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ORAL PRESENTATIONS

OP1
Resting-state neural correlates of fatigue in "drug-naïve" patients with Parkinson's disease

Alfonso Giordano[1,2], Rosa De Micco[1], Giuseppina Caiazzo[3], Antonio Russo[1,2], Mario Cirillo[4], Fabrizio Esposito[5,6], Gioacchino Tedeschi[1], Alessandro Tessitore[1]

[1]Department Medical, Surgical, Neurological, Metabolic and Aging Sciences, Second University of Naples, Naples, Italy; [2]IDC Hermitage Capodimonte, Naples, Italy; [3]MRI Research Center SUN-FISM, Second University of Naples, Naples, Italy; [4]Neuroradiology Service, Second University of Naples, Naples, Italy; [5]Department of Medicine and Surgery, University of Salerno, Baronissi, Salerno, Italy; [6]Department of Cognitive Neuroscience, Maastricht University, Maastricht, The Netherland

Introduction: Distressing fatigue is a common problem in patients with Parkinson disease (PD) [1]. Despite its clinical relevance, our understanding of fatigue pathophysiology is limited due to the frequent overlap with other confounding non motor symptoms (NMS) [1] and the lack of previous structural or functional studies.
Objective: The aim if this study was, using resting-state (RS) fMRI, to investigate the functional correlates of distressing fatigue in a restricted cohort of "drug-naïve" PD patients non-depressed, with no sleepiness and cognitively unimpaired.
Methods: 20 PD patients with (f-PD) and without (nf-PD) fatigue and 20 healthy controls (HCs) were enrolled in the study. The presence of distressing fatigue was defined based on the 16-item Parkinson fatigue scale (PFS-16) [2]. Single-subject and group-level independent component analysis was used to investigate functional connectivity differences within the major RS networks between patients subgroups and HCs. Moreover, based on previous studies, a region of interest analysis (ROI) in the supplementary motor area (SMA) was also performed. Voxel-based morphometry was used to detect structural abnormalities.
Results: Distressing fatigue was associated with an increased connectivity in the prefrontal and posterior cingulate cortices within the DMN and a decreased connectivity in pre-motor cortex within the SMN. ROI analysis showed a decreased connectivity in the SMA between all PD patients and HCs and when f-PD were compared with nf-PD. Fatigue severity was associated with DMN and SMN changes. VBM analysis did not reveal any significant volume differences between all PD patients and HCs and between f-PD and nf-PD patients.
Conclusions: In "drug-naïve" PD patients primary PD-related fatigue was associated with an altered connectivity within DMN and SMN. We hypothesize that RS functional changes may play a compensatory or a maladaptive role into the pathogenesis of this disabling NMS.
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OP2
GPi-DBS using frame-based versus frameless stereotaxy in dystonia: a single centre experience

Christian Lettieri[1], Sara Rinaldo[1], Grazia Devigili[1], Federica Pisa[2], Massimo Mondani[3], Stanislao D'Auria[3], Miran Skrap[3], Roberto Eleopra[1]

[1]Neurology Unit, "S. Maria della Misericordia" University Hospital, Udine, Italy; [2]Institute of Hygiene and Clinical Epidemiology, "S. Maria della Misericordia" University Hospital, Udine, Italy; [3]Neurosurgery Unit, "S. Maria della Misericordia" University Hospital, Udine, Italy

Background: Bilateral globus pallidus deep brain stimulation (GPi-DBS) represents a well established and effective therapy for primary refractory dystonia. The aim of this study was to assess, retrospectively, the effect of two different surgical procedures during GPi-DBS in 20 patients affected by primary generalized or multi segmental dystonia.
Materials and methods: 10 patients were operated with a frame-based stereotaxy whilst the other 10 patients underwent surgery with a frameless technique. Clinical features were evaluated for each patient at baseline, 6 and 12 months after surgery by means of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS).
Results: During GPi-DBS frame-based and frameless stereotaxy provided comparable clinical outcomes without any surgical complications.
Conclusions: Frameless surgery is safe and effective during GPi-DBS for primary dystonia and it could be a better choice as compared to frame-based surgery owing the higher patient compliance.

OP3
Gastroesophageal dysmotility in advanced Parkinson's disease

Francesca Mancini[1], Luigi Manfredi[1], Anna Bianchi[1], Marco Lacerenza[1], Carlotta Colombo[2], Alberto Bestetti[2]

[1]Centro Parkinson e Disordini del Movimento, Servizio di Neurologia, Casa di Cura San Pio X, Fondazione Opera San Camillo, Milano, Italy; [2]Servizio di Medicina Nucleare, Dipartimento di Scienze Cliniche e Biomediche, Università di Milano, Casa di Cura San Pio X, Fondazione Opera San Camillo, Milano, Italy

Introduction: Gastrointestinal dysfunction is the most common non-motor symptom of Parkinson's disease (PD), and has been often attributed to gastroparesis. In PD patients, gastroparesis has the potential to affect the absorption of medications and, consequently, motor function.

