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I, The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism, J Child Psychol Psychiatry. 2001 Feb;42(2):241-51
[3] Pardini M, Emberti Gialloreti L, Mascolo M, Benassi F, Abate L, Guida S, Viani E, Dal Monte O, Schintu S, Krueger F, Cocito L, Isolated theory of mind deficits and risk for frontotemporal dementia: a longitudinal pilot study, J Neurol Neurosurg Psychiatry. 2012 Nov 8.
[4] Poletti M, Enrici I, Bonuccelli U, Adenzato M, Theory of Mind in Parkinson's disease, Behav Brain Res. 2011 Jun 1;219(2):342-50

P43

Psychological intervention group with Parkinson's disease patients and their caregivers

Fabiana Giada Radicati, M. Torti, L.Vacca, F. Stocchi

IRCCS San Raffaele Pisana, Roma

Background: The clinical course and psychological impact of Parkinson's disease (PD) for those affected but also for caregivers require a specialized group of professionals capable of dealing with various issues. It is essential to improve the quality of life and help people get benefits that go beyond those coming from drugs and learn to deal adequately and proactively with stress, disability and psychological limitations.

Objective: Promoting a better quality of life in people with PD and their caregivers through a psychological support group.

Materials and Methods: One group of 5 patients, 4 males and 1 female, with diagnosis of PD and 5 caregivers were enrolled into the study. The age ranged from 50 to 70 years and the age at the time of diagnosis ranged between 48 and 67 years. The project lasted 12 months; the group was meeting once a week for one hour and a half. Cognitive and psychological evaluation of PD patients were performed at baseline and at the end of the study through tests and individual meetings. Caregivers underwent psychological assessment through tests and individual meetings at baseline and at the end of the study.

Results: At the end of the study analysis of data showed a worsening especially in skill performance (excutive functions), a slight deterioration of depressive symptoms and quality of life. In caregivers we did not notice any statistically significant change.
Patients reported an improvement in quality of socialization as highlighted by strong cohesion of the group, and developed a greater awareness of disease. During the meetings, the participants were particularly interested and involved, as confirmed by the punctuality and by the regular attendance to the group by each of them.

Conclusion: This pilot study showed that a support group doesn't affect the classical PD symptoms. It acquires value and meaning as a source of support and it may improve the quality of life both in patients and caregivers if it is prolonged over time.

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Long-term rotigotine treatment in progressive supranuclear palsy

Fana Alemseged, T. Schirinzi, V. Pisani, G. Madeo, A. Pisani

Department of Neuroscience, University of Rome "Tor Vergata", Rome

Introduction: Progressive supranuclear palsy (PSP) is a rare neurologic disorder presenting with motor disturbances, cognitive deficits, psychiatric dysfunction, and low quality of life. No effective symptomatic, disease-modifying or neuroprotective therapy is currently available.

Objective: Preliminary observations made during our clinical practice suggested some interesting therapeutic results in PSP patients after administration of rotigotine, a non-ergolinic dopamine-agonist already available for Parkinson's disease. Hence, we performed a systematic and detailed evaluation of therapeutic response on PSP patients following a 42 weeks period of treatment with rotigotine.

Methods: We enrolled six subjects with a diagnosis of PSP, according to clinical consensus criteria, at Movement Disorders Center of Policlinico Tor Vergata, Rome. After titration of rotigotine transdermal patch up to 6mg/24h, patients were clinically monitored during a 42 weeks period. The study included five visits, in which Montreal Cognitive Assessment, UPDRS scale (section II-III), PSP rating scale (PSPRS), Activity of daily living (ADCS-ADL) and Caregiver distress status (CDS) were systematically collected.

Results: Our preliminary results suggest that UPDRS-III and PSPRS scores seem to remain stable during treatment. Interestingly, while ocular motility worsened, limbs agility seemed to improve, as supported by the scores at UPDRS-II subscale. Cognitive performances remain unchanged even if it is unclear whether this finding depends on treatment or disease course.
Notably, caregiver perception of clinical worsening measured by ADCS-ADL and CDS scales, resulted to be more pronounced than medically perceived.

Conclusion: In our study we performed a clinical evaluation of the therapeutic response to rotigotine in a limited number of PSP patients. According to our observations, administration of rotigotine might be considered useful in maintaining stable motor capabilities and giving patients a perception of improved health status.

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Stimulation of subthalamic nuclei restores a near normal planning strategy in Parkinson's patients

Giovanni Mirabella[1,2], *S. Iaconelli*[1], *N. Modugno*[1], *G. Giannini*[1], *F. Lena*[1], *G. Cantore*[1]

[1]IRCCS Neuromed, Pozzilli (IS)
[2]Department of Physiology and Pharmacology "V. Erspamer", La Sapienza University, Rome

A fundamental function of the motor system is to gather key information from the environment in order to implement behavioral strategies appropriate to the context. Although several lines of evidence indicate that Parkinson's disease affects the ability to modify behavior according to task requirements, it is currently unknown whether deep brain stimulation (DBS) of the subthalamic nucleus (STN) affects context-related planning.
To explore this issue, we asked 12 Parkinson's patients with bilateral STN DBS and 13 healthy subjects to execute similar arm reaching movements in two different paradigms: go-only and countermanding tasks. In the former task patients had to perform speeded reaching movements to a peripheral target. In contrast, in the countermanding task participants had to perform the same reaches unless an infrequent and unpredictable stop-signal was shown during the reaction time (RT) indicating that they should withhold the ongoing action. We compared the performance of Parkinson's patients in different DBS conditions. We found that patients with both DBS-ON behaved similarly to healthy subjects, in that RTs of no-stop trial increased while movement times (MTs) decreased with respect to those of go-only-trials. However, when both DBS were off, both RTs and MTs were longer in no-stop trials than in go-only trials. These findings indicate that bilateral DBS of STN can partially restore the appropriate motor strategy according to the given cognitive contexts.

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Clinical course and pharmacologic treatment in aromatic L-Aminoacid decarboxylase deficiency

Mario Mastrangelo[1], *Cl. Carducci*[2], *A. Polizzi*[3], *Ca. Carducci*[2], *V. Sofia*[4], *R. Barone*[5], *M. Zappia*[3], *M. Ruggeri*[6], *V. Leuzzi*[1]

[1]Dipartimento di Pediatria e Neuropsichiatria Infantile, Sapienza Università di Roma, Roma
[2]Dipartimento di Medicina Sperimentale, Sapienza Università di Roma, Roma
[3] Dipartimento di Scienze Neurologiche, Consiglio Nazionale delle Ricerche, Catania
[4] Dipartimento di Neurologia, Università di Catania, Catania
[5] Divisione di Neuropsichiatria Infantile, Università di Catania, Catania
[6] Dipartimento di Scienze dell' Educazione, Università di Catania, Catania

Background: Aromatic L-Aminoacid decarboxylase (AADC) deficiency (OMIM#608643) is a disorder of biogenic amine metabolism presenting with developmental delay, hypotonia, dystonia, oculogyric crisis, orthostatic hypotension, sleep disturbances, sweating, temperature instability, reduced HVA and 5HIAA and increased 3 OMD in CSF and hyperprolactinaemia.

Case reports:
Family 1 included a 12 years old and a 18 years old boy carrying the homozygous mutation c.1543C>T; p.SER250PHE in exon 7 of AADC gene. The elder brother had an absent motor and language development. He had also a severe dystonia, hypo/bradikinesia and oculogyric crises. The younger brother had a delayed psychomotor and mental development, diurnal fluctuation of tonus, muscle strength, hypokinesia, limbs and trunk dystonia, choreic movements, dystonic dysarthria, orthostatic hypotension, sleep disturbances, asthenia, akinesia, oculogyric crises and on-off phenomena. Different drugs were used since early infancy with poor benefits in both brothers. At the age of 11 years the association of transdermal rotigotine, tranylcypromine and folinic acid resulted in an improvement of gross motor functions in the younger brother but not in the elder one who had started treatments later.
Prolactinaemia was normalized in both brothers.
Family 2 included two never previously treated adult sisters, aging respectively 22 and 32 years, carryng a compound heterozygosis for two novel pathogenic gene mutations on *AADC* gene [p.P35FS (c.105delC) and p.F237S (c.710 T>C). Their clinical history included early onset oculogyric crisis, ptosis, mild intellectual disability, dysarthria, muscular hypotonia and hyposthenia, orthostatic hypotension, bradykinesia, oculogyric crisis, multifocal spontaneous myoclonic jerks, and mild derangement of postural reactions. The association of rotigotine, pyridoxine, escitalopram resulted in a relevant improvement of gross motor disorders and in the normalization of blood prolactin.

Conclusion: Present cases are relevant portraits of natural history of AADC deficiency and suggest that its gross motor symptoms are responsive to pharmacologic treatment independently by the age of the patients.

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Diabetes in Parkinson disease is associated with cognitive worsening and postural instability

Martina Giuntini, F. Baldacci, A. Vergallo, R. Ceravolo, U. Bonuccelli

Department of Clinical and Experimental Medicine, Neurological Unit, University of Pisa, Pisa

Background: Several experimental and epidemiological studies have investigated the association between Parkinson's disease (PD) and diabetes mellitus type II (DM) with conflicting results. However, few data are available regarding the possible clinical differences between PD patients with DM (PD-DM) and PD patients without DM (PD-nDM).

Objective: Aim of our study was to investigate differences in motor and non motor features between PD-DM patients in respect to PD-nDM patients.

Methods: We performed a case-control study. From the cohort of drug naïve PD patients referred to our institute over a 3-year period, we identified 50 patients with a diagnosis of diabetes before PD onset and 50 PD subjects without diabetes, matched for sex, age, disease duration and severity. All patients were free from cardiovascular disease. All subjects performed SPECT with FP-CIT to assess nigrostriatal function. Motor symptoms have been evaluated by UPDRS II/III and the cognitive state by MMSE, at baseline and after 3 years follow-up. Chi²test with continuity correction or Fisher's exact test was used for categorical variables and Mann-Whitney U for continuous variables.

Results: The group of PD-DM patients had a significant higher postural scores (items "posture", "postural instability" and "gait") when compared to the group PD-nDM, both at baseline (1,66 ± 1,41 vs 1,09 ± 0,81; p= 0,015) and follow-up (2,31 ± 1,73 vs 1,58 ± 0,97; p=0.033). Significant lower MMSE scores were found only at follow-up (26,5 ± 3,08 vs 27,4 ± 3,20; p=0,019). In the comparison between the two groups no significant differences were found as regards the dopaminergic nigrostriatal denervation.

Conclusion: Onset of diabetes before the onset of PD might be associated with more severe postural and cognitive impairment. We suggest that PD-DM could have a different clinical phenotype respect to PD-nDM patients, however larger studies taking into account even the cerebrovascular burden are warranted.

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Psychogenic movement disorders in a tertiary referral center: incidence and role of disease modelling

Maria Superbo, R. Pellicciari, D. Liuzzi, P.V. Mancino, A.F. Gigante, G. Defazio

Department of Basic Medical Sciences, Neurosciences and Sensory Organs, "Aldo Moro" University of Bari, Bari

Background: Psychogenic movement disorders (PMDs) have become increasingly recognized. Incongruency with organic movement disorders (OMD), inconsistency over time, sudden onset and rapid progression of symptoms and history of other functional symptoms are features suggestive of PMD. Recently, it was also suggested that a positive history of exposure to a disease modelling supports the diagnosis of PMD. However it remains unclear whether this feature is independent of or relates to other basic psychogenic features.

Objective: Aim of this study were: (i) to assess the incidence of PMDs in a tertiary referral center; (ii) to confirm the association of PMD with disease modelling; and (iii) to see whether disease modelling relates to other basic features of PMD.

Methods: PMDs were diagnosed according to Fahn and Williams criteria. For the purposes of the incidence study, we reviewed the clinical records of all patients seen for the first time at our movement disorders center during 2012. For the purposes of the case-control study, we administered a standardized questionnaire assessing relevant demographic/clinical features to 33 PMD patients and 50 OMD patients.

Results: During 2012, 19/149 (14%) first referred patients were diagnosed with a PMD. Tremor, ataxia and dystonia were the most frequent misdiagnosis. Case-control comparison yielded a lower age at PMD onset (41+19 vs. 52+11, p=0.0002), and greater frequency of sudden onset of symptoms (13/33 vs. 0/50, p ‹ 0.001) and disease modelling (23/33 vs. 18/50, p=0.003) in the PMD group. Disease modelling was associated with lower age at PMD onset (37+16 vs. 52+21 years, p=0.02). The association remained significant even after adjusting for age, sex, sudden onset of symptoms, and presence of psychiatric disturbances on multivariable linear regression analysis.

Conclusion: PMDs can be frequently encountered in the practice of a movement disorder clinic. Disease modelling may contribute to the pathophysiology of PMD, particularly in younger patients.

References

[1] Fahn S., Williams D., Psychogenic dystonia, Adv Neurol 1988; 50: 431-455
[2] Shill H., Gerber P., Evaluation of Clinical Diagnostic Criteria for Psychogenic Movement Disorders, Movement Disorders 2006 21 (08), 1163-1168
[3] Kranick S, Ekanayake V, Martinez V, Ameli R, Hallett M, Voon V. Psychopathology and psychogenic movement disorders, Movement Disorders 2011 26 (10): 1844-50

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Pseudoathetosis - dystonia in a 76 years old woman with a severe cervical malformation

Carlo Rossi[1], *R. Galli*[1], *U. Bonuccelli*[2]

[1]UOC Neurofisiopatologia - ASL5, Pisa
[2]Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa

Movement disorders secondary to intrinsic spinal cord or to nerve roots diseases have been infrequently described.
A 76-year-old woman was admitted to our service to investigate difficulties in walking and movement disorder at upper arms started 2 years before. On neurological examination she presented postural instability, axial rigidity, right proximal arm weakness, reduced deep sensation at both arms, dysmetria in upper limbs, hyperreflexia. Romberg's sign was present.
At the inspection a scapulohumeral joint and arms muscle atrophy and a great toe extension with plantar flexion of remaining toes (striatal foot) were observed. The movement disorder was characterized by a dystonic posture at both arms, jerky movements that resemble myoclonus and, finally, constant slow movements at the fingers (athetosis), expecially at the left side, that worsened with eyes closure. She underwent to a Brain Magnetic Resonance Imaging without any remarkable results, an electromyography with a chronic neurogenic damage in all upper limbs muscles. Cervical MRI highlighted a congenital severe cervical spine malformation with an inversion of the physiological curvature on C5-C6 and a severe sthenosis C3-C5.
Dystonia, athetosis and myoclonus are rarely associated to several cervical cord lesions such as tumors, demyelination, trauma and syrinx formation. In these cases the site and nature of pathogenetic mechanisms underlying the abnormal movements are still not clear and might include abnormal sensory input, altered processing at the spinal interneurone circuits, primary disorder of spinal motoneurones or at a supraspinal level.

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Two cases of focal trapezius muscle atrophy after repeated injection of botulinum toxin-A

Pamela Latino[1], *F.E. Pontieri*[1,2], *M. Giovannelli*[1]

[1]Movement Disorder Unit, Sant'Andrea Hospital, Rome
[2]Department of Neuroscience, Mental Health and Sensory Systems, Sapienza University, Rome

Introduction: Cervical dystonia represents the most common focal dystonia. Botulinum toxin (BoNT) injection is the first-line therapy for its treatment.

Objective: We report two cases with selective atrophy of the descending portio of the trapezius following repaeted injection of BoNT for cervical dystonia. In both cases, right laterocollis with consensual abnormal contraction of trapezius, splenius-capitus and levator-scapulae were present.

Method: The two patients were evaluated with clinical examination, electromyographic exam and ultrasound of the affected muscle and controlateral/ispilateral shoulder girdle muscles.
The evaluations were performed at baseline (time when the symptoms have occurred) and repeated after two months.

Results: The clinical evaluation at baseline revealed a focal atrophy of the right trapezius and a consensual weakness of elevation/adduction of the shoulder. Strength and muscle mass of the left trapezius was normal as well as that of the other muscles of the shoulder girdle bilaterally. The electromyography at baseline showed the presence of myopathic damage on the right trapezius muscle; the ultrasound revealed a trapezius hyperechogenicity in the right side, a reduction in the thickness of the muscle.
Instrumental exams of the remaining girdle muscles on both sides were normal. Two months after the last BoNT injection, weakness was completely resolved at clinical examination. The electromyography and ultrasound showed an incomplete recovery of muscle atrophy.

Conclusion: The patients presented a visible trapezius muscle atrophy following BoNT-A injection. The cause of atrophy may be due to the effects of the toxin on the neuromuscular junction. In these cases, the atrophy developed in the most lateral region of the muscle, where little soft tissue exists. Both patients presented a transient and reversible atrophy of trapezius.
The gap between persistent muscular atrophy and regained function remains unclear. Local plasticity, including increased activation of neighboring neuromuscular junctions not inactivated by BoNt, may play a role.

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Normal pressure hydrocephalus presenting as behavioural-variant frontotemporal dementia: a case report

Vincenzo Moschella[1], *M.C. Massimetti*[1], *A. Di Chirico*[2], *C. Anile*[2], *A. Stefanini*[1]

[1]Neurological Service, San Camillo de Lellis General Hospital. AUSL di Rieti, Rieti
[2]Neurosurgical Department, Azienda Ospedaliera S. Maria, Terni

Background: Idiopathic Normal Pressure Hydrocephalus (iNPH) is characterized by a varying combination and degrees of gait disturbance, urinary incontinence and dementia and is caused by enlargement of cerebral ventricles. It can mimic neurodegenerative or psychiatric disorders.

Aims: To describe a case of behavioural-variant Frontotemporal Dementia-like syndrome due to iNPH.

Methods and Results: In 2008, a diabetic and dyslipidaemic 57-years old man, after been laid off, started complaining of apathy, aboulia and diurnal somnolence. A diagnosis of depression of mood was done. Subsequently, decline in social manner, impairment in regulation of personal conduct, emotional blunting, behaviour and speech change insidiously arose and slowly progressed. General and neurological examination were normal and no urinary difficulties were present. A clinical diagnosis of behavioural-variant Frontotemporal Dementia was done and patient started assuming galantamine extended release until 16mg per day. In 2012 patient presented to our ambulatory referring a moderate worsening of behavioural and cognitive problems, unclear gait difficulties and urinary incontinence.
Neurological examination revealed slow, wide-based and shuffling gait with mild disequilibrium. Neuropsychological assessment revealed deficits in attention, executive function, memory and visuospatial functions. Cerebral MRI showed ventriculomegaly, thinning and upward elevation of corpus callosum and periventricular hyperintensities in FLAIR-sequences. Diagnosis of iNPH was made (iNPH-grading scale was 8) and supported by cine phase-contrast MRI and CSF hydrodynamics, evaluated by intraventricular infusion test. Ventriculo-peritoneal shunt was performed. A six months follow-up revealed significant improvement of gait and urinary disturbances and improvement of global neuropsychological profile, especially executive functions (iNPH-grading scale was 3).

Conclusion: Since idiopathic normal pressure hydrocephalus is one of the rare form of potentially reversible dementia, clinicians should keep in mind it can display a pure psychiatric or cognitive onset and such remain for a long time. Complete neurological, neuropsychological, neuroradiological and neurosurgical analysis is essential to avoid a late diagnosis.

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Sleep motor activity in parkinsonisms at disease onset: a possible marker for differential diagnosis. *BO-ProPark* study preliminary results

Maria Alessandria, *G. Calandra-Buonaura*, *A. Cecere*, *L. Sambati*, *R. Terlizzi*, *P. Guaraldi*, *F. Provini*, *P. Cortelli*

IRCCS Istituto delle Scienze Neurologiche and Department of BioMedical and NeuroMotor Sciences, Bologna University, Bologna

Introduction: The differential diagnosis of each form of parkinsonism at onset may be difficult for clinicians because the evolution of different features may vary widely and clinical and instrumental markers predictive for a specific syndrome are still lacking.

Objective: To describe the possible diagnostic value of videopolysomnographic (VPSG) motor findings in patients with recent-onset parkinsonism.

Patients: 41 consecutive patients with parkinsonian features and disease duration up to 3 years were included in the *BO-ProPark* study (Bologna-motor and non motor Prospective study on Parkinsonisms at onset). Each patient was evaluated twice, at baseline and 16 months later. The diagnosis was made at the second evaluation following international diagnostic criteria. Patients were diagnosed as: Parkinson disease (PD, 24 patients), PD plus (PD with cognitive impairment and/or dysautonomia) (5 patients), parkinsonian syndrome (PS, 9 patients). 3 patients dropped out.

Methods: All patients underwent a full night VPSG, scored by a neurologist blinded to the diagnosis. We compared the VPSG data between two groups of patients: PD versus PS patients.

Results: All patients showed reduced sleep efficiency. RBD episodes were recorded in 4 patients (2/24 PD; 2/9 PS). 15/24 PD patients and 6/9 PS patients presented REM without atonia (RWA). The mean percentage of time with enhanced tonic and/or phasic muscle EMG activity during REM sleep was higher in PS than in PD patients (10,95±21,49% vs 24,97±42,13). The PLMS index was ≥ 10 in 23 patients (15/24 PD; 8/9 PS). 7 patients (3/24 PD; 4/9 PS) showed excessive fragmentary myoclonus (EFM). PS patients showed whole body jerks during sleep more frequently than PD patients.

Conclusion: Our preliminary data suggest that impaired sleep motor control is more frequent at disease onset in patients with PS compared to PD patients. More data are needed to establish whether these features may have a diagnostic value in the differential diagnosis of parkinsonisms.

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A cavernous angioma with thalamic localization: a cause of hemicorea/kemiballismus associated with mutation in PDCD10/CCM3 gene

Antonella Antenora[1], *L. Bilo*[1], *S. Peluso*[1], *P. Ruosi*[1], *M. Quarantelli*[2], *G. De Michele*[1]

[1]Department of Neurological Sciences, Federico II University, Naples
[2]Biostructure and Bioimaging Institute, National Research Council, Naples

Background: Cerebral cavernous malformations (CCMs) are vascular abnormalities characterized by enlarged capillary cavities without intervening brain parenchyma. In familial cases (20%) three genes have been identified: KRIT1/CCM1, MGC4607/CCM2, and PDCD10/CCM3. Symptomatic individuals typically present cerebral hemorrhages, focal neurological deficits, and headaches. Extra-cerebral vascular malformations, most commonly retinal and cutaneous, are detected only in a small portion of patients.

Case report: A 33-old-man came to our observation complaining of sporadic proximal and distal rapid involuntary movements of the right arm. Similar movements arose abruptly during childhood, and completely disappeared after few months. At 25 years he was diagnosed with an idiopathic thrombocytopenia. Familial history was negative for neurological diseases.
Physical examination showed dysphonia, due to right vocal cord paralysis, and multiple hemangiomas, some with overlying hyperkeratosis, confirmed as angiokeratomas on skin biopsy. Brain MRI showed multiple cerebral angiomas mainly located in the subcortical and periventricular white matter of both cerebral hemispheres but also in the left thalamus. A contrast-enhanced neck and mediastinal CT scan was negative. Molecular analysis revealed a heterozygous nonsense mutation (c.103C/T; Arg35X) in the PDCD10 gene.

Conclusion: Right side dyskinesias of our patient may be described as choreic/ballic movements, which may be an occasional complication of different vascular disorders affecting the contralateral basal ganglia, their connections, or both. Therefore, a cavernous angioma with thalamic localization may be an unusual cause of hemicorea/hemiballismus. Vocal cord palsy may be rarely caused by a brainstem cavernoma, but brain MRI of our patient did not evidence brainstem lesions. However, we excluded lesions of the recurrent laryngeal nerve.
We suspect that the associated thrombocytopenia might be due to platelet trapping into the multiple cerebral and cutaneous angiomas. It should be emphasized that the presence of multiple CCMs, even more if associated with cutaneous angiomas, requires molecular genetic analysis, also in patients without positive familiar history.

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Hereditary spastic paraparesis 11 (SPG11)-associated parkinsonian symptoms and sapropterin responsiveness

Andrea Celato[1], *B. Tavazzi*[2], *F.M. Santorelli*[3], *E. Bertini*[4], *Cl. Carducci*[5], *V. Leuzzi*[1]

[1]Dipartimento di Pediatria e Neuropsichiatria Infantile, Sapienza Università di Roma, Roma
[2]Dipartimento di Diagnostica e Medicina di Laboratorio, Policlinico Gemelli, Roma
[3]Laboratorio di Medicina Molecolare, IRCCS, Stella Maris, Pisa
[4]Dipartimento di Neuroscienze, IRCCS, Ospedale Pediatrico Bambino Gesù, Roma
[5]Dipartimento di Medicina Sperimentale, Sapienza Università di Roma, Roma

Background: Hereditary spastic paraparesis due to mutations of *KIAA1840* gene is the most frequent form of complicated autosomal recessive paraplegias. SPG11 phenotype includes: thin corpus callosum, peripheral neuropathy and cognitive impairment. *KIAA1840* gene encodes for spatacsin, a protein whose function is unknown. To date nine SPG11 patients were described presenting parkinsonian-like symptoms. Six were treated with L-DOPA-carbidopa and 2 with L-DOPA-carbidopa together with sapropterin. CSF analysis was performed in four patients and revealed, in three cases, low homovanillic acid and biopterin levels. CSF biogenic amines, retested after treatment, normalized under sapropterin in two patients.

Methods: We report on a 28 years-old boy affected by spastic paraparesis from the age of sixteen. Brain MRI showed thin corpus callosum and *KIAA1840* gene sequencing confirmed the diagnosis (compound heterozygosity: c.1951C>T; c.6898_6899delCT). Later in the disease the patient developed bradykinesia, hypomimia and mild cognitive impairment. A phenylalanine oral loading test was performed showing a profile overlapping those observed in Segawa disease with a delayed clearance of Phe and a marked increase of Phe levels and Phe/Tyr ratio. Urine Neopterin was low while biopterin was normal. CSF analysis detected low HVA and BH4 levels. The patient started sapropterin (10 mg/Kg/day for ten days and 20 mg/kg/day for further 10 days). Unified Parkinson Disease Rating Scale, timed get-up and go test and video recordings were used to check the results of the treatment.

Results: A marked improvement of gait speedness as well as bradykinesia was detected with lower dosage of sapropterin with an additional improvement under 20 mg/kg/day.

Discussion: In SPG11 patients presenting extrapiramidal symptoms, a trial with sapropterin should be considered. CSF analysis probably may discriminate SPG11 patients responsive vs nonresponsive to BH4. Our case support previous reports concerning sapropterin effectiveness. Further studies are required to better understand the relationship between spatacsin and neurotransmitter disorders.

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Respiratory disorders in Parkinson's disease

Antongiulio Gallina, N. Tambasco, G. Muzi, N. Murgia, E. Sacchini, E. Marsili, E. Luchetti, E. Brahimi, F. Ripandelli, P. Nigro, S. Simoni, A. Rossi, P. Calabresi

Clinica Neurologica, Azienda Ospedaliera-Università di Perugia, Perugia

Respiratory disorders (RD) represent one of the less investigated non-motor symptoms in Parkinson's disease (PD). They are distinguishable in restrictive alterations, most likely caused by reduced chest wall compliance, due to the rigidity of the respiratory muscles and obstructive disorders, with more uncertain pathogenesis. The patients may complain of shortness of breath, decreased cough reflex, abnormal rhythm of breathing and respiratory drug-induced dyskinesias.

Objective: The aim of our study was to identify both clinical and sub-clinical respiratory alterations and to assess the effect of therapy with L-Dopa on the respiratory dynamic in PD.

Methods: We selected 20 patients with PD (H&Y scale 1-3), aged between 40 and 85, responsive to dopaminergic stimulation (L-Dopa, apomorphine), non-smoking and not affected by other respiratory diseases. A simple spirometry and an UPDRS assessment, both in "OFF" phase and after L-Dopa administration, were performed.
We also used modified 0-10 Borg scale in assessing the degree of dyspnea in both OFF and ON states. The statistical analysis of the test was performed with SPSS 13.0 statistical software, the influence of categorical variables through the non-parametric test of Mann Whitney U, and numeric variables with the Spearman rank correlation.

Results: The spirometric data showed indices of respiratory function in the lower limits compared to normal subjects. More interestingly, the subjective valutation indicated that about 50% of PD patients have a significant degree of dyspnea (Borg scale between 1 and 4). After intake of dopaminergic therapy, there is an improvement in subjective respiratory discomfort.

Conclusion: Our data suggest that the dopaminergic dysfunction in PD plays an important role in the regulation of respiration both at local and central level, causing respiratory discomfort and that dopamine replacement therapy can reverse this condition.

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Fatigue and correlations with other non-motor symptoms in Parkinson's disease patients

Paolo Solla, A. Cannas, C.S. Mulas, L. Meleddu, S. Argiolas, F. Marrosu

Clinica Neurologica, Università di Cagliari, Cagliari

Background: Among non-motor symptoms observed in Parkinson's disease (PD) patients, fatigue represents an insidious disturbance. Although common, its correlations with motor and other non-motor symptoms of PD are still largely unclear.

Objective: To assess fatigue in PD patients studying the possible correlation with motor and other non-motor symptoms.

Methods: Eighty-one Sardinian PD patients were included in the study. Motor impairment and disability were assessed using the Modified Hoehn & Yahr (HY) staging and the Unified PD Rating Scale (UPDRS) part-III. Presence of motor complications was evaluated by using UPRDS part-IV. The PD Fatigue Scale (PFS) and the Fatigue Severity Scale (FSS) scale were used to measure fatigue.
Non-motor symptoms were assessed with the Non-Motor Symptoms Scale (NMSS). The correlation between fatigue and other variables was studied and possible predictors of severity of fatigue were determined with different models of multiple regression analyses.

Results: Fatigue was significant higher in female patients compared to males. Among motor symptoms, significant correlations between fatigue and HY stage, UPDRS-III score, bradykinesia and postural UPDRS-III subscores were found. Among non-motor symptoms, significant correlations between fatigue and fainting, daytime sleep, difficulty falling asleep, lost interest in surroundings, apathy, sadness, anhedony, swallowing, and the NMSS score were found. NMSS score, HY stage and gender were the significant predictors of fatigue. Among non-motor symptoms, the strongest predictors in the PFS model were apathy ($p<.000$), anxiety ($p<.016$), and daytime sleep ($p<.015$), while those revealed in the FSS model were anhedony ($p<.004$) and difficulty falling asleep ($p<.014$).

Discussion: To our knowledge, this is the first paper which correlated the specific assessment of fatigue with a holistic scale of non-motor symptoms such as the NMSS. Fatigue was a frequent non-motor symptom in parkinsonian patients, affecting 40% to 50% of the population with a significant higher severity in female patients. Although a definite correlation of severity of fatigue with the motor impairment was detected, a more significant increase in severity of fatigue related to severity of non-motor symptoms (mainly affective and sleep disorders) was observed.

Conclusion: The better individuation of factors underlying fatigue, also with the systematic administration of holistic evaluation scales such as the NMSS, may improve the current strategies used in the treatment of this disabling condition.

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Note out of tune in the score of Parkinson’s disease

Kai Stephan Paulus, G. Carpentras, M. Meloni, E. De Natale, P. Galistu, V. Agnetti

Centro dei Disordini del Movimento, UO Clinica Neurologica, AOU, Sassari

Parkinson's disease (PD) is defined as a neurodegenerative pathology with a progressive evolution. There are motor signs such as rest tremor, rigidity, bradikinesia and postural instability, and nonmotor signs with pain, and psychiatric manifestations with anxiety, depression, insomnia and psychosis. These last signs are more common in later disease stages and in the off-states. Nonmotor signs are known to be as disabling as the motor symptoms. Commonly a solid dopaminergic therapy with motor improvement can ameliorate the nonmotor signs, but in some cases the association of antidepressants and/or anxiolitics can be useful; sometimes antipsychotics are necessary.
We present the case of a 57-years old man, married, upper education level, with a 15-years history of parkinsonian syndrome and typical right body onset of extrapyramidal symptoms, without genetic evidence. In the last decade no clinical disease progression was evident, but anxiety and insomnia increased without any benefit of BDZ, SSRI's and SNRI's. Psychological evaluation established absence of conversion or somatization. Our hypothesis of two different pathologies is based on the observation that before PD onset the patient was used to be precise and correct, also obsessed by the research of perfection at work and at home. Now, with the disease and the physical dysability, he is no more able to be what he was used to be before. This situation probably do create an enormous tension which could be the origin of his anxiety. Our man is convinced that his PD is the reason of the failure of his life's goal. In conclusion, in this case anxiety seems not to be a consequence of PD but, on the contrary, PD seems to be overloaded by anxiety which could explain the poor treatment response of both PD and anxiety. So, there have to be made two diagnoses which need two different treatments with possible benefits. In our opinion, take in mind this possibility could be useful in terms of healths economy and disease management.

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Hemiparkinsonism due to frontal meningioma with normal striatum PET[^{18}F]DOPA uptake

Rosa De Micco[1], *A. Tessitore*[1], *M. Cirillo*[1], *A. Giordano*[1,2], *G. Tedeschi*[1]

[1]Department of Neurological Sciences, Second University of Naples, Naples
[2]Neurological Institute for Diagnosis and Care "Hermitage Capodimonte", Naples

Materials and Methods: Case report: a 46-year-old female was referred to our Movement Disorders outpatient clinic for the occurrence of slowness of movements in the right upper limb and writing difficulties during the last three months. The patient was also complaining of a depressed mood. Her familial history was unremarkable.

Results: Neurological examination revealed hypomimia; right hemiparkinsonism with bradykinesia and slight cogwheel rigidity (more pronounced in the upper limb); upper limbs postural and hypostenic tremor (right>left); symmetrical brisk deep tendon reflexes; no Babinski sign; dysgraphia. She denied constipation, hyposmia and sleep difficulties. A brain MRI demonstrated a large left frontal meningioma causing significant compression on the left striatum, middle and superior frontal gyri, precentral and postcentral gyri, cingulate gyrus; PET[^{18}F]Dopa uptake was normal in the bilateral striatum but the tumor showed a high and inhomogeneous tracer uptake. PET [^{18}F]FDG revealed a focal hypometabolism of the right striatum and a decreased tracer binding of the tumor.

Conclusion: The diagnosis of idiopathic Parkinson's Disease (PD) is, at present, based mostly on the clinical findings. However, PET[^{18}F]Dopa detects a tracer binding reduction in the striatum controlateral to the parkinsonian syndrome in patients with PD; conversely, PET[^{18}F]FDG usually shows spared striatum glucose metabolism. In our patient [^{18}F]Dopa uptake was normal and the glucose metabolism was decreased in the left striatum, suggesting that the tumor may have impaired striatal synaptic function without an involvement of the presynaptic side. Thus, we believe that the parkinsonism might be due to compression of the frontal gyri, which encompass primary motor area (M1) and supplementary motor area (SMA), with their striatal connections, causing an hypometabolism of these structures. Moreover, our case underlines the importance of performing structural neuromaging in any case of parkinsonism, especially in those with some clinical "red flag".

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Health comorbidities in geriatric patients with Parkinson's disease

Chiara Fossati, *L. Vacca*, *P. Grassini*, *M. Torti*, *F. Stocchi*

IRCCS San Raffaele Pisana, Roma

Introduction: Parkinson's disease (PD) is a neurodegenerative disease with increasing incidence. In geriatric patients this chronic and progressive disease is frequently associated with the presence of several comorbidities which contribute to establish a clinical condition of frailty, raising the risk of functional disability and adverse outcomes.

Objective: The aim of our study was to investigate the presence of health comorbidities in 100 PD geriatric patients by a multidimensional geriatric assessment and to examine their influence on quality of life, functional abilities, cognition and eventually on disease course.

Materials and Method: We included in our study 100 outpatients ≥ 65 years old with a diagnosis of PD according to UK Brain Bank criteria. Health comorbidities were assessed by Cumulative illness Rating Scale for Geriatrics (CIRS-G) that measures the chronic medical illness burden while considering their severity in 14 items representing individual body systems. PD was not rated as a comorbid disease. Cognition was assessed by Mini-Mental State Examination, health-realted quality of life (HRQoL) by EQ-5D, functional ability by ADL and IADL scales.

Results: Our sample was made of 45% males and 55% females. Mean disease duration was 7,35±5.38 years; Hoen and Yahr stage ranged from 1 to 4. Mean number of drugs used for treating PD was 2.08±1.06, and 55.4% of our patients were treated with ≥ 2 drugs for comorbid diseases. Preliminary data showed that all our patients had some comorbidities, with 90.5% of them with at least one moderate/severe comorbid disease. Most of patients with worse scores in EQ-5D resulted to have 2 or more moderate/severe health comorbidities.

Conclusion: Our results highlight the great importance of a global health assessment in PD patients. We suppose that the large prevalence of coexisting disorders could influence HRQoL of geriatric parkinsonian patients. Health comorbidities may also have an impact on disase course, prognosis, outcome of treatment and costs.

P60

Autoimmune neurological syndromes presenting with acute movement disorders: our experience

Simone Gallerini, M. Bartalucci, L. Giovanditti, S. Pieri, K. Plewnia, C. Scarpini, R. Marconi

UO Neurologia, Ospedale Misericordia, Grosseto

Autoimmune syndromes of CNS are a heterogenous group of diseases that can occur as a postinfectious, paraneoplastic or idiopatic process. The onset can be acute ore subacute with rapid progressive disease evolution. The clinical features are extremely variable ranging from cognitive or psychiatric symptoms and seizures to movement disorders. In some of these patients movement disorders are predominant with hypercinetic or hypocinetic pattern. We describe eight patients admitted in the Neurological Unit of Grosseto from Emergency Department with complex movement disorders or neuropsychiatric syndromes and an acute or subacute onset. An extensive diagnostic program was done. It included extensive blood exams, brain and spinal MRI, EEG, neurophysiological studies, CSF examination, chest, abdomen and pelvis CT and PET to reveal associated tumors, detection of antineuronal antibodies. Finally an alternative diagnosis was excluded and an autommiune basis was considered: 1) opsoclonus-mioclonus-ataxia from gastric cancer 2) antiphospholipid-related ataxia 3) autoimmune myoclonus and delirium (two patients) 4) anti-GAD associated ataxia and delirium 5) anti-YO associated ataxia 6) antiphospholipid-related chorea 7) acute parkinsonism and dementia from CAA-related inflammation. The patients were treated with corticosteroids or intravenous immunoglobulin with improvement in four of them.
The differential diagnosis and investigation approach of acute-onset movement disorders are discussed.

P61

Clinical, cognitive and behavioural correlates of white matter damage in progressive supranuclear palsy

Sebastiano Galantucci[1], *F. Agosta*[1], *M. Svetel*[3], *M.J. Lukić*[3], *M. Copetti*[4], *K. Davidovic*[1,3], *A. Tomić*[3], *E.G. Spinelli*[1,2], *G. Comi*[2], *V.S. Kostić*[3], *M. Filippi*[1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[3]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[4]Biostatistics Unit, IRCCS-Ospedale Casa Sollievo della Sofferenza, Foggia

Introduction: Progressive supranuclear palsy (PSP) is characterized by an extensive white matter (WM) pathology. Diffusion tensor (DT) magnetic resonance imaging (MRI) provides information on the organization and integrity of brain WM tracts. DT MRI-derived measures might be useful as markers of disease severity and clinical symptoms in PSP.

Aims: To assess the relationship between WM tract abnormalities and clinical, cognitive, and behavioural changes in patients with PSP using diffusion tensor DT MRI tractography and Random Forest (RF) analysis.

Methods: Thirty-seven patients with PSP and 34 matched healthy controls underwent a MRI scan and a standardized clinical testing to evaluate the severity of physical disability, cognitive impairment and apathy. The contribution of WM tract damage to motor, cognitive and behavioural disturbances was assessed using RF.

Results: Relative to healthy controls, PSP patients showed diffusivity abnormalities of the corpus callosum and superior cerebellar peduncle (SCP) bilaterally. Alterations were also observed in the cingulum and uncinate fasciculus bilaterally. DT MRI metrics of the corpus callosum and SCP were the best predictors of global disease severity scale scores. The global cognitive test scores were associated with DT MRI abnormalities of the corpus callosum, superior longitudinal (SLF), uncinate, and inferior longitudinal (ILF) fasciculi bilaterally. DT MRI metrics of the corpus callosum, right SLF and ILF, and left uncinate were the best predictors of executive dysfunction. Apathy severity was related to the damage to the corpus callosum, right SLF and uncinate fasciculus.

Conclusion: PSP patients harbor structural connectivity abnormalities in the cerebellum and in a distributed neural network, involving commissural and association WM tracts of all cerebral lobes. Our findings indicate that WM tract damage contributes to the motor, cognitive and behavioural deficits in PSP.

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P62

Subcortical and deep cortical brain atrophy in *GRN*-related pathology

Enrico Premi[1], *V. Garibotto*[2], *S. Gazzina*[1], *A. Formenti*[1], *S. Archetti*[3], *R. Gasparotti*[4], *B. Borroni*[1], *A. Padovani*[1]

[1]Centre for Ageing Brain and Neurodegenerative Disorders, Neurology Unit, University of Brescia, Brescia
[2]Department of Medical Imaging, Geneva University Hospital, Geneva, Switzerland
[3]III Laboratory of Analyses, Brescia Hospital, Brescia
[4]Neuroradiology Unit, University of Brescia, Brescia

Background: Parkinsonism is often associated with cognitive and behavioural symptoms in Frontotemporal dementia (FTD), but its pathogenesis has been largely neglected. In genetic inherited disorder, such as in *Granulin* (GRN) mutations, Parkinsonism is an early sign and it is more common than in sporadic FTD. The precise pattern of atrophy in *GRN* related Frontotemporal dementia has not been fully defined yet. Aim of the present work was to study gray matter (GM) volume changes in subcortical and deep cortical regions in the *Granulin*-related FTD.

Method: Thirty-three FTD patients, i.e. 13 carriers of *GRN* mutation (*GRN*+) and 20 non-carriers (*GRN*)-, and 12 healthy controls (HC) were consecutively enrolled. Each subject underwent MRI scan for 1) an automated whole brain voxelwise analysis by Voxel Based Morphometry and Statistical Parametric Mapping to study the GM differences in cortical and subcortical regions; 2) a Region of interest (ROI) approach using a probabilistic *a- priori* atlas of subcortical regions (caudate, putamen, thalamus and amygdala) to assess the regional differences in GM volumes.

Results: GRN+ showed greater damage of frontotemporal regions as compared *GRN*- group. Overall, FTD patients had greater bilateral GM atrophy in the caudate and in the thalamus, bilaterally, even considering total grey matter atrophy; the other subcortical regions resulted spared. Damage in these subcortical and deep cortical regions was greater in FTD-*GRN*+ than in FTD-*GRN*- patients.

Discussion: This study confirms that subcortical and deep cortical involvement is a key-feature of FTD, more pronounced in monogenic *GRN* disease.
Caudate damage in *GRN*+ patients may explain the dopa non-responsive parkinsonism always associated since the early disease stages.

P63

Genetic screening for R1441C and G2019S *LRRK2* mutations in parkinsonian patients from Campania

Anna De Rosa[1], *A. Guacci*[1], *R. Carbone*[1], *A. Giordano*[2], *F. Salemi*[2], *R. De Micco*[2], *M. Picillo*[1], *P. Barone*[3], *M. Moccia*[1], *A. Tessitore*[2], *M.T. Pellecchia*[3], *M. Lieto*[1], *S. Peluso*[1], *G. De Michele*[1], *C. Criscuolo*[1]

[1]Department of Neurological Sciences, Federico II University, Naples
[2]Movement Disorders Center, Department of Neurology, Second University of Naples, Naples
[3]Center for Neurodegenerative Diseases, University of Salerno, Salerno

Introduction: PARK8 is the most common mendelian form of Parkinson's Disease (PD) being responsible for 5% of familial and 1-2% of sporadic PD. It is due to mutations in the *leucine-rich repeat kinase 2 (LRRK2)* gene and G2019S is considered the most common mutation in the Caucasian population.

Objective: Here we assess the G2019S and R1441C/H/G mutations frequency in a large number of PD patients recruited from Campania.

Methods: We studied 513 (311 M and 202 F) unrelated PD patients. At the time of screening, mean age (± SD) of the patients was 64.7 (±10.7) years, and disease onset was 58.12 (± 11.13) years. Twenty-one cases reported parental consanguinity, 337 patients presented a sporadic disease, whereas 176 reported a familial history of PD or tremor. Three hundred and eighty-one cases originated from Naples. Mutations were checked by restriction endonuclease digestion and the mutations were confirmed by direct sequencing in both directions.

Results: Thirteen patients (8 M and 5 F) carried a heterozygous R1441C mutation. The prevalence of the R1441C mutation was 2.5% in the whole sample, 5% in the familial group, and 1.2% in the sporadic cases. The G2019S mutation was identified in 4 patients (3 M and 1 F), with an overall prevalence of 0.7%, 1.7% in the familial group, and 0.3%. in the sporadic PD patients. All carriers originated from the province of Naples. R1441H/G mutations were not found.

Discussion: R1441C and G2019S mutations may be considered a common cause of PD in Campania, especially in the province of Naples and in the familial cases, where the overall prevalence was about 7%. We confirm that R1441C is much more frequent in Campania than G2019S. Region-specific mutation prevalence data should be taken into account for a sensitive and cost-effective molecular diagnosis and counseling of patients with PD.

P64

Imaging of the substantia nigra at 7T in the diagnosis of Parkinson's Disease

M. Cosottini[1,2], *Daniela Frosini*[3], *I. Pesaresi*[2], *M. Costagli*[1], *R. Ceravolo*[3], *U. Bonuccelli*[3], *M. Tosetti*[1,4]

[1]IMAGO7 Foundation, Pisa
[2]Neuroradiology Unit, Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa
[3]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa
[4]Stella Maris Scientific Institute, Pisa

Background: The morphological correlate of dopaminergic degeneration in Parkinson's Disease (PD) is the neuronal loss in the pars compacta of the substantia nigra (SN).
Standard neuroimaging techniques fail in defining anatomy of the SN and have a marginal role in the diagnosis of PD.

Purpose: Our purpose is to evaluate the anatomy of SN in healthy subjects (HS) and the diagnostic accuracy of Ultra High Field (UHF) MRI targeted imaging of the SN in the diagnosis of PD.

Patients and Methods: 21 HS and 17 PD patients were enrolled in this UHF MRI protocol approved by the Italian Ministry of Health and by the local ethics committee. 3D gradient-recalled multi-echo (SWAN) images were acquired for both groups. The images from 8 HS were used to define the normal UHF MRI appearance of SN. Changes in the normal anatomy of the SN were used to calculate the sensitivity and specificity of UHF MRI in diagnosing PD by comparing 13 HS (Mean age: 54.7years) and 17 PD patients (Mean age: 56.0years, Mean PD-duration: 27.2 months, Mean UPDRSIII:17.8) by two independent raters. Intra- and inter-raters agreement were calculated.

Results: SWAN UHF MRI of the SN allows to define a three layered organization of the SN at the lower level and an hyperintense ventro-lateral spot at the intermediate level. The loss of hyperintense intermediate layer and of the lateral hyperintense spot of the SN has a sensitivity of 100% for both raters and specificity of 100% and 92.3% for the two neuroradiologists respectively. Intra- and inter-raters agreement are both excellent.

Conclusion: UHF MRI allows high resolution characterization of the SN and its fine local organization into three layers presumably corresponding to pars reticulata, pars compacta-ventralis and pars compacta-dorsalis.
By the use of SWAN images it is possible to accurately differentiate HS from PD patients.

P65

Dyskinesia detection and monitoring by a single inertial sensor in patients with Parkinson's Disease

Giovanna Lopane[1,2], *S. Mellone*[3], *L. Chiari*[3,4], *P. Cortelli*[1,2], *S. Mohamed*[1,2], *C. Candela*[1,2], *M. Contin*[1,2]

[1]IRCCS - Institute of Neurological Sciences of Bologna, Bologna
[2]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna
[3]Biomedical Engineering Unit, Department of Electrical, Electronic, and Information Engineering, University of Bologna, Bologna
[4]Health Sciences and Technologies - Interdepartmental Center for Industrial Research, University of Bologna, Bologna

Introduction: Levodopa (LD) induced dyskinesia (LID) is a recognized adverse effect of long-term treatment in Parkinson's disease (PD). In the current clinical practice its assessment is based on semi-quantitative scales administered by physicians.

Aims: To assess the feasibility, clinical validity and patient usability of a single inertial sensor (SIS) in LID detection and monitoring in PD patients.

Methods: Forty-six PD patients (28 males; 63±9 yrs; Hoehn-Yahr 1-3) on chronic LD underwent kinetic-dynamic monitoring based on the intake of their usual morning LD dose followed by serial measurements of motor and postural performances and dyskinesia rating (Clinical Dyskinesia Rating Scale-CDRS).
Eighteen de novo PD patients (13 males; 59±9 yrs; Hoehn-Yahr 1-2) and 18 healthy controls (CTRL; 9 males; 60±11 yrs) performed the same motor and posturography serial tests. Posturography included Quiet Standing (QS) trials, with Eyes Open (EO), Eyes Closed (EC) and Eyes Open Dual Task (EODT). Functional tests were instrumented using a SIS embedding a triaxial accelerometer and gyroscope (McRoberts Dynaport Hybrid) worn on the lower back.

Results: Sex distribution and age were comparable among patients and CTRL. Thirteen patients out of 48 on chronic LD were identified as dyskinetic according to the CDRS. A subset of 10 instrumental parameters was selected for clinical applications (Intraclass Correlation Coefficients, ICC ? 0.7 in EO, EC, and EODT condition). Best results in detecting dyskinesias during QS trials were obtained considering mean angular velocity in medio-lateral direction in EODT condition (97.5% of overall accuracy). Time to onset, offset and intensity of limb and axial dyskinesias assessed by CDRS vs SIS showed a good intrasubject correlation (Spearman Rank Correlation coefficient = 0.79, $p<0.01$; 0.95, $p<0.001$; 0.76, $p<0.001$, respectively). SIS specifity was low in case of very mild involuntary movements affecting distal body segments (face, feet).

Conclusion: A wearable SIS may be a reliable and clinically applicable tool to detect and monitor dyskinesias in PD patients.

P66

Cannabinoid CB_1 receptor dysfunction alters synaptic activity and plasticity in PINK1-deficient mice

Tommaso Schirinzi[1], *G. Madeo*[1], *F. Alemseged*[1], *M. Maltese*[1], *G. Martella*[1], *J. Shen*[2], *E.M. Valente*[3], *F. Fezza*[4,5], *M. Maccarrone*[5,6], *A. Pisani*[1]

[1]Department of System Medicine, University of Rome "Tor Vergata", Laboratory of Neurophysiology and Synaptic Plasticity, Santa Lucia Foundation I.R.C.C.S., Rome
[2]Center for Neurologic Diseases, Brigham & Women's Hospital, Program in Neuroscience, Harvard Medical School, Boston, U.S.A.
[3]IRCCS Casa Sollievo della Sofferenza, Mendel Laboratory, San Giovanni Rotondo, and Dept. of Medicine and Surgery, University of Salerno, Salerno
[4]Department of Experimental Medicine & Surgery University of Rome "Tor Vergata", Rome
[5]European Center for Brain Research (CERC), Santa Lucia Foundation, Rome
[6]Center of Integrated Research, Campus Bio-Medico University of Rome, Rome

Introduction: Loss-of-function in PTEN-induced kinase 1 (PINK1) gene is causative of an autosomal recessive form of Parkinson's disease (PD). Both the decrease in dopamine (DA) release and the impairment of corticostriatal synaptic plasticity in PINK1 knockout mice ($PINK1^{-/-}$) suggest a critical role for PINK1 in striatal circuit function. Growing evidence supports a close interplay between the endocannabinoid (eCB) and dopaminergic systems both in the modulation of striatal function and regulation of motor behavior.

Objective: In the present work we investigated the interaction between eCB and dopaminergic signalings underlying disruption of striatal synaptic plasticity in $PINK1^{-/-}$ mice.

Methods: By a multidisciplinary approach we characterized CB_1-signaling within the striatum of $PINK1^{-/-}$ mice and their respective littermates. We performed an electrophysiological characterization of striatal synaptic activity by using patch clamp and conventional recordings of striatal medium spiny neurons (MSNs) from corticostriatal slice. Recordings were paralleled by biochemical measurements of the two main endogenous cannabinoids, 2-arachidonylglycerol (2-AG) and anandamide (AEA).

Results: Despite normal levels of 2-AG and AEA, we found a significant impairment of CB_1 receptor-mediated responses. As compared to controls, where a presynaptic inhibition was recorded, CB_1 receptor agonists failed to modulate both spontaneous and evoked synaptic activity in $PINK1^{-/-}$ mice, at all concentrations. Physiologic CB_1-dependent responses were restored after either *in vitro* or chronic treatment with drugs able to restore a normal dopaminergic tone.

Conclusion: Our findings suggest a selective dysfunction of CB_1-signaling underlying the impairment of dopamine-dependent synaptic activity and the loss of synaptic plasticity in $PINK^{-/-}$ mice. The rescue of a physiologic CB_1-response, after modulation of dopaminergic tone, supports the notion of a dynamic interaction between eCB and dopaminergic systems.
Our work provides further clues to the understanding of mechanisms behind the dysfunction of basal ganglia circuitry underlying pathophysiology of PD.

P67

Functional connectivity of the basal ganglia circuit in early Parkinson's disease: a resting-state fMRI study

Francesca Caso[1], *F. Agosta*[1], *A. Inuggi*[1], *I. Stankovic*[3], *I. Petrovic*[3], *G. Comi*[2], *V.S. Kostic*[3], *M. Filippi*[1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[3]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: In PD, the dopamine depletion leads to an abnormal modulation of basal ganglia (BG)-thalamocortical circuit.

Objective: To evaluate the functional connectivity (FC) of the BG circuit in early, levodopa treated (t-PD) and drug-naïve (n-PD) PD patients.

Methods: 44 t-PD and 25 n-PD patients, and 27 healthy controls (HC) were studied. Since PD patients showed lateralized parkinsonian features, images from 24 patients with left (L)-sided symptoms were left-right (R)-flipped. FC analysis from resting-state fMRI was performed using BG bilaterally as seed regions of interest. FC differences were investigated among groups. In PD, the correlation between FC and motor performance was assessed ($p < 0.05$ FWE).

Results: In n-PD vs. HC: L-("affected") and R-("unaffected") putamen and caudate were hyperconnected with the contralateral counterparts; L-thalamus was hypoconnected with ipsilateral prefrontal and insular cortices and R-cerebellum, while R-thalamus was hyperconnected with the controlateral. In t-PD vs. HC: R-caudate was hyperconnected with R-temporal regions and hypoconnected with R-pallidus and bilateral-(B) thalamus; L-pallidus was hyperconnected with L-temporo/parietal/occipital regions; L-thalamus was hypoconnected with L-insula and hyperconnected with B-sensorimotor/visual cortices. In both groups vs. HC, L-caudate was hypoconnected with L-prefrontal cortex. In n-PD vs. t-PD, we detected hyperconnectivity between: L and R-caudate; R-putamen and R-insula and orbitofrontal cortex; L and R-thalami. Compared with t-PD, n-PD showed hypoconnectivity between R-caudate and R-parietoccipital cortex. We found positive correlations between UPDRS III and FC between: R-pallidus and R-putamen in n-PD and L/R putamen and R-thalamus in t-PD with B-temporo/parieto/occipital cortex; R-caudate with L-sensorimotor cortex, L-insula, and B-precuneus in t-PD.

Conclusion: Abnormal connectivity within the BG circuit was found in early PD patients with significant differences between n-PD and t-PD. These findings support the evidence of a modulation of the BG-thalamocortical circuit by levodopa in PD.

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P68

Resting state functional connectivity in patients with focal dystonia

Federica Agosta[1], *A. Inuggi*[1], *L. Sarro*[1,2], *A. Tomić*[3], *M. Svetel*[3], *N. Kresojević*[3], *G. Comi*[2], *V.S. Kostić*[3], *M. Filippi*[1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[3]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: Neuroimaging and electrophysiological studies have shown patterns of locally altered activity within the sensorimotor network of patients with focal dystonia.

Objective: To investigate the functional connectivity of the sensorimotor, default mode (DMN) and bilateral frontoparietal networks in patients with focal dystonia using resting state (RS) fMRI.

Methods: Fifty patients with focal dystonia and 36 healthy controls were studied. Focal dystonia group included 17 patients with blepharospasm, 15 patients by spastic torticollis and 18 patients with writer's cramp. RS fMRI data were analyzed using a model free (MELODIC) approach in FSL ($p < 0.05$ FWE corrected).

Results: Compared with controls, patients with blepharospasm showed an increased functional connectivity of the sensorimotor network in the supplementary motor area bilaterally and left primary sensorimotor cortex, frontal eye field, and superior parietal lobule.
Blepharospasm showed no RS fMRI changes in the frontoparietal network. Patients with writer's cramp showed a decreased functional connectivity of the bilateral superior parietal gyri within the frontoparietal networks and posterior cingulate cortex within the DMN, while they did not show altered functional connectivity of the sensorimotor network. No RS fMRI abnormalities were detected in patients with spastic torticollis.

Conclusion: This study showed specific patterns of altered functional connectivity in patients with focal dystonia. Blepharospasm was associated with an increased functional connectivity of regions of the sensorimotor network consistent with motor and visuospatial integration of stimuli. On the contrary, writer's cramp patients showed a disconnection of regions involved in somatosensory guidance of hand movements. These findings add novel elements to the pathophysiological substrates of these conditions.

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P69

Mesocortical dopaminergic dysfunction in Parkinson's disease-depression: evidence from a ^{123}I-FP-CIT-SPECT investigation

Elisa Unti[1], *D. Frosini*[1], *C. Del Gamba*[1], *E. Fiasconaro*[2], *D. Volterrani*[2], *U. Bonuccelli*[1], *R. Ceravolo*[1]

1 Department of Experimental and Clinical Medicine, Neurological Clinic, University of Pisa, Pisa
2 Department of Nuclear Medicine, University of Pisa, Pisa

Introduction: Pathogenesis of depression in Parkinson's Disease (PD) is not fully understood although neurochemical structural changes have been suggested. Both striatal and extra-striatal dopaminergic deficits could play a major role although results on striatal dopamine transporter (DAT) density are conflicting.

Objective: To assess with an exploratory approach, without an a priori hypothesis the striatal and extrastriatal DAT availability by using SPM on ^{123}I-FP-CIT-SPECT images in a population of PD patients and depression (PD-d), compared to PD patients without depression (PD-nd).

Methods: We evaluated retrospectively the baseline FP-CIT-SPECT of 40 consecutive de novo PD patients; among then 11 had a diagnosis of depression (DSM IV criteria) assessed by Beck Depression Inventory (BDI) (Mean age at SPECT scan 66.8 ys ± 5.4; Mean disease duration 1.0 ys ± 0.7; UPDRS III at SPECT scan 15.7 ± 5.3; BDI 16.8 ± 3.8), the remaining 29 had no depression (Mean age at SPECT scan 68.3 ys ± 7.1; Mean disease duration 1.2 ys ± 1.5; UPDRS III at SPECT scan 15.6 ± 7.0; BDI 2.5 ± 2.1). SPM2 and VOI analysis were then used for group comparisons and correlations.

Results: The two groups were comparable in all clinical and demographical parameters except for BDI score higher in PD-d group ($p < 0.01$).
A cluster, with statistically significant ($p < 0.05$) lower binding of FP-CIT in PD-d with respect to PD-nd patients was found in right cingulate cortex, persistent after correction for age, disease severity and duration. When cingulate VOI radiotracer uptake was correlated with BDI scores in the whole group, an inverse correlation was observed (r -0.367, $p < 0.01$).

Conclusion: Our data indicate no differences in striatal dopaminergic denervation in PD-d and PD-nd, however a significant association between depression and cingulate dopaminergic denervation was observed, confirming the dopaminergic hypothesis of PD-depression.

P70

A longitudinal study of sensorimotor cortical plasticity and intracortical inhibition in early Parkinson's disease

Matteo Bologna[1], *M. Kojović*[2,3], *P. Kassavetis*[2], *I. Pareés*[2], *I. Rubio-Agusti*[2], *A. Berardelli*[1,4], *M.J. Edwards*[2], *J.C. Rothwell*[2], *K.P. Bhatia*[2]

[1]Neuromed Institute (IRCCS), Pozzilli (IS)
[2]Sobell Department of Motor Neuroscience & Movement Disorders, UCL, Institute of Neurology, The National Hospital for Neurology & Neurosurgery, London, U.K.
[3]Department of Neurology, University of Ljubljana, Slovenia
[4]Department of Neurology and Psychiatry, Sapienza University of Rome, Rome

We have recently described a functional reorganisation of primary motor cortex in early, clinically asymmetric patients with Parkinson's disease: less affected hemisphere had increased long-term potentiation (LTP)-like sensorimotor cortical plasticity and normal intracortical inhibition. In contrast, the more affected hemisphere had reduced plasticity and reduced intracortical inhibition. It however remained unsolved whether these functional changes are compensatory or maladaptive. Thus, the present study was designed to assess the relationship between the longitudinal changes in electrophysiological and clinical measures of early Parkinson's disease patients. Our hypothesis was that enhanced cortical plasticity on the less affected side reflects a process of compensation. We therefore predicted a positive association between changes in motor cortex plasticity and changes in measures of disease severity over time. Twelve patients with clinically asymmetric idiopathic PD underwent serial TMS experiments including baseline, 6 month and 12 month follow-up measurements. At each time point, patients were tested in separate sessions over both hemispheres, corresponding to clinically more and less affected sides. We measured motor thresholds, input-output curves, short interval intracortical inhibition, intracortical facilitation and cortical silent period and sensorimotor cortical plasticity by using excitatory paired associative stimulation protocol (PAS25). Disease severity was assessed clinically (UPDRS-III scale). We found no difference in resting and active motor thresholds between sides and no longitudinal changes of these. IO curve was steeper on the more affected side and this interhemispheric difference remained constant through the period of follow up. SICI was reduced on the more affected side and preserved on the less affected side and these asymmetries also persisted at 1 year. On the contrary, initially reduced CSP on the more affected side increased over time, resulting in side- to- side equalisation of CSP after 1 year. A decrease in interhemispheric difference in CSP was associated with increase in disease severity scores, suggesting that initially shorter CSP on more affected side was a compensatory change. Importantly, the interhemispheric difference in sensorimotor cortical plasticity detected at baseline, and defined by increased plasticity on the less affected side and decreased plasticity on the more affected side, was still present after 1 year. There was a positive association between change in PAS interhemispheric ratio and change in UPDRS-III scores, showing that decrease in PAS response was related to progression of motor symptoms. We conclude that enhanced cortical plasticity in early PD may represent a compensatory change.

P71

Modulation of cortical excitability by high-frequency deep rTMS with H-coil in Parkinson's disease

Mario Fichera[1,2], *F. Spagnolo*[1,2], *E. Houdayer*[1], *R. Chieffo*[1,2], *D. Dalla Libera*[1,2], *L. Straffi*[1], *E. Coppi*[1,2], *A. Nuara*[1,2], *L. Ferrari*[1,2], *G. Di Maggio*[1,2], *M. Bianco*[1,2], *S. Velikova*[1], *A. Zangen*[3], *G. Comi*[1,2], *M.A. Volonté*[1], *L. Leocani*[1]

[1]Institute of Experimental Neurology and Neurological Department, Scientific Institute Hospital San Raffaele, Milan
[2]Vita-Salute University, Milan
[3]Neuroscience Laboratory, Ben-Gurion University of the Negev, Israel

Introduction: Cortical excitability, resulting from widespread involvement of cortical-subcortical loops, is often altered in Parkinson's Disease (PD) and can be considered not only as a marker of the disorder, but also as an objective measure for potential treatments. H-coils, allowing deeper and wider magnetic fields compared to traditional coils, may be of potential advantage for application in PD.

Objective: To evaluate safety and clinical-neurophysiological effects of repetitive Deep Transcranial Magnetic Stimulation (rdTMS) in PD, using the novel H-coil.

Patients and Methods: 14 PD-patients underwent 12 sessions 10 Hz-DTMS during a 4 weeks-period. rdTMS was applied over primary motor area opposite to their most affected side (W-M1) and over the prefrontal cortices, bilaterally. Clinical assessment (UPDRSIII; timed-tests including arm/foot tapping-AT/FT) and neurophysiological evaluation (Resting Motor Threshold-RMT, input-output curves-IO, Cortical Silent Period-CSP, intracortical inhibition-ICI/facilitation-ICF) were performed for worse (WS) and less affected (BS) sides. Patients were evaluated OFF therapy at baseline (Pre) and before the last rdTMS session (Post).

Results: No adverse events were reported. We found significant clinical improvements in UPDRSIII (41.9±9.4 vs. 31.4±7.9; $p<0.001$), lateralized scores ($p<0.001$ for both sides) and timed-test ($p<0.05$ for AT and FT in both sides). Neurophysiological measures disclosed modifications in M1 excitability only in the worse hemisphere. RMT lowered from 36.5±6.7 to 34.3±6.4 ($p=0.04$), MEP amplitude (at 120% RMT) increased ($p=0.04$) and CSP shortened ($p=0.05$). No significant changes were observed for IO curves and for ICF and ICI.

Conclusion: Despite the lack of blindness, deep TMS appears as a safe and promising new therapeutic perspective for non-invasive stimulation in PD. Our results show that rdTMS improves clinical symptomatology and induces neurophysiological changes in cortical excitability.

P72

Dopamine and its metabolites in Parkinson's and Alzheimer's disease CSF

Enrica Olivola[1], *P. Imbriani*[1], *M. Stampanoni Bassi*[1], *A. Martorana*[1], *M. Pierantozzi*[1,2], *A. Stefani*[1,2]

[1]Department of Neuroscience, University of Rome ‘‘Tor Vergata’’, Rome
[2]Santa Lucia Foundation, I.R.C.C.S., Rome

Introduction: In Parkinson’s disease (PD), the possibility to detect specific alterations in the cerebrospinal fluid content of dopamine (DA) and its metabolites is questioned. Further, recent evidence supports that an altered dopaminergic transmission occurs also in Alzheimer’s disease (AD).

Objective: To investigate DA and its major metabolites (DOPAC and HVA) concentration in cerebrospinal fluid (CSF) in PD and AD to verify whether the dopaminergic imbalance may 1) correlate with PD stages and 2) represent a convergent mechanism leading to neurodegeneration.

Methods: 26 subjects with PD according to the UK PD Society Brain Bank criteria (supported by asymmetry of the dopaminergic deficit in 123-I-FP-CIT-SPECT), 12 patients with probable AD, based on NINCDS-ADRDA criteria and 14 age-matched control subjects underwent lumbar puncture between 8 and 9 AM after 3 days withdrawal of possible dopaminergic or anticholinergic treatment. CSF levels of monoamines were determined by HPLC Monoamines AnalyzerTM .

Results: CSF DA concentration, in PD patients, is significantly reduced compared to controls only when considering stage 2-2,5 according to Hoehn & Yahr (0,09 nM vs 0,19; p=0,04) whilst no significant difference highlight stage 1 (in agreement with Goldstein et al., 2012).
DOPAC and HVA concentration, instead, are significantly lower in most of PD patients, suggesting early impairment of presynaptic machinery. AD patients showed a mean CSF DA content (0,17 nM) similar to control, although a surprising low concentration was detectable in specific cases.

Conclusion: These findings support the contention by which CSF concentrations of DA (and major metabolites) may correlate with disease progression and motor performance. The limited sample of demented subjects impedes further comments (but it is possible that DA alterations highlight rapidly progressive dementia or dementia complicated by early hallucinosis). If validated on larger cohort, this approach might be utilized to verify the potential neuro-protective capabilities of new therapeutic agents.

P73

Age should be considered for midbrain measures using magnetic resonance imaging morphometry analysis in Parkinson's disease

Calogero Edoardo Cicero, A. Nicoletti, G. Mostile, T. Cavallaro, E. Bruno, V. Dibilio, A. Luca, G. Sciacca, L. Raciti, D. Contrafatto, M. Zappia

Department GF Ingrassia, Section of Neurosciences, University of Catania, Catania

Background: Morphometry analysis of midbrain area combined with other specific brainstem regions measurements using conventional magnetic resonance imaging (MRI) has been extensively used to differentiate Parkinson's disease (PD) from atypical parkinsonisms.
However, few studies have systematically analyzed possible clinical predictors of such instrumental measures in PD.

Objective: To investigate clinical and radiological predictors of selected brain MRI measurements in PD patients.

Methods: We retrospectively selected clinical and radiological data of N = 102 PD patients diagnosed according to the Gelb's diagnostic criteria. (age: 63.3 ± 10.4 years; age at onset: 58.3 ± 10.6 years) who performed a standardized brain MRI during their clinical admission.
Analysis of selected brain structures morphometry included midbrain and pons area as well as middle and superior cerebellar peduncle. A multivariate analysis was performed using linear regression analysis.

Results: MRI midbrain area negatively correlated with age ($r = -0.413$, $p < 0.001$) while morphometric measures of selected brain structures directly correlated with midbrain area. A multivariate regression linear model was obtained setting midbrain area as dependent variable. Based on multivariate analysis, a 0.8 mm2 decrease per year in midbrain area was expected.

Conclusion: MRI midbrain area measurements in PD may depend on age and diffuse brain morphometric changes. Morphometric measures of midbrain area should require correction factors for PD patients with old age and diffuse brain atrophy.

P74

A multicentre, randomised, open-label, comparative phase 4 trial to assess changes in dementia diagnostic category and diagnostic confidence after DaTSCAN imaging in subjects with an uncertain diagnosis of dementia with Lewy bodies (possible DLB)

Roberto Ceravolo[1], *D. Volterrani*[2], *B. Paghera*[3], *G. Di Santo*[4], *L. Kiferle*[1], *A. Alberici*[5], *M. Banica*[6], *A. Padovani*[7], *G. Pizzolato*[6], *U. Bonuccelli*[1]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa
[2]Nuclear Medicine Unit, University of Pisa, Pisa
[3]Nuclear Medicine Unit, AO Spedali Civili di Brescia, Brescia
[4]Nuclear Medicine Unit, Azienda Ospedaliero-Universitaria Trieste, Trieste
[5]Neurology Unit, AO Spedali Civili di Brescia, Brescia
[6]Neurologic Clinic, University of Trieste, Trieste
[7]Department of Clinical and Experimental Sciences, University of Brescia, Brescia

Background: The clinical diagnosis of Dementia with Lewy bodies (DLB) has good specificity but low sensitivity. This is particularly an issue in patients with an uncertain diagnosis (possible DLB). Single-photon emission computed tomography (SPECT) may increase diagnostic confidence in the evaluation of dementia. DaTSCAN™ (Ioflupane 123I) is a radiopharmaceutical for brain SPECT imaging which binds to the dopamine transporter receptors located on the presynaptic terminals of dopaminergic neurons and it is useful to differentiate AD from DLB with sensitivity and specificity around 85 %.

Objective: To evaluate the impact of DaTSCAN™ SPECT imaging on dementia diagnostic category and on clinicians' diagnostic confidence in patients with a diagnosis of possible DLB.

Design/Methods: 187 patients with a diagnosis of possible DLB, recruited from 21 centers in 6 European countries, were randomized to have a DaTSCAN™ at baseline (127 patients; imaging group) or to have no-imaging (60 patients; control group). The proportion of patients with changes in clinical diagnosis (to probable DLB or non-DLB) and changes in the confidence in diagnosis from baseline was compared between the two groups at 8 and 24 weeks of follow-up.

Results: DaTSCAN™ imaging showed dopaminergic deficit in 49 /114 (43%) subjects.
Significantly more patients in the DaTSCAN™ group had a change in diagnostic category after 8 weeks (62% vs 4%; p ‹ .0001) and after 24 weeks (71 % vs 16%; p ‹ .0001) compared to the control group. Clinicians were more likely to change the diagnostic category if the DaTSCAN™ was abnormal (82%) than if the result was normal (46 %).Confidence in diagnosis measured by a VAS (0-100, mean baseline 49) significantly increased in the imaging group during follow-up compared to the control group (+17.5 vs 1 at week 8 and +21 vs 3 at week 24; both p ‹ .0001).

Conclusion: DaTSCAN™ SPECT imaging drove the clinicians to change the diagnostic category and improved diagnostic confidence in patients with possible DLB. The follow-up confirmed the DaTSCAN™ SPECT diagnostic utility showed at 8 and 24 weeks.

P75

Functional connectivity in the default mode network relates to the severity of depression in autosomal recessive Parkinson's disease

Simona Petrucci[1,2], *E. Makovac*[3], *L. Serra*[3], *M. Torso*[3], *B. Spanò*[3], *L. Ricciardi*[4], *C. Caltagirone*[5,6], *T. Ialongo*[4], *A. Guidubaldi*[4], *A.R. Bentivoglio*[4], *E.M. Valente*[1,7], *M. Bozzali*[3]

[1]CSS-Mendel Institute, IRCCS Casa Sollievo della Sofferenza, Rome
[2]Dept. of Experimental Medicine, Sapienza University, Rome
[3]Neuroimaging Laboratory, IRCCS Santa Lucia Foundation, Rome
[4]Dept. of Neurosciences, Catholic University, Rome
[5]Dept. of Clinical and Behavioural Neurology, IRCCS Santa Lucia Foundation, Rome
[6]Dept. of Neuroscience, University of Rome 'Tor Vergata', Rome
[7]Dept. of Medicine and Surgery, University of Salerno, Salerno

Background: Biallelic mutations in the *Parkin* and *PINK1* genes are frequent causes of early onset, autosomal recessive Parkinson's disease (ARPD), characterized by slow progression of motor signs, good response to dopaminergic therapy and often psychiatric disturbances, including depression. While only homozygous or compound heterozygous patients show the typical ARPD phenotype, single heterozygous carriers may remain asymptomatic or manifest subtle signs related to the disease. Here we used functional MRI (fMRI) to explore the pathophysiological basis of depression and other behavioral problems in ARPD.

Methods: We enrolled eight *Parkin* or *PINK1* homozygous PD patients (HOM) and nine heterozygous healthy relatives (HET). All subjects underwent neuropsychological and behavioral assessments including Hamilton Depression scale (Ham-d) and Hamilton Anxiety scale (Ham-a). An MRI assessment at 3T, including EPI images for resting state fMRI, was obtained in each patient. Independent component analysis (ICA) was used to identify the Default Mode Network (DMN). The second level analysis was performed in SPM8 using a two sample T test, with group (HOM or HET) as factor, Ham-d or Ham-a scores as covariates of interest, and total grey matter volume as covariate of no interest.

Results: HOM patients presented significantly higher scores than HET subjects at all behavioral measures. In resting-state fMRI analyses, Ham-d scores were negatively correlated with functional connectivity within the DMN across the whole population in the BA (Brodmann areas) 23/31 and in the BA 9/46. A significant "group by score" interaction was also observed, within DMN connectivity, in the precuneus of HOM vs HET subjects.

Conclusion: Our data indicate that, in *Parkin* and *PINK1* ARPD, depression is pathophysiologically associated with brain tissue abnormalities by the disconnection mechanism, not only in affected patients but also in non-affected heterozygous carriers. As expected, depression and brain disconnection were more severe in HOM than in HET subjects.

P76

Parkinson's disease: extensive evaluation of pre-motors potential markers in REM behaviour disorders population

Roberta Zangaglia[1,2], *R. De Marzi*[1,2], *N. Gabriele Pozzi*[1,2], *B. Minafra*[1,2], *M. Terzaghi*[3], *R. Manni*[3], *E. Guaschino*[4], *N. Ghiotto*[4], *M. Picascia*[2,5], *E. Sinforiani*[2,5], *C. Pacchetti*[1,2]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia
[2]Interdepartmental Research Center for Neurodegenerative Disease, National Institute of Neurology Foundation "C. Mondino", Pavia
[3]Sleep Unit, National Institute of Neurology Foundation," C. Mondino", Pavia
[4]Neurovascular Unit, National Institute of Neurology Foundation, "C. Mondino", Pavia
[5]Laboratory of Neuropsychology, National Institute of Neurology Foundation, "C. Mondino", Pavia

REM sleep behaviour disorder (RBD), which is regarded as another non-motor symptom of Parkinson's Disease (PD), precedes motor symptoms in some patients and seems to be one of the strongest premotor markers for PD. The risk of developing a neurodegenerative disease in idiopathic RBD ranges from 40 to 65% after 10 years of follow-up. However, the specificity of symptom screens for RBD is not established and there are only limited ways to predict which RBD patients will develop PD. At present there is no single tool that allows to predict if an RBD- patient will develop PD over time.
Aim of the study is an extensive evaluation of clinical sign, neurophysiological finding and neuroimaging associated with RBD.
We recruited subjects with a diagnosis of RBD confirmed by video-polysomnography. These subjects were evaluated with Transcranial B-mode ultrasonography (TCS), dopamine transporter SPECT, brain MRI 3 Tesla, visual evoked potentials, UPSIT for hyposmia, autonomic testing, extensive neuropsychological test, clinical evaluation with UPDRS motor score.
21 subjects (20 male and 1female) were recruited of mean age 69.71 ± 6.27 and average duration of RBD about 9 years. 36,4% of subjects had a low $^{[123]}$ I-FP-CIT-SPECT uptake; mean UPDRS motor score was 14.8 ± 9.7, and in this group all showed SN hyperechogenicity except two subjects.
14 RBD-subjects showed hyperechogenicity of the substantia nigra (SN) at TCS and among these 6 subjects also presented a reduced striatal $^{[123]}$ I-FP-CIT-SPECT binding; in all these subjects UPDRS III scores was higher than 4 points. Among RBD patients, 13 had hyposmia and among these 61,5 % showed a hyperechogenicity of SN, while only 4 had a abnormal $^{[123]}$ I-FP-CIT-SPECT uptake.
In this study we summarize an extensive picture of pre-motors potential markers of PD in subjects with RBD. All patients will be followed with annual follow-up.

P77

Voxel-based morphometry (VBM) in Parkinson's disease with freezing of gait

Alfonso Rubino[1,2], *F. Assogna*[3], *R. Scatozza*[1,2], *V. Montemurro*[1,2], *E. Di Battista*[1,2], *F. Fattapposta*[2], *G. Meco*[1,2]

[1]Centro Malattia di Parkinson Policlinico "Umberto I", Roma
[2]Dipartimento di Neurologia e Psichiatria "Sapienza" Università di Roma, Roma
[3]I.R.C.C.S. Fondazione Santa Lucia, Roma

Background: Freezing of gait (FOG), defined as a ''brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk.'', is part of an intricate clinical picture in Parkinson's disease (PD). Structural neuroimaging studies on FOG in PD with VBM yielded variable and partially conflicting findings; the inconsistent results obtained probably reflect the heterogeneity and complexity of the phenomenon. The aim of the present study was to further explore the differences in local GM volume in patients with PD with and without FOG by using VBM.

Materials and Methods: We investigated 26 patients (7 women and 19 men) with a diagnosis of PD in stable treatment with dopaminergic therapy. Thirteen patients classified as exhibiting FOG (FOG+) were matched for age, disease severity (UPDRS scores and H&Y stage), disease duration and educational attainment with 13 nonfreezers (FOG-) patients. All 26 participants underwent a detailed cognitive assessment and a grey matter volumetry using VBM derived from T1 weighted 3T MRI.

Results: The patient groups did not significantly differ for age, disease duration; H&Y stage; UPDRS part-III, educational attainment or gender. No significant differences of cognitive assessment emerged. There were no differences in global GM between groups. PD-FOG+ patients showed a pattern of GM relative atrophy in left posterior parietal gyrus (using the statistical threshold $p < 0.001$-uncorrected) compared with PD-FOG-.

Discussion: The findings of this study suggest that a specific pattern of cortical volume reduction involving posterior parietal cortices contributes to the occurrence of FOG in PD. These data agree with the growing body of evidence that considers the parietal posterior cortex as an association area involved in spatial control of motor behavior, integrated in sensory evaluation and response selection.

P78

SWEEDs within the same family. Casual event or is there anything else still to make out?

Vincenzo Toni, A. Vasquez, A. Bernardi, M.C. Pastore, R. Scarpello

U.O.C. Neurologia – Ospedale "Francesco Ferrari" Casarano (LE) – ASL LE, Lecce

Introduction: Parkinson's Disease (PD) shows well recognized clinical features but diagnosis is susceptible to misdiagnosis. After the introduction of DAT-SPECT, a group of patients with features that challenge a diagnosis of PD but with a normal scan has been identified (SWEDDs: Scans-Without-Evidence-of-Dopaminergic-Deficit).

Objective: To describe the cases of two sisters with features resembling PD but normal DAT- PECT, without any other conclusive diagnosis.

Patients: PATIENT 1- C.C.:

-Female, 71years-old
-10 years ago left hand postural and resting tremor with mild slowness of voluntary movements
-During follow-up no progression of symptoms
-Motor examination: mild hypomimia; mild, bilateral hand postural tremor with dystonic posturing of fingers; mild slowness without clear fatigue or decrement; reduced right arm swing
-No response to dopamineric drugs

PATIENT 2- C.M.:

-Female, 62years-old
-9 years ago bilateral hand postural tremor, head tremor, mild slowness and "rigidity" of left hand
-During follow-up very slow progression of symptoms
-Motor examination: mild hypomimia; head tremor; moderate postural and resting tremor of both hands with mild dystonic posturing of fingers; slowness of repetitive movements without clear fatigue or decrement; reduced arm swing
-No response to dopaminergic drugs and, then, to Propranolol (160 mg/day) and Primidone (750 mg/day).

In both cases DAT-SPECT, brain-MRI or brain-CT were normal and dopaminergic drugs were withdrawn without worsening of symptoms.

Discussion: Hitherto, to our knowledge, cases of SWEDD within the same family have not been described.
So, in our opinion two questions arise from the study of these cases.

1. Do they meet the diagnostic criteria for PD or other movement disorder or can they be referred to as SWEDDs?
2. If they are diagnosed as SWEDDs, is their unusual recurrence within the same family casual or could it suggest the existence of anything else we have to make out about the origin of these clinical pictures?

Further and larger observations are needed.

P79

Cerebello-thalamo-cortical circuits and basal ganglia interactions in Parkinson's patients with bilaterally implanted deep brain stimulating electrodes into subthalamic nuclei: a TMS-EEG study

Giacomo Koch[1,2], *V. Ponzo*[1], *M. Stampanoni Bassi*[2], *A. Stefani*[2], *A. Peppe*[1], *L. Brusa*[3], *D. Veniero*[1]

[1]Laboratorio di Neurologia Clinica e Comportamentale, IRCCS Fondazione Santa Lucia, Roma
[2]Dipartimento di Neuroscienze, Policlinico "Tor Vergata", Roma
[3]UOC Neurologia, Ospedale S. Eugenio Hospital, Roma

Parkinson's disease (PD) is characterized by a degeneration of dopaminergic neurons of substantia nigra. Deep brain stimulation (DBS) into subthalamic nucleus (STN) is an effective treatment for advanced PD. However, our knowledge about STN stimulation effects over cortical activity is lacking. In a previous study, we demonstrated that levodopa-induced dyskinesia in PD can be reduced by cerebellar continuous theta burst stimulation (cTBS), through the modulation of cerebello-thalamo-cortical (CTC) circuits activity, thus suggesting an interaction between CTC and basal ganglia circuits.
Our aim was to investigate the effects of DBS and cerebellar cTBS over the cortical activity of STN-DBS treated PD patients with a combined Transcranial Magnetic Stimulation (TMS)/EEG approach.
We studied 6 PD patients with DBS. Three conditions were tested on different days. In the Off-OFF condition first?morning levodopa medication was suspended and DBS was turned off. In the Off-ON condition the dopaminergic medication was suspended but DBS was on. In the On-ON condition, patients continued their usual dopaminergic medications and the DBS was on. In each condition before and after cerebellar cTBS, 80 single pulse TMS were delivered over M1, contralateral to the clinically more affected side while acquiring EEG. Response to TMS were calculated for theta (4-7Hz), alpha (8-12Hz) and beta (13-30Hz) band.
During On-ON condition, TMS induced a higher beta synchronization when compared to all other conditions (p=0.006) and Off-OFF condition was associated with lower level of beta. After cTBS there was an increased beta synchronization regardless the condition (p
In conclusion, the increase of beta level after cerebellar stimulation suggests a possible interaction between CTC and basal ganglia circuits.

P80

Correlation between occipital cortex alpha activity lateralization and L-dopa motor response in Parkinson's disease

Giovanni Mostile, V. Dibilio, A. Luca, I. Pappalardo, L. Giuliano, C.E. Cicero, G. Sciacca, L. Raciti, D. Contrafatto, E. Bruno, V. Sofia, A. Nicoletti, M. Zappia

Department GF Ingrassia, Section of Neurosciences, University of Catania, Catania

Background: Quantitative EEG (qEEG) studies have shown Parkinson's disease (PD) may be associated with alterations of oscillatory brain activity which could be normalized by L-dopa treatment. However, few studies have focused on relationship between L-dopa motor response and cortical activity asymmetry using qEEG in L-dopa untreated PD.

Objective: To assess correlation between cortical activity asymmetry and L-dopa motor response in de novo PD patients using a qEEG asymmetry index.

Methods: We retrospectively selected N = 34 L-dopa untreated PD patients who performed a standardized EEG assessment during their clinical admission. N = 18 subjects matched by age, sex and hand dominance with a normal EEG study and no parkinsonism and/or cognitive decline were also selected as control group. For all patients, EEG signals were recorded from homologous pairs of electrodes over each hemisphere. A Welch's periodogram was applied to artefacts-free detrended signals epochs visually selected off-line from continuous EEG recordings during eyes-closed and eyes-open tasks. An Index of Lateralization (IL) was then obtained as the absolute value of the EEG asymmetry index, computed by subtracting left from right sided log power spectral density for each homologous site and frequency bands (delta to beta). A standardized L-dopa acute challenge test was also performed to all PD patients and the motor response magnitude computed.

Results: In occipital region of PD patients, we obtained lower IL for the alpha band compared to controls ($p = 0.024$). Such parameter correlated with L-dopa motor response magnitude ($r = 0.456$; $p = 0.007$).

Conclusion: Lateralization of occipital cortex alpha activity may correlate with L-dopa motor response in PD.

P81

Utility of an electroencephalographic asymmetry index in Parkinson's disease

Giovanni Mostile, V. Dibilio, A. Luca, I. Pappalardo, L. Giuliano, C.E. Cicero, G. Sciacca, L. Raciti, D. Contrafatto, E. Bruno, V. Sofia, A. Nicoletti, M. Zappia

Department GF Ingrassia, Section of Neurosciences, University of Catania, Catania

Background: In Parkinson's disease (PD), enhancement of topographically defined frontal cortex beta activity by cortical-subcortical oscillatory networks has been implicated in motor program dysfunction. Few studies have focused on cortical activity asymmetry using quantitative EEG (qEEG) in PD.

Objective: To assess feasibility and clinical correlates of a qEEG asymmetry index in de novo PD patients compared to controls.

Methods: We retrospectively selected N = 34 L-dopa untreated PD patients who performed a standardized EEG assessment during their clinical admission. Clinical data of enrolled PD patients were collected. N = 18 subjects matched by age, sex and hand dominance with a normal EEG study and no parkinsonism and/or cognitive decline were also selected as control group. For all patients, EEG signals were recorded from homologous pairs of electrodes over each hemisphere. A Welch's periodogram was applied to artefacts-free detrended signals epochs visually selected off-line from continuous EEG recordings during eyes-closed and eyes-open tasks. An Index of Lateralization (IL) was then obtained as the absolute value of the EEG asymmetry index, computed by subtracting left from right sided log power spectral density for each homologous site and frequency bands (delta to beta).

Results: In mid/lateral frontal regions of PD patients, we obtained higher IL for the beta band ($p = 0.015$) whereas lower IL for the theta band ($p = 0.036$) during the eyes-closed task compared to controls. Both parameters correlated with Hoehn-Yahr stage (respectively: $r = 0.428$, $p = 0.012$; $r = -0.464$; $p = 0.006$).

Conclusion: Our data suggest a specific lateralization of frontal cortex beta activity in PD correlating with disease progression. We suggested IL may represent a useful index of cortical neural activity in PD.

P82

Subthalamic oscillations during monetary reward in patients with Parkinson's disease with and without pathological gambling

Manuela Fumagalli[1], *M. Rosa*[1], *G. Giannicola*[1], *S. Marceglia*[1], *C. Lucchiari*[2], *D. Servello*[3], *A. Franzini*[4], *C. Pacchetti*[5], *L.M. Romito*[4], *A. Albanese*[4], *M. Porta*[3], *G. Pravettoni*[2,6], *A. Priori*[1,7]

[1]Centro Clinico per la Neurostimolazione, le Neurotecnologie ed i Disordini del Movimento, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano
[2]Dipartimento di Economia, Management e Metodi Quantitativi, Università degli Studi di Milano, Milano
[3]Neurochirurgia Funzionale e Clinica Tourette, IRCCS Galeazzi, Milano
[4]Fondazione IRCCS Istituto Nazionale Neurologico Carlo Besta, Milano
[5]Unità Operativa Parkinson e Disordini del Movimento, IRCCS Istituto Neurologico Mondino, Pavia
[6]Applied Research Unit for Cognitive and Psychological Science, Istituto Europeo di Oncologia, Milan
[7]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano, Milano

Introduction: Although parkinsonian patients who gamble have an increased sensitivity to risk, the precise neural mechanisms underlying pathological gambling remain unknown.
Scientific evidence suggested these mechanisms involve the dopaminergic reward circuit, a circuit that mediates reward processing - the information processing phase that follows decision-making when subjects face choice outcomes. This circuit includes the subthalamic nucleus (STN) but its role in the circuit remain unclear.
In a previous study investigating local field potentials (LFPs) recorded from the STN in parkinsonian patients engaged in an economics task we recorded a specific low-frequency STN LFP activity during conflictual economics decisions in gamblers. No study has investigated neurophysiological changes in the STN during monetary reward.

Aims: We designed this study to investigate whether the human STN is involved in monetary reward, and to seek a possible reward system dysfunction in parkinsonian patients who gamble.

Methods: We recorded STN LFPs in 12 parkinsonian patients who had deep brain stimulation (DBS) electrodes implanted in the STN, 6 gamblers and 6 non gamblers, engaged in an economics task entailing positive and negative risky and positive and negative non risky rewards.

Results: When engaged in the task, parkinsonian patients who gambled adopted a risk-taking, whereas non gamblers used a risk-avoiding behavioral strategy. In all patients, STN LFP low-frequency power increased from baseline during feedback. In particular, whereas in STN LFP recordings from gamblers low-frequency power increased during all types of reward tested, in recordings from non gamblers during the risky positive reward it remained unchanged from baseline.

Conclusion: This study provides hitherto unavailable neurophysiological evidence that the human STN is involved in monetary reward. Our findings also suggest that pathological gambling reflects a brain reward system dysfunction that impairs the ability to discern different rewards so that patients become unable to learn from previous experience involving rewards.

P83

Can serotoninergic antidepressants prevent or delay the development of L-dopa induced dyskinesias in PD patients?

Sonia Mazzucchi[1], *D. Frosini*[1], *A. Ripoli*[2], *U. Bonuccelli*[1], *R. Ceravolo*[1]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa
[2]Fondazione Monasterio, Pisa

Introduction: Several studies investigated the role of serotoninergic system in the pathogenesis of L-dopa induced dyskinesias (LID) in patients with Parkinson's Disease (PD).
Serotoninergic neurons can act as “surrogates” of dopaminergic neurons in the advanced phase of the disease, releasing dopamine irregularly because of lack of autoreceptors. LID attenuation has been reported in hemiparkinsonian rats after administration of Selective Serotonine Reuptake Inhibitors (SSRIs); the serotonine transporter (SERT) could represent a future anti-dyskinetic target.

Objective: To investigate the potential effect of SSRIs, assumed previously and during dopaminergic treatment, in reducing the frequency and severity or delaying the development of LID in a cohort of PD patients.

Methods: 135 consecutive PD outpatients, with a minimum follow-up of 10 years since diagnosis, were retrospectively evaluated in a single-centre study. We considered age at PD onset, LD exposure (duration and maximum daily dose), SSRIs exposure, LID onset.

Results: 49 patients received SSRIs (S+ Group) and 86 did not (S- Group). In the S+ Group 26 developed LID (53,1%) within 10 years vs 48 (55,8%) in the S-. A comparison with Chi Square Test did not reveal any statistically significant difference in the prevalence of LID.
Dyskinetic patients in the S+ Group develop dyskinesias later: 6 vs 5 years since introduction of LD (p=0.02). LID patients were furtherly divided into Early and Late Onset (EOG vs LOG) and SSRIs exposure was associated with an OR = 3,48 (1.24 – 10.98, p=0.02) to belong to the LOG.

Conclusion: In our study the previous/concomitant use of SSRIs in PD patients did not protect from LID, however our preliminary data suggest a later onset of LID either with respect to PD diagnosis or LD start supporting that modulation of the serotoninergic system could represent a possible anti-dyskinetic strategy.

P84

Extradural stimulation of primary motor cortex in patients with Parkinson's disease: motor and cognitive assessments in a 3-year prospective open-label study

Francesco Bove[1], *C. Piano*[1], *B. Cioni*[2], *T. Tufo*[2], *C. Piccininni*[1], *C. De Simone*[2], *M. Meglio*[2], *A. Fasano*[1], *A. Daniele*[1], *A.R. Bentivoglio*[1]

[1]Institute of Neurology, Catholic University, Rome
[2]Institute of Neurosurgery, Catholic University, Rome

Background: Extradural stimulation of primary motor cortex (EMCS) [1], which is part of the corticobasal ganglia loops, may be an alternative option for the surgical treatment of Parkinson's disease (PD).

Objective: To investigate motor and cognitive effects of EMCS in PD patients with a 3-year postoperative follow-up.

Methods: A quadripolar electrode strip was placed extradurally over the motor cortex in 9 patients with PD. Before surgery and postoperatively (3, 6, 12, 18 e 36 months after surgery) patients underwent assessments of motor symptoms (Unified Parkinson's Disease Rating Scale, UPDRS), cognition (Mental Deterioration Battery) and behavior, quality of life (Parkinson's Disease Quality of Life Questionnaire, PDQL).

Results: Three, 6, 12, 18 e 36 months after surgery, a significant postoperative motor improvement (reduction of UPDRS-III scores) was observed only in the off-medication condition. A significant postoperative improvement of motor axial symptoms was detected 18 e 36 months after surgery. Moreover, quality of life improved postoperatively at 3, 6, 12 months.
A slight but significant postoperative improvement of cognitive performance was observed on the Mini-Mental State Examination and on a task of verbal episodic memory at 18 months, possibly due to practice effect. No surgical complication, no adverse event, and no postoperative behavioural change were observed.

Discussion: Extradural motor cortex stimulation is a safe procedure. After 36 months, the patients demonstrated a moderate improvement of motor symptoms (particularly axial symptoms) and quality of life.

Conclusion: EMCS may be a safe alternative option in PD patients who refuse DBS or in whom DBS is contraindicated [2].

References

[1] Bentivoglio AR, Fasano A, Piano C, Soleti F, Daniele A, Zinno M, Piccininni C, De Simone C, Policicchio D, Tufo T, Meglio M, Cioni B (2012). Unilateral extradural motor cortex stimulation is safe and improves Parkinson's disease at 1 year. Neurosurgery, vol. 71, p. 815 -825
[2] Fasano A, Daniele A, Albanese A (2012). Treatment of motor and non-motor features of Parkinson's disease with deep brain stimulation. The Lancet Neurology, vol. 11, p. 429-442

P85

Botulinum toxin in sialorrhea is safe and effective in the long term use

Martina Petracca[1], *A. Guidubaldi*[1], *L. Ricciardi*[1,2], *T. Ialongo*[1], *E. Di Stasio*[3], *A.R. Bentivoglio*[1]

[1]Istituto di Neurologia, Università Cattolica del Sacro Cuore, Roma
[2]Dipartimento di Neuroscienze, Psichiatria e Scienze Anestesiologiche, Università di Messina, Messina
[3]Istituto di Biochimica e Biochimica Clinica, Università Cattolica del Sacro Cuore, Roma

Introduction: In the last years, either botulinum toxin (BoNT) A and B resulted efficacious and safe in the treatment of excessive drooling, but scanty data are available on the long term use.

Aims: To investigate the adverse events (AEs), to discriminate differences in safety and to evaluate the efficacy in the long term use of both BoNT A (AbobotulinumtoxinA) and B (rimabotulinumtoxinB) for sialorrhea in a retrospective study.

Patients and Methods: Consecutive patients affected by Amyotrophic Lateral Sclerosis (ALS) or parkinsonism (PD) with severe sialorrhea were included. Patients received at least two ultrasound-guided (USG) intrasalivary glands AboBoNT-A 250 U or RimaBoNT-B 2500 U injections.
Clinical and demographical data were collected. Safety and tolerability were assessed on the basis of patients' self-reports. Efficacy was assessed by recording the duration of benefit and by means of Drooling Severity Scale (DSS) and Drooling Frequency Scale (DFS) 4 weeks after intervention.

Results: Sixty-five patients (32 ALS and 33 PD) were treated in a total of 317 sessions (189 RimaBoNT-B and 132 AboBoNT-A). Either AboBoNT-A or RimaBoNT-B treatments gave a clear-cut benefit in all patients. The mean benefit duration was similar for both serotypes, but significantly shorter in ALS group (67.2 ± 25.5 days) compared to PD (108.7 ± 35.3 days; p p= 0.003). The only BoNT related AEs was a change of saliva thickness, mostly rated mild to moderate and more frequent in ALS patients (p = not significant).

Discussion: Either 250 U AboBoNT-A or 2500 U RimaBoNT-B USG intrasalivary glands injection are safe and effective in treating sialorrhea, even in the long-term follow-up. Older age is significantly associated with longer benefit duration. PD patients showed a more favorable safety-efficacy ratio than ALS, due to lower AEs rate (p= not significant) and longer benefit duration (p ‹ 0,0001).

P86

Cognitive impairment in Parkinson's disease: a study of subthalamic deep brain-stimulated patients

Carlo Alberto Artusi, A. Romagnolo, A. Merola, L. Rizzi, M. Zibetti, S. Angrisano, F. Dematteis, M. Lanotte, M.G. Rizzone, L. Lopiano

Department of Neuroscience, Università degli Studi di Torino, Torino

Objective: The aim of this study was to identify baseline clinical and neuropsychological predictors of poor long term cognitive outcome in parkinsonian patients treated with STN-DBS.

Materials and Methods: 174 patients with Parkinson's disease (PD) who underwent STN-DBS were evaluated by means of UPDRS and a standardized battery of neuropsychological tests carried out at baseline (before surgery) and after 1, 3 and >5 years after surgery. Kaplan–Meier survival analyses and a Cox regression model were performed to estimate the risk of developing dementia after surgery and to evaluate the predictors of dementia.

Results: At baseline no patients showed dementia, even though 23% subjects met the criteria for PD-MCI. During follow-up, we observed an increasing incidence of cognitive impairment: the percentage of MCI rose to 34% at 1 year, 45% at 3 years, 41% at last follow-up, while dementia was found in 0%, 15% and 32% respectively. A significantly different cognitive evolution was observed between baseline MCI and no-MCI patients: 22,5% PD-MCI patients developed dementia during follow-up, versus 11,9% of the other group, with a different time needed to develop dementia (6,03 and 11,08 years since surgery respectively; p:0,028). Cox model showed a correlation between the HR of dementia and both the UPDRS-I baseline scores (p:0,045) and the executive functions alteration (p:0,010).

Discussion: Many PD features are recognised risk factors for the development of dementia but definitive data on STN-DBS cognitive outcome are lacking. This study showed a higher rate of dementia development in subjects with PD-MCI before surgery and revealed that baseline impairment of executive functions and higher UPDRS-I score are independent risk factors for dementia. These preliminary results confirm preceding literature data, highlighting the role of PD-MCI and in particular of the executive functions as predictors of dementia; they also point out the importance of the UPDRS-I to predict a possible evolution to dementia.

P87

Acute challenge with rotigotine in Parkinson's disease: effects on motor symptoms and cognitive functions

Mario Stampanoni Bassi[1], *P. Imbriani*[1], *E. Olivola*[1], *M. Pierantozzi*[1], *A. Stefani*[1,2]

[1]Department of Neuroscience, University of Rome ‘‘Tor Vergata’’, Rome
[2]Santa Lucia Foundation, I.R.C.C.S., Rome

Introduction: In Parkinson´s Disease (PD) a dysexecutive syndrome with deficient attentional resource allocation is frequently present, in addition to motor symptoms. Specifically, deficits in the executive components of attention associated with an overall slowing and greater reaction time variability can be observed. This is associated with poor ability to focus attention, divide attentional resources and resist interference. Only a few studies explored the effect of dopaminergic medication on this cognitive impairment and with discordant results. Moreover, the role of acute challenge tests both with levodopa and some dopamine agonists such as pramipexole and apomorphine have been investigated as an important diagnostic instrument in PD, but none with rotigotine.

Objective: To test the effect of acute rotigotine administration both on motor symptoms, evaluated with Unified Parkinson's Disease Rating Scale part III (UPDRS-III) score and finger tapping frequency, and cognitive functions, in terms of simple and choice reaction time. Using a Simon task, we investigated the effects on both on-line and proactive control efforts to reduce interference produced by the activation of an incorrect response.

Methods: 20 non-demented early PD patients (Hoehn & Yahr ‹ 2) were evaluated under two different treatment conditions: off therapy and 60 minutes after administration of rotigotine 8 mg or placebo, randomly distributed. Moreover they underwent levodopa challenge test.

Results: Acute rotigotine exerted modest effect on motor performance (for instance, about 12% improvement in finger tapping frequency). On the contrary, administration of rotigotine versus placebo showed a positive influence on cognitive reaction time and a reduced interference effect at Simon task.

Discussion: Albeit preliminary, the results obtained support the notion that acute rotigotine administration may positively affect cognitive performance in PD. Moreover, when validated on larger cohort of patients, this test might become a useful instrument to challenge cognitive facets of the PD syndrome.

P88

Evaluation of analgesic effectiveness of oxycodone/naloxone prolonged release (OXN RP) *versus* gabapentin in Parkinson's disease patients with central chronic pain

Graziella Madeo, T. Schirinzi, F. Alemseged, A. Pisani

Department of System Medicine, University of Rome "Tor Vergata", Laboratory of Neurophysiology and Synaptic Plasticity, Santa Lucia Foundation I.R.C.C.S., Rome

Introduction: Pain and other non-motor symptoms are increasingly recognized as a major cause of reduced quality of life (QoL) in patients with Parkinson's disease (PD). PD-patients frequently report different types of pain, including musculoskeletal, dystonic, radicular neuropathic and central pain. Although a correct management of dopaminergic therapy is often associated to a mitigation of symptoms, the different underlying pathogenesis may represent a major therapeutic challenge.

Objective: Aim of this study is to investigate the effectiveness of treatment with oral oxycodone prolonged-release (PR)/naloxone PR (OXN PR) versus oral gabapentin (GBP) on pain symptoms' management, as well as the impact of analgesic effect on both QoL or PD-symptoms.

Methods: PD-patients suffering from chronic pain are recruited in a consecutive manner and clinically observed for a period of 32 weeks. PD-patients will undergo clinical examination of pain, motor and cognitive status, by using Number rating scale for pain (NRS), Unified Parkinson's disease Rating Scale part III (UPDRS-III), Mini Mental Status Examination (MMSE), Hoehn and Yahr scale (H&Y). Moreover, self-scored scales will be administered: DN4, McGill Pain Questionnaire, Brief Pain Inventory (BPI), Beck Depression Inventory (BDI), Clinical Global Impression (CGI), Pittsburg Quality of Index (PSQI), Quality of Life (SF-36), Bowel Function Index (BFI).

Results: Primary endpoints: evaluation and comparison of analgesic effectiveness of OXN RP 5 mg/2.5 mg every 12h compared to GBP 300 mg every 8h, analysis of relationship between pain intensity and modification of dopaminergic therapy dose, and drug-safety. Secondary endpoints: maintenance of therapeutic effectiveness of RP OXN 5mg/2.5 compared to GBP, impact on QoL, mood and sleep, reduced use of "rescue" analgesic drugs, and constipation.

Conclusion: Pain in PD is a frequent and important non-motor symptom. The availability of novel therapeutic tools is of crucial importance to ensure a better QoL to PD patients.

P89

Seldinger technique for PEG devices replacement in PD patients in treatment with Levodopa/Carbidopa intestinal gel infusion

Rossella Scatozza[4], *G. Levi Della Vida*[1], *M. Morucci*[2], *A. Tesi*[3], *V. Montemurro*[4], *A. Rubino*[4], *G. Meco*[4]

[1]U.O.C. Governo Clinico in Geriatria Az. Osp. S. Camillo Forlanini, Roma
[2]U.O.C. Radiologia Vascolare Az. Osp. S. Camillo Forlanini, Roma
[3]U.O.C. Gastroenterologia Az. Osp. S. Camillo Forlanini, Roma
[4]Centro Malattia di Parkinson, Dipartimento Scienze Neurologiche e Psichiatriche "Sapienza" Università di Roma, Roma

Background: Levodopa/carbidopa intestinal gel infusion (LCIG) is a recent therapeutic advance for patients with Parkinson's disease (PD) and severe motor fluctuations. Aiming at continuous dopaminergic stimulation, the drug-containing gel is steadily pumped into the upper jejunum through a Jet-PEG, an extension tube inserted through a percutaneous endoscopic gastrostomy (PEG). A growing body of evidence suggests considerable potential adverse effects under LCIG, related to surgical procedures and deterioration or dislocation of enteral devices.

Aims of study: We propose an easy procedure for the management of replacement of Jet-PEG in order to minimize adverse effects during the treatment course with duodenal levodopa infusion.

Materials and methods: Four PD patients underwent this procedure for the developing of complication during treatment course with duodenal levodopa infusion (2 device displacements, 1 duodenal bezoar, 1 leak of gastric fluids). All patients gave their written informed consent before the treatment. The replacement procedure was achieved using a wire-guided that passed thought the existing gastrostomy. Subsequently, a ballon tip tube (GASTROTOMY TUBE FLOCARE) featuring an "adapted" nasodigiunal tube (FLOCARE BENGMARK) was inserted along the wire guide. Then wire-guide was removed. Wire-guide allowed to confirm the correct placement of the devices (Seldinger technique) using radioscopic examination. Replacement procedures described have been repeated periodically every four months.

Results: In all four patients enteral tubes were successfully replaced; no adverse effect was reported after an average observation period of six months.

Discussion: PEG management may be safely accomplished by a variety of techniques, each one showing advantages and disadvantages. This simple method, avoiding the need of sedation and the discomfort due to endoscopic procedures, allows periodic mini-invasive PEG tube replacement. This approach could prevent devices deterioration (calcification, vulcanization) as well as reduce the risk of bacterial/fungal aggregates and bezoars. Long-term follow-up with cost-effectiveness evaluation of this procedure is mandatory.

P90

A 7-years experience with Levodopa/Carbidopa intestinal gel infusion

Serena Angrisano[1], *M. Zibetti*[1], *A. Merola*[1], *C. A. Artusi*[1], *L. Rizzi*[1], *D. Reggio*[2], *C. De Angelis*[2], *M.G. Rizzone*[1], *L. Lopiano*[1]

[1]Dipartimento di Neuroscienze, Università of Torino, Torino
[2]Divisione di Endoscopia, Città della Salute e della Scienza, Torino

Introduction: Levodopa/carbidopa intestinal gel (LCIG) infusion is an established therapeutic option for advanced Parkinson's disease (PD) patients with fluctuating motor symptoms unresponsive to conventional oral and transdermal treatment. Since the implementation of LCIG is increasing, there is a need of safety and efficacy data from clinical practice.

Methods: We analyzed all PD patients treated with LCIG at our Center over a 7-years period to determine the duration of treatment, retention rate, reasons for discontinuation, efficacy on motor complications, modifications of concomitant therapy and adverse events.

Results: Of 59 patients, 7 (12%) died of causes unrelated to LCIG infusion, 11 patients (19%) discontinued therapy prior to the cutoff date. LCIG improved motor complications in all patients. Over 90% of patients reported a great or moderate improvement of their quality of life, autonomy and clinical global status. The most common adverse events were dislocation and kinking of the intestinal tube.

Conclusion: LCIG infusion is effective in the long-term treatment of advanced PD patients with a clinically relevant effect on motor complications and a relatively low dropout rate.

P91

L-Dopa pharmacokinetic profile with effervescent Melevodopa/Carbidopa versus standard-release Levodopa/Carbidopa tablets in Parkinson's Disease

Margherita Torti, P. Grassini, L.Vacca, M. Casali, F.G. Radicati, F. Stocchi

IRCCS San Raffaele Pisana, Roma

Background and purpose: This study was conducted to characterize the pharmacokinetic profile of levodopa (L-Dopa) after repeated doses of effervescent tablet containing melevodopa and carbidopa compared to standard-release L-dopa/carbidopa in patients with fluctuating Parkinson's disease.

Experimental approach: Patients with a clinical diagnosis of Parkinson's disease were included in this single-centre, randomized, double-blind, double-dummy, two-period crossover study. Treatment consisted of molar equivalent doses of melevodopa 125.6 mg/carbidopa 25 mg and L-Dopa 100 mg/carbidopa 25 mg, with 7 doses given over 24 hours (Cohort 1), 4 doses given over 12 hours (Cohort 2), or 2 doses given over 12 hours in combination with entacapone 200mg (Cohort 3). Blood samples were collected every 20-30 minutes postdose.

Key results: 25 patients were randomized and received at least one dose of study medication. L-Dopa was rapidly absorbed after administration of both of melevodopa 125.6 mg/carbidopa 25 mg and L-dopa/carbidopa, although absorption tended to be more rapid with the former. Values for t_{max}, C_{max} and AUC tended to be less variable after melevodopa 125.6 mg/carbidopa 25 mg versus L-Dopa/carbidopa, both across the dosing period and between patients. This was particularly noticeable after the early afternoon and evening doses.
Accumulation of L-Dopa in plasma was less noticeable with melevodopa 125.6 mg/carbidopa 25 mg. Carbidopa exposure and interpatient variability was lower when melevodopa 125.6 mg/carbidopa 25 mg or L-Dopa/carbidopa was given in combination with entacapone (compared with either drug alone). Both treatments were well tolerated.

Conclusions and implications: The effervescent formulation of melevodopa/carbidopa, provides a more reliable L-Dopa pharmacokinetic profile versus standard-release L-Dopa/carbidopa, with less apparent drug accumulation and less variability.

P92

Comparison of botulinum neurotoxins for clinical use

Antonio E. Elia, A. Albanese

Movement Disorders, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan

Objective: To compare efficacy and safety of different botulinum neurotoxin (BoNT) brands in all the available clinical trials.

Background: The four marketed BoNT brands differ for specific activity, packaging, constituents and excipients, pH, complex size and preparations; yet they have overlapping clinical indications and are all marketed for cervical dystonia.

Methods: Computerized MEDLINE searches were performed. All publications combining a pre-specified string with at least two of the following terms were selected: Botox OR onabotulinumtoxinA; Dysport OR abobotulinumtoxinA; Xeomin OR incobotulinumtoxinA; Myobloc OR Neurobloc OR rimabotulinumtoxinB. Controlled trials with direct comparison of different BoNT brands were selected.

Results: Twenty six randomized controlled trials were selected: 15 on facial wrinkles or hyperhidrosis, 9 on primary dystonia, one on hemifacial spasm and one on achalasia. In blepharospasm and cervical dystonia Abo was found to be more efficacious and less tolerated than Ona. No difference were reported between Ona and Inco in dystonia. Abo was found to be more efficacious and with longer effect than Ona in most studies for facial wrinkles or hyperhidrosis. Rima was associated to larger anhidrotic areas than Ona in one study.

Conclusion: In trials with direct comparisons Abo seems to be more efficacious and less tolerated than Ona. Few head to head trials are available for movement disorders compared to cosmetics and dermatology. The data reviewed here do not allow to draw conclusions on the relative potency of the four toxin brands.

P93

Pallidal stimulation for generalized dystonia: primary dystonia compared to dystonic cerebral palsy

Luigi M. Romito[1,4(*)], *G. Zorzi*[1(*)], *M.L. Ciceri*[1,2], *C.E. Marras*[3], *A. Franzini*[1], *N. Nardocci*[1], *A. Albanese*[1,4]

[1]Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano
[2]Clinica Neurologica, Università degli Studi, Milano
[3]Neurosurgery Unit, Department of Neuroscience and Neurorehabilitation, IRCCS Bambino Gesù Children's Hospital, Roma
[4]Istituto di Neurologia, Università Cattolica, Milano

(*) *These authors equally contributed to the study*

Background: There are increasing evidences that globus pallidus internus (GPi) deep brain stimulation (DBS) is effective in patients with dystonic syndromes. Clinical and demographic outcome predictors are however still poorly defined.

Methods: The aim of this work was to examine the long-term efficacy and safety of GPi DBS for the treatment of generalized primary dystonia (GPD) or generalized dystonia due to cerebral palsy (GDCP). We studied 25 patients with GPD (20 idiopathic, 5 DYT1) and 15 with GDCP, up to 6 years after DBS surgery.
Presence of severe spasticity was an exclusion criterion for GDCP patients. Mild brain MRI abnormalities were acceptable only in patients with GDCP. At regular intervals, dystonia severity was assessed by the motor section of the Burke-Fahn-Marsden dystonia rating scale (BFMDRS-M), amount of energy delivered computed and adverse events and side effect collected.

Results: At last FU, BFMDRS-M score improved in DYT1 group by 75% while the other groups improved on average by 41%. Age at implant or onset, disease duration and baseline dystonia severity, did not correlate to outcome. In GDCP patients, occurrence of spasticity was associated to poorer outcome. GDCP patients received lower energy compared to GPD patients while DYT1 patients received less energy than idiopathic GPD patients. Incidence of adverse events and side effects was comparable between groups.

Conclusion: In the long-term there were no outcome differences between idiopathic GPD and GDCP patients, but DYT1 patients improved more than all other groups. Most patients maintained a stable motor improvement. Safety profile was reassuring.

P94

Current status of Wilson Disease: does early treatment protect from nervous system impairment?

Marcello Esposito[1], *F. Manganelli*[1], *R. Dubbioso*[1], *G. Ranucci*[2], *F. Di Dato*[2], *M.G. Puoti*[2], *R. Iorio*[2], *L. Santoro*[1]

[1]Department of Neurological Sciences, "Federico II" University, Naples
[2]Pediatric Liver Unit "Federico II" University, Naples

Background: During the course of WD neurological disorders (ND) have been described frequently especially when treatment is delayed. In the last years most of WD cases have been diagnosed in childhood at the occurrence of hypertransaminasemia (HT) receiving an early treatment and apparently not showing a progression of the disease afterwards.

Objective: Aim of this study is to assess the impact on nervous system of Wilson disease (WD) in early treated (ET) patients with long duration of disease.

Methods: A clinical, neurophysiologycal and neuroradiological assessment has been conducted in patients with WD with long duration of disease and therapy. Clinical neurological evaluation was performed using the neurological section of "global assessment scale" (GAS) for WD. Transcranial magnetic stimulation (TMS) was performed in all patients and 7 healthy volunteers to study motor corticospinal pathways and cortical excitability. The former was examined measuring central motor conduction time (CMCT) for upper and lower limbs (UL, LL), the latter was explored studying active motor threshold (AMT), rest motor threshold (RMT), cortical silent period (CSP) and, using the paired pulse technique, short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). A brain MRI scan was performed for each patient.

Results: 27 patients (16 M, age range 13-47 y) and a mean disease duration of 16.5 years (range 7-28) have been assessed from 2011 to 2012. All patients started treatment soon after the diagnosis and currently are on pennicillamine (6 patients) or zinc acetate (21 patients). TMS and brain MRI studies were normal in 23 subjects who received diagnosis of WD for the occurrence of HT in childhood and never reporting ND, and in 2 patients presenting both liver and neurological disorders with brain MRI abnormalities at WD onset but currently without ND. Two patients presenting ND as onset in adolescence and still showing neurological signs (GAS 16-18) had brain MRI alterations while neurophysiological studies showed only abnormal SICI.

Conclusion: During the recent decades WD natural history seems to be changed as nervous system could be not affected when patients are diagnosed in childhood receiving early treatment [1, 2]. Our study confirms that early treated patients ,not presenting ND at the onset, do not show neurological clinical signs even after a long disease duration. The normality of TMS and brain MRI studies also suggests the absence of subclinical nervous system impairment. Patients with current ND receiving an almost ET presented neurophysiological features only consisting with a cortical excitability dysfunction, this data may be of interest and needs to be confirmed in further studies.

References

[1] Ala, A. P. Walker, K. Ashkan, J. S. Dooley, M. L. Schilsky. Wilson's disease. Lancet 2007; 369: 397–408
[2] I.O. Kim, W.S. Kim, J.E. Cheon, S.G. Moon, J.W. Kwon, J.K. Seo, K.M. Yeon MR Imaging of the Brain in Wilson Disease Childhood: Findings Before and After Treatment with Clinical Correlation AJNR Am J Neuroradiol 2006 27:1373–78

P95

Rotigotine effect on early morning akinesia. Gait Analysis study

Antonella Peppe[1], *F. Marchetti*[1], *M. Stampanoni Bassi*[2], *A. Stefani*[2]

[1]IRCCS Fondazione Santa Lucia, Roma
[2]Clinica Neurologica Policlinico Tor Vergata, Roma

It is already known the transdermal efficacy of rotigotine on reducing the parkinsonian symptoms as well as the efficacy of Gait Analysis on evaluating the Parkinson's disease (PD) stages. In fact, Gait analysis has been used to validate the effects on locomotion produced by functional neurosurgery and/or L-Dopa medication with/without attentional strategies and rehabilitation program. Therefore, Gait Analysis is to be considered a consistent tool for measuring at first the gait and balance impairment, and consistently objectifying their ameliorations. The present study focuses on the assessment of the efficacy of rotigotine on the amelioration of gait in the morning in a group of moderately advanced Parkinson's disease patients (H&Y:>2) suffering by "early morning akinesia". Further, the study evaluates by specific clinical scales the time/daily spent in ON and the amelioration of Quality of life. Ten PD patients, recruited from Movement Disorder Outpatients Centre at the Neurological Department of the University of Rome Tor Vergata and from Parkinson Disease clinic centre at the Fondazione IRCCS Santa Lucia, Rome. Patients suffering for Idiopathic Parkinsons Disease. H&Y stage > or = 2 with un-satisfactory control by on-going pharmacological therapy (Levodopa, COMT & MAO-inhibitors, see I/E criteria), characterized by an incomplete control of motor signs, in particular presence of early morning akinesia. Gait analysis was performed always in the morning (.30-9.30 am.) twice, at the beginning and after at least to week of stable administration of 16 mg of rotigotina system, no changes of previous antiparkinsonian therapy were made.
The Gait Variables, statistically analyzed by non parametric tests(Freedman and Wicoxon, were: Mean Velocity, Stride percentages (Stance, Swing, Double stance, separately Right and Left side) The data obtained in this group before and after Rotigotine showed: Mean Velocity reduced (p=0.005): Swing R increased (p=0.05), Double support R reduced (p=0.02); Stance L reduced (p=0.02; Swing L increased (p=0.04). Our data, by a validate tool as is Gait Analysis, indicate the efficacy of rotigotina transdermal system for relieve the morning extrapiramidal signs; and support the importance of long lasting action of dopaminergic stimulation.

P96

Peduncolopontine deep brain stimulation in primay progressive freezing of gait: a case report

Nicolò Gabriele Pozzi[1,2], *B. Minafra*[1,2], *R. Zangaglia*[1,2], *R. De Marzi*[1,2], *D. Servello*[3], *G. Sandrini*[4,5], *C. Pacchetti*[1,2]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia
[2]Interdepartmental Research Center for Neurodegenerative Disease, National Institute of Neurology Foundation "C. Mondino", Pavia
[3]Division of Functional Neurosurgery and Tourette Center, IRCCS Galeazzi Institute Milan, Milano
[4]Unit of Neurorehabilitation, National Institute of Neurology Foundation "C. Mondino", Pavia
[5]Department of Public Health and Neurosciences, University of Pavia, Pavia

Primary progressive freezing gait (PPFG) is a neurodegenerative disorder that causes gait freezing during the first 3 years and later results in postural instability and a wheelchair-bound state. It is accompanied by bradykinesia and rigidity and it is unresponsive to dopaminergic medications severely affecting the quality of life [1]. Pedunculopontine nucleus (PPN) is a small nucleus located at the pontomesencephalic junction adjacent to the decussation of the superior cerebellar peduncles. It has extensive connections to the basal ganglia and bilateral outputs to the spinal cord. In 2005, starting from the preliminary observation in primates animal-models of Parkinson disease, PPN stimulation in human was performed [2].
Subsequently reports of improvement in axial symptoms especially gait and postural instability, in patients with Parkinson's disease began to be pubblished [3]. We report a case of a 67-years old caucasian woman affected by PPFG. She developed gait bradykinesia in 2008, evolved in gait freezing unresponsive to L-Dopa therapy. Several NMR images negative for atypical parkinsonism findings, bilaterally asymmetric reduction of radionucleotide capitation in SPET DAT SCAN study and normal myocardial MIBG scintigraphy, with clinical 4 year-follow-up period with only worsening of freezing of gait (FOG) without abnormalities at neuroophtalomological exam were high suggestive for primary progressive freezing of gait disease. In 2013 for the severe limitation in activity of daily living due to FOG, PPN-DBS was done. Ad-hoc low frequency double-negative bipolar stimulation were selected. MDSUPDRS, Gait and fall questionnaire (GFQ) and a gait analysis performed before DBS were retaken. Reduction in MDS-UPDRS III: from 28 to 33, GFQ from 43 to 21, and number of FOG episodes at gait analysis evaluation was reported. Our findings, like other in literature [4], suggest that PPN-DBS in patients with PPFG, a medication-refractory disorder with severe axial symptoms, should represent a reliable therapeutic option.

References

[1] Factor SA, Jennings DL, Molho ES, Marek KL. The natural history of the syndrome of primary progressive freezing gait. Arch Neurol 2002; 59:1778–1783
[2] Mazzone P, Lozano A, Stanzione P, Galati S, Scarnati E, Peppe A, Stefani A. Implantation of human pedunculopontine nucleus: a safe and clinically relevant target in Parkinson's disease. Neuroreport. 2005 Nov 28;16(17):1877-81
[3] Benabid AL, Torres N.New targets for DBS. Parkinsonism Relat Disord. 2012 Jan;18 Suppl 1:S21-3
[4] Wilcox RA, Cole MH, Wong D, Coyne T, Silburn P, Kerr G Pedunculopontine nucleus deep brain stimulation produces sustained improvement in primary progressive freezing of gait. J Neurol Neurosurg Psychiatry. 2011 Nov;82(11):1256-9

P97

Wearing-off and dyskinesia reduction by switching L-Dopa therapy from “pulsatile” to “pulse” in complicated Parkinson’s disease

Giovanni Mostile, A. Nicoletti, V. Dibilio, A. Luca, L. Raciti, G. Sciacca, D. Contrafatto, E. Bruno, M. Zappia

Department GF Ingrassia, Section of Neurosciences, University of Catania, Catania

Background: Conventional modality of L-Dopa administration consisting in intermittent multiple daily small doses (the so called “pulsatile” treatment modality) may determine an intermittent stimulation of dopamine receptors leading to motor fluctuations. A therapeutic regimen consisting in standard oral doses at specific inter-doses intervals exploiting the long-duration response to the drug and designated as oral “pulse” L-Dopa therapy could instead result in a more physiological and tonic stimulation of dopamine receptors, reducing motor fluctuations and dyskinesia.

Objective: To evaluate wearing-off and dyskinesia in complicated Parkinson’s disease (PD) after switching from “pulsatile” to “pulse” L-Dopa administrations.

Methods: Thirty-four patients with motor complications (N = 21 fluctuating; N = 13 dyskinetic) underwent two consecutive standardized waking day motor status evaluations using UPDRS-ME and the Abnormal Involuntary Movement Scale (AIMS) after switching from “pulsatile” to “pulse” L-Dopa administrations. To quantify predictable motor fluctuations, a Wearing Off Index (WOI) was computed based on changes in L-Dopa response magnitude between the two assessments.

Results: We found a significant reduction in number of daily doses while an increase in average single dose between the two assessments, with no differences in cumulative daily dosage of L-Dopa. Maximal AIMS score detected during the motor status monitoring was significantly lower at the second assessment. In fluctuating patients, there was a significant reduction in UPDRS-ME average score as well as in WOI. In dyskinetic patients, there was a significant reduction in average and maximal AIMS scores with no changes in average and maximal UPDRS-ME scores.

Conclusion: Switching L-Dopa therapy from “pulsatile” to “pulse” avoiding small and frequent L-Dopa doses during the day reduces wearing-off and dyskinesia in complicated PD.

P98

Brain structural changes in focal dystonia

Lidia Sarro[1], *F. Agosta*[1], *S. Galantucci*[1], *A. Tomic*[3], *M. Svetel*[3], *N. Kresojevic*[3], *G. Comi*[2], *V.S. Kostic*[3], *M. Filippi*[1]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan
[3]Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: On conventional MRI, focal dystonia is not accompanied by structural brain abnormalities. Voxel-based morphometry (VBM) and diffusion tensor (DT) MRI reported inconsistent findings on grey (GM) and white matter (WM) damage in these patients.

Objective: To investigate GM and WM abnormalities in patients with primary focal dystonia using T1-weighted and DT MRI.

Methods: 75 focal dystonia patients (20 blepharospasm [BL], 15 spasmodic disphonia [SD], 21 spasmodic torticollis [ST], 19 writer's cramp [WC]) and 83 healthy controls were studied.
GM and WM abnormalities were assessed using VBM and tract-based spatial statistics (TBSS). Basal ganglia (BG) volume and diffusivity metrics were measured.

Results: Compared with controls, all dystonia patients showed left postcentral and supramarginal gyrus atrophy. BL patients vs. controls showed decreased GM in the right postcentral gyrus, rolandic operculum, bilateral cerebellum. In BL, GM atrophy was associated with clinical severity. SD patients vs. controls showed decreased GM in bilateral superior frontal gyrus and rolandic operculum/ insula, and right temporal lobe. WC patients vs. controls showed GM density increase in the right middle frontal gyrus and insula, left superior frontal and postcentral gyri, bilateral thalami, which correlated with disease duration and severity. ST patients did not show GM abnormalities. TBSS showed a widespread WM damage in BL and SD patients, and right internal and external capsule damage in ST and WC patients vs. controls. No difference in BG volumes was found in dystonia patients. BG diffusivity metrics were altered bilaterally in B and ST patients, while in WC cases alterations were localized on the right side. Damage to the caudate nucleus and globus pallidus correlated with disease severity in all patients.

Conclusion: Patients with focal dystonia exhibit GM and WM alterations in regions highly relevant to motor function, sensory processing, and cognitive modulation of motor behavior.

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Deep brain stimulation of the subthalamic nucleus and behavioral complications of Parkinson's disease: a 2-year prospective study

Chiara Sorbera, M. Barbuto, L. Ricciardi, A. Epifanio, P. Girlanda, L. Morgante, F. Morgante

Dipartimento di Neuroscienze, Università di Messina, Messina

Introduction: The effect of deep brain stimulation (DBS) on behavioral complications of Parkinson's disease (PD) is controversial so far. Either improvement or worsening after surgery of impulse control disorders (ICD) and dopamine dysregulation syndrome (DDS) has been reported. Prospective long-term studies are lacking, nor the clinical variables or the stimulation setting associated to modulation of these symptoms are known.

Objective: In this 2-year prospective study, we evaluated the effect of bilateral DBS of the subthalamic nucleus (STN) on behavioral complications of PD.

Methods: 17 PD patients undergoing STN-DBS underwent prospective clinical, cognitive and behavioral assessment at baseline and after surgery (at 6,12,18,24 months). Specifically, for behavioral symptoms we applied the following scales: apathy evaluation scale (AES), punding rating scale, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), Barratt Impulsiveness Scale (BIS), Snaith-Hamilton Pleasure Scale. Correlational analysis was used to explore which clinical variable was associated to improvement/worsening of behavioral complications.

Results: After STN-DBS, motor UPDRS in OFF medication improved without worsening of cognitive status. Preoperative DDS disappeared in 4/6 and behavioral addictions in 6/7.
Apathy developed after DBS in 12/17 patients, improving at 1 and 2-year follow-up. Reduction of levodopa (LEDD) and dopamine agonists (LEDD-ag) equivalent daily dose was correlated with improvement of DDS and ICD after surgery.

Conclusion: Our data demonstrated that successful STN-DBS is efficacious in treating behavioural complications of PD, through a decrease of dopaminergic medications.

P100

Imaging of the dopamine transporter predicts pattern of disease progression and response to levodopa in patients with schizophrenia and parkinsonism: a 2-year follow-up multicenter study

Angela Matinella[1], *F. Morgante*[2], *T. Bovi*[1], *A. Cannas*[3], *P. Solla*[3], *A. Nicoletti*[4], *M. Zappia*[4], *A. Luca*[4], *A. Di Stefano*[4], *L. Morgante*[5], *C. Pacchetti*[6], *B. Minafra*[6], *M. Sciarretta*[6], *C. Dallocchio*[7], *S. Rossi*[8], *M. Ulivelli*[8], *R. Ceravolo*[9], *D. Frosini*[9], *A. Cipriani*[10], *C. Barbui*[10], *M. Tinazzi*[1]

[1]Department of Neurological, Neuropsychological, Morphological and Motor Sciences, University of Verona,Verona
[2]Dipartimento di Medicina Clinica e Sperimentale, University of Messina, Messina
[3]Department of Cardiovascular and Neurological Sciences, Section of Neurology, University of Cagliari, Cagliari
[4]Department "GF Ingrassia", Section of Neurosciences, University of Catania, Catania
[5]Department of Neurosciences, University of Messina, Messina
[6]Parkinson's Disease and Movement Disorders Unit, Instituto di Ricovero e Cura a Carattere Scientifico (IRCCS) C. Mondino National Institute of Neurology Foundation, Pavia
[7]A.O.Pavia, Division of Neurology, The Civil Hospital, Voghera
[8]Department of Neurosciences, Section of Neurology, University of Siena, Siena
[9]Department of Neurosciences, University of Pisa, Pisa
[10]Department of Public Health and Community Medicine, Section of Psychiatry and Clinical Psychology, University of Verona, Verona
[11]Department of Public Health and Community Medicine, Section of Psychiatry, University of Verona, Verona

Patients chronically exposed to antipsychotic drugs might develop parkinsonism that may persist even after drug withdrawal. We recently demonstrated evidence of nigro-striatal denervation by single photon emission computed tomography of the dopamine transporter (^{123}I-FP-CIT SPECT) in patients with schizophrenia and parkinsonism, and raised the possibility of an underlying degenerative condition. In the present study, we longitudinally assessed progression of motor disability in the same cohort of patients, over a 2-year follow-up. We aimed to define clinical and neuroimaging features associated with disease progression. Clinical data were correlated to findings at ^{123}I-FP-CIT SPECT. Sixty patients who had been scanned at baseline visit were re-evaluated by motor Unified Parkinson's Disease Rating Scale (UPDRS) at 2-year follow-up (range 19-44 months). Patients were divided in two groups according to ^{123}I-FP-CIT SPECT results (normal = 33; abnormal = 27). Clinical response to levodopa over 3 month periods was probed in 35 patients (normal = 16; abnormal = 19).
Motor UPDRS at follow-up significantly increased only in patients with ^{123}I-FP-CIT SPECT. Levodopa treatment was associated to significant decrease of motor UPDRS only in the group with abnormal SPECT. After adjustment for possible confounders, linear regression analysis demonstrated that abnormal SPECT finding at baseline was the only predictor of motor disability progression and of better outcome of levodopa treatment.
Our results support the notion that a degenerative disease underlies parkinsonism in a sub-group of schizophrenic patients chronically exposed to antipsychotics, who may be identified by functional imaging of the dopamine transporter and might benefit from levodopa therapy.

P101

Quality of life in patients with craniocervical dystonia. Italian validation of the "Cervical Dystonia Impact Profile (CDIP-58)", and "Craniocervical Dystonia Questionnaire (CDQ-24)"

Margherita Fabbri[1], *M. Superbo*[2], *G. De Fazio*[2], *C.L. Scaglione*[1], *E. Antelmi*[1], *G. Basini*[1], *S. Nassetti*[1], *R. Plasmati*[1], *R. Liguori*[1]

[1]IRCCS Istituto delle Scienze Neurologiche e Dipartimento di Scienze Biomediche e NeuroMotorie, Università di Bologna, Bologna
[2]Department of Neuroscience and Sensory Organs, 'Aldo Moro' University of Bari, Bari

Introduction: Patients with craniocervical dystonia (CD) face a lifetime of chronic visible disability and impaired health related quality of life (HR-QoL). Two disease-specific scales: "The Cervical Dystonia Impact Profile (CDIP-58)" and the "Craniocervical Dystonia Questionnaire (CDQ-24)" were recently validated for measuring QoL in craniocervical dystonia patients.

Objective: To validate the Italian version of the CDQ-24 and the CIDP-58.

Method: A back translation of the CDQ-24 and CDIP-58 was performed. Patients with idiopathic CD were recruited from two Botulinum Toxin Units of the Universities of Bologna and Bari. CD patients received the SF-36, CDIP-58 and CDQ-24 scales before (T0) botulinum toxin A treatment (BTA) and four weeks after treatment (T1). Patients with blepharospasm (BSF) received SF-36 and CDQ-24 at T0 and T1, while 42 age, sex and comorbidity-matched controls received the SF-36.

Results: 75 patients were enrolled in the study, 41 with CD and 34 with BSF with a mean age of 61± 12 years and a mean disease duration of 21± 16 years. Five patients abandoned the study due to questionnaire-induced anxiety. SF-36 score was significantly worse in patients than controls. SF-36 score significantly correlated with CDQ-24 and CDIP-58. Statistical differences between T0 and T1 scores were observed in: a) CDQ-24 total score and in three subscales ("emotional wellbeing", "pain" and "activities of daily living"); b) "pain and discomfort" subscale of CDIP-58; c) "role-physical" subscale of SF36. CD patients had a worse score for "emotional wellbeing" and "activities of daily living" subscales compared with BSF patients.

Conclusion: We validated the Italian version of the CDQ-24 and CDIP-58. HR-QoL measurement is pivotal in the management of CD patients.
The SF-36 could not detect the therapeutic efficacy of BTA. CDQ-24 effectively detected the QoL-modified aspects pre and post BTA whereas we did not obtain the same results for CPID-58.

P102

A long-term follow-up echocardiographic study of the cardiac valvulopathies related to ergot-derived dopamine agonists (EDA) in Parkinson's disease (PD) patients

Elena Marchesi[1], *A. Negrotti*[1], *W. Serra*[2], *M. Angelini*[1], *S. Calzetti*[1]

[1]UO Neurologia, Azienda Ospedaliero-Universitaria, Parma
[2]UO Cardiologia, Azienda Ospedaliero-Universitaria, Parma

Introduction: Restrictive valvular heart disease has been reported in PD patients in association to the chronic use of ergot-derived dopamine agonists, such as pergolide and cabergoline. The estimated prevalence of this adverse reaction is nearly 26%, but its potential reversibility after drug discontinuation has been poorly investigated. Furthermore, there is no data regarding the long term outcome of the cardiac valvulopathy.

Objective: This study is aimed at evaluating the long term reversibility of the valvular disfunctions related to EDA 3-5 years after drug discontinuation and replacement with non ergot DA agonists or L-dopa.

Methods: 15 PD patients (8 male and 7 female, mean age 66.47 years, mean disease duration 6.5 years), on chronic therapy with pergolide or cabergoline (mean duration of treatment 52.26 months ± 9.54 S.E.M., mean daily dosage 1.77 mg ± 0.19 S.E.M. expressed in pergolide equivalent), discontinued the EDA after echocardiographic detection of uni or multivalvular regurgitation and/or thickening of mitral valve. The patients were reevaluated after a mean follow-up period of 49 months. The following echocardiographic parameters were considered: severity of mitral, tricuspid and aortic valve regurgitation, sum of regurgitation, mitral valve tenting area and thickening of the mitral valve anterior leaflet (LAM).

Results: 80% of the patients showed a long-term echocardiographic improvement. A statistically significant reduction of the following parameters as compared to pre-withdrawal evaluation was found: severity of mitral and tricuspid valve regurgitation, sum of regurgitation, mitral tenting area and thickening of LAM. Neither a significant change in aortic valve regurgitation nor a relationship between valve disease regression and therapeutic variables, such as duration and dosage of EDA, were found.

Conclusion: Unlike previous studies, we detected a significant improvement of all the morphological and functional aspects of restrictive cardiac valve disease except one.
However, these valvulopathies seem to be not completely reversible despite a long term drug withdrawal.

P103

Cortical and brainstem plasticity in Gilles de La Tourette Syndrome and obsessive compulsive disorder

Flavio Di Stasio[1], *A. Suppa*[1,2], *L.Marsili*[1], *A. Latorre*[1] , *I. Berardelli*[1], *V. Roselli*[1], *M. Pasquini*[1], *F. Cardona*[3], *G. Fabbrini*[1,2], *A. Berardelli*[1,2]

[1]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome
[2]Neuromed Institute, "Sapienza" University of Rome, Pozzilli (IS)
[3]Department of Pediatrics, Child Neurology and Psychiatry, "Sapienza" University of Rome, Rome

Introduction: Patients with Gilles de la Tourette Syndrome (GTS) may manifest psychiatric comorbidity including Obsessive-compulsive disorder (OCD). In a small cohort of GTS patients, we have demonstrated abnormal cortical and brainstem plasticity as tested by the theta-burst stimulation (TBS) of the primary motor cortex (M1) and the high frequency stimulation (HFS) of the supraorbital nerve (SN).

Objective: Whether in GTS, the presence of OCD influences responses to TBS and SN-HFS remains unclear. We investigated M1 and brainstem plasticity in patients with "pure" motor GTS, GTS/OCD and OCD alone.

Methods: We studied 20 patients with "pure" motor GTS, 20 with GTS/OCD, 15 with OCD alone and 20 healthy subjects. We tested M1 plasticity by conditioning the left M1 with intermittent (iTBS) or continuous (cTBS) TBS. We recorded 20 motor evoked potentials (MEPS) from the right first interosseous muscle, before and after TBS. We tested brainstem plasticity by conditioning the right supraorbital nerve with facilitatory or inhibitory SN-HFS. We recorded 10 blink reflexes (BR) from the right orbicularis oculi muscle, and calculated the late response (R2) area, before and after SN-HFS.

Results: iTBS increased and cTBS decreased MEPs in healthy subjects and OCD. By contrast, iTBS failed to increase and cTBS failed to decrease MEPs in patients with "pure" motor GTS and GTS/OCD. The BR-R2 area increased after facilitatory SN-HFS and decreased after inhibitory SN-HFS, in healthy subjects and OCD. Conversely, in patients with "pure" motor GTS and GTS/OCD, facilitatory and inhibitory SN-HFS left the BR-R2 area unchanged.

Conclusion: Unlike healthy subjects, patients with "pure" motor GTS and GTS/OCD have reduced cortical and brainstem plasticity. By contrast, patients with OCD have normal cortical and brainstem plasticity. In GTS, the abnormal cortical and brainstem plasticity does not reflect the presence of OCD supporting the hypothesis that in GTS abnormal cortical and brainstem plasticity contribute to motor symptoms.

P104

Cerebellar transcranial direct current stimulation in Parkinson's disease

Marta Bianchi[1], *R. Ferrucci*[2,3], *T. Bocci*[2,4], *R. Turrone*[1], *D. Pitteri*[2], *E. Tomasini*[2], *F. Cogiamanian*[2], *G. Ardolino*[2], *A. Di Fonzo*[2], *M. Vergari*[2], *F. Mameli*[2], *M. Fumagalli*[2], *E. Scelzo*[2,3], *M. Rosa*[2,3], *B. Borroni*[1], *A. Padovani*[1], *A. Priori*[2,3]

[1]Clinica Neurologica, Spedali Civili di Brescia, Università degli Studi di Brescia, Brescia
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan
[3]Università degli Studi di Milano, Milan
[4]Università degli Studi di Pisa, Pisa

Background: Increasing evidence suggests that the cerebellum plays a role in the pathophysiology of Parkinson's disease (PD). Transcranial cerebellar Direct Current Stimulation (tcDCS) is a recently validated, noninvasive method for modulating the activity of the human cerebellum.

Objective: To assess whether daily tcDCS can induce motor improvement in patients with PD.

Methods: 6 patients [(aged 37-85)(male=3)] diagnosed as having idiopathic PD were recruited. We delivered two different types of stimulation, anodal and sham tDCS, in random order, in two separate experimental sessions at intervals of at least 1 month. The stimulating current was anodal DC at 2 mA intensity, delivered for 20 minutes for five consecutive days. In each session, the Unified Parkinson's Disease Rating Scale (UPDRS-III and –IV), the Parkinson' Disease Questionnaire-8 (PDQ8) and the Beck Depression Inventory (BDI) were administered before (baseline) and after the treatment.

Results: After five days of anodal tcDCS the UPDRS total score improved by about 24% while sham tDCS left it unchanged [(mean±SEM); Anodal vs Sham: -24%±7.6 vs 8% ±3.2; p=0.03)]. Anodal tcDCS did not change PDQ8 and BDI.

Conclusion: Our results showed an improvement of motor function after anodal tcDCS. This conclusion argues in favor of a role of the cerebellum in the pathophysiology of PA and opens the possibility of using the cerebellum as novel target for treating PD with a simple, non-invasive, brain stimulation technique.

P105

Ventral visual stream is more impaired than dorsal stream in prodromal DLB: a cognitive study

Silvia Favaretto, N. Jelcic, F. Gnoato, S. Parise, G. Rolma, G. Zorzi, M. Tagliapietra, A. Cagnin

Department of Neurosciences, University of Padova, Padova

Background: The pattern of cognitive decline in dementia with Lewy bodies (DLB) is typically characterized by attentive, executive and visual-spatial deficits.

Aim: To investigate the presence and type of deficit in visual abilities (spatial-perceptual-constructive) in the prodromal phase of DLB.

Materials and methods: 25 patients with non-amnestic Mild Cognitive Impairment (MCI) (MMSE ›27/30) diagnosed as prodromal DLB were enrolled (mean age: 75.5±6.1 years; mean MMSE score: 28.5±1). The diagnosis of DLB was confirmed at 3-year follow-up visit according to established criteria. A group of 60 patients with mild to moderate DLB dementia (MMSE ‹ 27/30) served as control group (mean age: 75±6.4 years; mean MMSE score: 22.4±2.6; p

Results: Visual perceptual deficits were detected in 83% of the DLB-MCI patients: the performance in the subtest 2 (silhouettes task) was pathological in 71% and borderline in 12% of MCI patients. This frequency was similar to that of the DLB-dementia group (p=0.14). In the subtests exploring visual-spatial abilities (subtests 5-8) the DLB-MCI patients scored differently from the DLB-dementia cases being within the normal range in more than 50% of cases. The scores at VOSP subtests did not correlate with disease duration, while they correlated with the disease severity (MMSE score) except for VOSP subtest 2 (p=0.14).

Discussion: Although visual-spatial deficits are claimed to be an hallmark of DLB since the early stages, a specific battery for visual-spatial and perceptual abilities showed that early deficits in visual perceptual abilities are more frequent than those in the visual-spatial and constructive spectrum. This findings suggest a progression of the cognitive deficits from the ventral to the dorsal visual pathway during the disease course, while specific perceptual deficits are detectable with dedicated tools in the very early stage of DLB.

P106

In vivo evidence of cerebello-thalamo-cortical network dysfunction in essential tremor

Valentina Nicoletti[1], *M. Cosottini*[2], *P. Cecchi*[2], *D. Frosini*[1], *I. Pesaresi*[2], *U. Bonuccelli*[1], *R. Ceravolo*[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa
[2]Neuroradiology Unit, Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa

Introduction: Essential tremor (ET) has been considered as a monosymptomatic disorder, characterized by only postural and kinetic tremor; however recently other motor and non-motor symptoms have been included in the clinical spectrum. Neuropathological findings and the increasing incidence of ET with age have also suggests a neurodegenerative basis.

Objective: To identify the brain structures involved in the pathogenesis of ET and to compare ET patients with (ET+R) and without (ET-R) resting tremor.

Methods: 32 patients with diagnosis of possible or probable ET (18 ET+R; 14 ET-R) and 12 healthy controls (HC) underwent a 3T-MRI with acquisition of a 3D T1-weighted sequence which were analyzed with Voxel-Based Morphometry (VBM). We also performed an fMRI examination during continuous writing of “8” with right dominant hand. We also performed a FP-CIT SPECT in all ET+R patients which excluded a dopaminergic degeneration.

Results: VBM-analysis showed no gray and white matter abnormalities when both ET patients were compared to HC and ET+R to ET-R patients. HC with respect to ET patients showed a significant higher activation in BOLD response related to the motor task in left precentral, frontal superior, postcentral and cinguli gyrus, in left supplementar motor area and inferior parietal cortex. Left thalamus and right cerebellum also presented areas of higher activation in HC compared to ET patients. Activation maps between ET-R and ET+R showed lower activation in the latter in precentral gyrus bilaterally, left postcentral and supramarginal gyrus and in globus pallidus internus.

Conclusion: Our results confirm for the first time with an imaging study a dysfunction in ET patients in the cerebello-thalamo-cortical network, which electrophysiological studies have shown to be implicated in many types of tremor, including ET. Globus pallidus, previously reported as involved in rest tremor in Parkinson’s disease, could be participate to rest tremor even in ET patients.

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Obsessive-compulsive personality disorder in never treated Parkinson's disease patients

Antonina Luca, A. Nicoletti, L. Raciti, G. Sciacca, V. Dibilio, G. Mostile, E. Bruno, D. Contrafatto, C.E.Cicero, M. Zappia

Dipartimento GF Ingrassia Sezione di Neuroscienze Università di Catania, Catania

Objective: Aim of the study was to evaluate the frequency of personality disorders in de novo Parkinson's disease (PD) patients and in a group of healthy subjects.

Methods: Never treated patients affected by PD diagnosed according to the United Kingdom Parkinson's disease Society Brain Bank diagnostic criteria and a group of healthy controls were enrolled in the study. PD patients with cognitive impairment were excluded from the study. To evaluate the presence of personality disorders, diagnosed according to the DSM-IV, the Structured Clinical Interview for Personality Disorders-II (SCID-II) has been performed and the diagnosis was confirmed by a psychiatric interview.

Results: 33 PD patients (18 men; mean age 61.7 ± 9.5 years) and 35 healthy subjects (15 men; mean age 57.1 ± 9.9 years) were enrolled in the study. The most common personality disorder was the obsessive-compulsive personality disorder (OCPeD) diagnosed in 21 PD patients and in 6 controls subjects (p-value,0.0001) followed by the depressive personality disorder (DPeD) recorded in 7 PD patients and 4 control subjects (p-value 0.2). OCPeD was not significantly associated with age, UPDRS-ME score and early onset.

Conclusion: never treated PD patients presented a high frequency of OCPeD that does not seem to be related with both age, age at onset and UPDRS-ME. Due to the high prevalence of OCPeD found in the de novo PD patients, personality disorders could be a non-motor early manifestation of PD.

P108

Correlation between Italian olfactory identification test (IOIT) scores and clinical features in Parkinson's disease

E. Brahimi[1], *N. Tambasco*[1], *C. Maremmani*[2], *P. Eusebi*[3], *Simone Simoni*[1], *E. Sacchini*[1], *A. Gallina*[1], *E. Marsili*[1], *E. Luchetti*[1], *F. Ripandelli*[1], *P. Nigro*[1], *A. Rossi*[1], *P. Calabresi*[1]

[1]Clinica Neurologica, Azienda Ospedaliera – Università di Perugia, Perugia
[2]U.O. Neurologia, ASL1 Massa Carrara, Massa Carrara
[3]Dipartimento di Epidemiologia, Regione Umbria, Perugia

Introduction: Olfactory dysfunction is an important biomarker for Parkinson disease (PD) because of the high prevalence (>90%) among PD patients. Hyposmia develops during the early stages of PD and, therefore, may be one of the most sensitive markers for the early diagnosis of PD.
Impairments in the sense of smell, in several modalities; odor detection, discrimination and identification, may even precede the development of overt motor symptoms by as long as 5 years, and this further emphasizes the potential value of hyposmia as a preclinical sign of PD [1]. Unfortunately, studies on the relationship between olfaction and motor and non-motor functions in PD are scarce and contradictory.

Objective: The aim of our study was to investigate the relationship between clinical variables (motor and non-motor functions) and olfactory dysfunction in PD patients.

Methods: Participants comprised of 98 patients with idiopathic PD (mean H&Y: 2, mean age 67 years, mean disease duration 5.8 years) and without dementia. We assessed the clinical features using different scales (UPDRS part III, PD non motor symptom scale – NMSS -, PD sleep scale – PDSS -, Beck depression inventory – BDI II, Montreal cognitive assessment-MOCA).
Odor identification ability was tested using Italian Olfactory Identification Test (33-testers) designed for the Italian population [2].

Results: The relationship between IOIT scores and clinical features was analyzed using the ANOVA test. The statistical analysis was conducted using SAS software (9.1 version, SAS Institute Inc.). The analyses revealed that odour identification test scores correlated positively with both motor, such as postural disturbances ($p < 0,05$) and dyskinesias ($p < 0,05$) and non motor-features (such as sleep disorders, $p < 0,05$). Using the IOIT we previously identified 3 odors (basil, coffee, watermelon) that PD patients most frequently failed to recognize compared to age and gender matched controls. We did not find any correlation between smell identification scores and disease duration and severity.

Conclusion: It remains unknown whether the variability in olfactory performance has prognostic significance for the later course of the disease. However it is possible the olfactory testing, also in association with other biomarkers, may be a useful marker to identify patients at risk for major complications correlated to PD (such as postural disturbances and dyskinesias). This test might also provide prognostic information possibly allowing in the future to better target these patients with disease-modifying therapies that might delay or mitigate these devastating effects.

References

[1] Ponsen MM, Stoffers D, Booij J, Van Eck-Smit BL, Wolters ECh, Berendse HW. Idiopathic hyposmia as a preclinical sign of Parkinson's Disease. Ann Neurol. 2004 Aug; 56 (2): 173-81
[2] Maremmani C, Rossi G, Tambasco N, Fattori B, Pieroni A, Ramat S, Napolitano A, Vanni P, Serra P, Piersanti P, Zanetti M, Coltelli M, Orsini M, Marconi R, Purcaro C, Rossi A, Calabresi P, Meco G. The validity and reliability of the Italian Olfactory Identification Test (IOIT) in healthy subjects and in Parkinson's disease patients. Parkinsonism Relat Disord. 2012 Jul;18(6):788-93

P109

Emergency in advanced Parkinson's disease: diagnostic pitfalls

Roberta Arca[1], *D. Murgia*[2], *V. Ricchi*[2], *F. Marrosu*[3], *M. Melis*[2], *G. Cossu*[2]

[1]Scuola di Specializzazione Medica in Neurologia, Università degli Studi di Cagliari, Cagliari
[2]Sezione di Neurologia e Stroke Unit, Azienda Ospedaliera G. Brotzu, Cagliari
[3]Dipartimento di Scienze Cardiovascolari e Neurologiche, Policlinico Universitario di Monserrato, Cagliari

Background: Patients with advanced Parkinson disease (APD) can develop a wide amount of disabling symptoms but their acute onset is infrequent. We report three patients with APD referred to our emergency department for the sudden worsening of their parkinsonian symptoms. A further evaluation by movement disorder experts allow to find out an alternative diagnosis.

Case 1: 65-years-old male with 12-years history of PD. He showed a rapid worsening in his postural stability with frequent falls and freezing of gait. On admission, a PD exacerbation was suspected. Due to the report of recent falls, a brain CT scan was performed showing a right subdural hematoma. He underwent neurosurgery with a rapid improvement in his clinical conditions.

Case 2: 78-years-old male with a 14-years hystory of PD. He developed a sudden deterioration of his parkinsonian symptoms with, in particular, impairment of bradikinesia, postural instability, tremor together with behavioral complications. He also referred a remarkable low back pain. Lumbar MRI showed a L1-L2 spondylodiscitis with right psoas muscle abscess extending to the gluteal muscles and intrapelvic area. He underwent appropriate antibiotic therapy with complete clinical recovery.

Case 3: 64-years-old male with 14-years history of PD. He complained of a prominent postural instability with difficultly in standing and gait and, expecially, of painful paresthesia and strength deficit at his left hemisoma. As hemiparesis is generally unrelated with PD, a cervical MRI has been carried out showing a severe spondylosis with partial synostosis in C3-C4-C5-C6 with a cord signal changes at C5-C6,suggestive of lower cervical myelopathy. He underwent neurosurgery (placement of a cervical metallic distractor) with clinical recovery.

Conclusion: Acute motor complications in APD could frequently be due to unrelated medical conditions. A failure or a delay to diagnose and treat concomitant illnesses can result in a significant sickness. Our work stresses the importance of collecting an accurate anamnesis and performing a full medical examination not limited to extrapyramidal system.

P110

A randomized, placebo-controlled study evaluating the effects of deep repetitive transcranial magnetic stimulation with H-Coil in Parkinson's disease

Francesca Spagnolo[1,2], *M. Fichera*[1,2], *R. Chieffo*[1,2], *E. Houdayer*[1], *L. Straffi*[1], *E. Coppi*[1,2], *A. Nuara*[1,2], *G. Di Maggio*[1,2], *M. Bianco*[1], *D. Dalla Libera*[1,2], *S. Velikova*[1], *M.A. Volonté*[1], *A. Zangen*[3], *G. Comi*[1,2], *L. Leocani*[1]

[1]Institute of Experimental Neurology and Neurological Department, Scientific Institute Hospital San Raffaele, Milan
[2]Vita-Salute University, Scientific Institute Hospital San Raffaele, Milan
[3]Neuroscience Laboratory, Ben-Gurion University of the Negev, Tel Aviv, Israel

Objective: To evaluate safety and efficacy of deep repetitive transcranial magnetic stimulation (rDTMS) performed with H-Coil as add-on treatment for motor symptoms of Parkinson's disease (PD). This is a double-blind, randomized placebo-controlled study.

Patients and Methods: Sixty patients affected by PD were randomized into 3 groups: Group 1, receiving real stimulation both on primary motor (M1) and prefrontal (PF) cortices; Group 2 receiving real rDTMS on M1 and sham on PF, and Group 3, receiving both sham stimulations; rDTMS at 10 Hz was applied for four weeks, for a total of 12 sessions. Primary outcome was percent reduction of Unified Parkinson's Disease Rating Scale (UPDRS) part III, OFF therapy. Secondary outcomes were: changes in UPDRS part III sub-scores; improvement in timed tests (Hand Tapping-HT, Foot Tapping-FT, Walking Time-WT at 20 meters, Nine Hole Peg Test -NHPT). Primary outcome was tested in hierarchical order, by comparing the two real groups (1-2) only if, combined, they significantly differ from sham.

Results: No drop-outs or serious adverse effects were recorded during the study. One patient randomized to real M1/PF stimulations was excluded soon after for uncontrolled diabetes. Patients receiving real rDTMS showed a significant improvement vs sham in UPDRS III (p=.007), tremor subscore (p=.011) and lateralized sub-scores (p=.042 and p.012 for worse and better sides respectively). Timed tests significantly improved in the real group when considering the worse side (HT p=.041, FT p=.012, NHPT p=.003). Following the hierarchical analysis, both real rDTMS groups (1 and 2) improved significantly more than sham in UPDRSIII (p.010 and p.045 respectively), while they did not significantly differ between them.

Conclusion: Repetitive deep brain stimulation with H-Coil is safe and potentially effective as add-on treatment in PD. The encouraging results of this preliminary study need to be further validated, especially regarding the duration of clinical improvement.

P111

Usefulness of Magnetic Resonance Parkinsonism Index in differentiating progressive supranuclear palsy from vascular parkinsonism

Giovanni Mostile, A. Nicoletti, C.E. Cicero, T. Cavallaro, E. Bruno, V. Dibilio, A. Luca, G. Sciacca, L. Raciti, D. Contrafatto, M. Zappia

Department GF Ingrassia, Section of Neurosciences, University of Catania, Catania

Background: Morphometry analysis of selected brain structures using conventional Magnetic Resonance Imaging (MRI) has been extensively proposed as reliable tool to differentiate Progressive Supranuclear Palsy (PSP) from Parkinson's disease and other atypical parkinsonisms using a Magnetic Resonance Parkinsonism Index (MRPI). However, no studies have focused on accuracy of such measures in differentiating PSP from Vascular Parkinsonism (VP).

Objective: To investigate accuracy of the MRPI in differentiating PSP from VP.

Methods: We retrospectively analyzed radiological data of N = 12 PSP patients (sex: 7 women, age: 70.1 ± 6.5 years) and N = 17 age and sex-matched VP patients (sex: 6 women, age: 71.4 ± 5.5 years) who performed a standardized brain MRI during their clinical admission. PSP patients satisfied the Litvan et al proposed diagnostic criteria (Neurology 1996;47:1-9). VP patients fulfilled the Zijlmans et al proposed diagnostic criteria (Mov Disord 2004;19:630-40) presenting a weak response to dopaminergic chronic therapy evaluated at the follow-up visits. Morphometry analysis of selected brain structures was performed to all study subjects and the MRPI was calculated for each selected patient.

Results: MRI midbrain area as well as superior cerebellar peduncle width were significantly lower in PSP patients compared to VP subjects. MRPI was significantly higher in PSP patients compared to VP subjects. MRPI value equal or greater than 13 distinguished the two groups with a sensibility of 100% (95%CI: 69.9 - 100) and a specificity of 100% (95%CI: 77.1 - 100).

Conclusion: MRPI may represent an accurate tool in differentiating PSP from VP.

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