Objectives: The aim of this study is to evaluate the patterns of gastroparesis in PD patients with motor fluctuations and dyskinesias.
Methods: Scintigraphy with radiolabeled sulfur colloid added to acidified orange juice was performed in 32 consecutive advanced PD patients 1 h after their usual dopaminergic therapy first dose in the morning, to evaluate, among others data, the gastric emptying half time T1/2 (GE). Clinical evaluations at scintigraphy time consisted of collection of demographic, neurological, gastrointestinal and pharmacological data.
Results: The 32 patients (14 women, mean age: 65.3 ± 10.5 years, mean disease duration: 10 ± 5.7 years, mean UPDRS III in ON: 17.7 ± 12.4, median H&Y 3) were divided into 2 groups, using the cut-off point of 40 min obtained in normal subjects. The subgroup 1 consisted of 15 patients (68 ± 9.3 years) with GE T1/2 of 26.6 ± 6.9 min (normal), the subgroup 2 (62.9 ± 11.2) showed a GE of 88.7 ± 58 min (delayed). There were no significant differences in demographic or clinical parameters between patients of two groups with the exception of disease duration, that was significantly lower in group 2 (8.24 ± 3.75 years vs 12.87 ± 6.5; $P < 0.03$). Linear regression showed a significant correlation between GE and dosage of peripheral inhibitors ($P = 0.013$).
Conclusions: This preliminary observational study outlines that delayed GE is present in approximately 50 % of PD patients with motor fluctuations (delayed-on, wearing off, on–off, no-on) and dyskinesias. The dosage of peripheral inhibitors may concur in GE delay and its consequent effect on drug delivery and efficacy.

OP4
Emotion recognition and emotion expression in Parkinson's disease

Lucia Ricciardi[1], Federica Visco-Comandini[1], Roberto Erro[1], Francesca Morgante[2], Matteo Bologna[3], Alfonso Fasano[4], Diego Ricciardi[5], Mark Edwards[1]* and James Kilner[1]

[1]Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, London, UK; [2]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [3]IRCCS Neuromed Institute, Pozzilli, Italy; [4]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital, UHN, Division of Neurology, University of Toronto, Toronto, Canada; [5]Department of Geriatry, Catholic University of Sacred Heart, Rome, Italy

Introduction: Parkinson's disease (PD) patients have impairment of facial expressivity (hypomimia) and difficulties in interpreting the emotional facial expressions produced by others, especially for aversive emotions.
Objectives: To evaluate whether in PD there is a deficit of specific emotions for both facial expressivity and recognition and whether these deficits are related to each other.
Methods: Twenty non-demented, non-depressed PD patients and 20 healthy subjects (HS) matched for demographic characteristics were studied. The ability of recognizing emotional facial expressions was assessed with Ekman-60-faces-test. Subjects were video-recorded while posing facial expressions of 6 primary emotions (happiness, sadness, surprise, disgust, fear and anger). The most expressive pictures of each subject for each emotion were derived from the videos. Ten healthy participants were asked to look at the pictures displayed on a computer-screen in pseudo-random fashion and to identify the emotional label in a six-forced-choice response format. Reaction time (RT) and accuracy of responses were recorded. At the end of each trial the participant was asked to rate his/her confidence in his/her perceived accuracy of response.
Results: *Emotion recognition*: PD reported lower score than HS for Ekman total score ($p < 0.001$) and for fear, anger and surprise subscores (all $p < 0.01$). *Emotion expressivity*: PD and HS significantly differed in facial emotion expressivity total score ($p < 0.001$) and happiness, sadness, anger (all $p < 0.001$) and surprise ($p < 0.05$) subscores. RT and level of confidence showed significant differences between PD and HS for the same emotions. *Correlation emotion recognition/expressivity:* there was a positive correlation between recognition and expressivity scores for surprise ($r = 0.55$, $p = 0.01$) and as a trend toward significance for disgust ($r = 0.4$, $p = 0.06$) in PD patients.
Conclusions: PD patients showed difficulties in recognizing facial emotional expressions produced by others and in posing emotional expressions. There was a positive correlation between recognition and expressivity of surprise. These results open important clinical and rehabilitation perspectives.

OP5
Correlation between non-motor symptoms and ^{123}I-FP-CIT SPECT in Sardinian Parkinson's disease patients

Paolo Solla, Antonino Cannas, Davide Fonti, Erika Erriu, Daniela Ciaccio, Rita Farris, Lorenzo Polizzi, Mario Meloni, Gianni Orofino, Gianfranco Costantini, Maria Giuseppina Ottolini, Francesco Marrosu

Movement Disorders Center, Department of Neurology, Institute of Neurology, University of Cagliari, Cagliari, Italy

Background: At present, there is not definitive evidence about possible correlation of data obtained at functional imaging of dopaminergic terminal obtained by nuclear medicine techniques such as ^{123}I-CIT-SPECT and non-motor symptoms in patients affected by Parkinson's disease (PD).
Objective: The aim of this study was the evaluation between the correlation of dopaminergic deficits assessed by ^{123}I-CIT-SPECT and non-motor symptoms in Sardinian PD patients.
Methods: Consecutive outpatients with a diagnosis of PD in accordance with the UK Brain Bank criteria were included in our study, with ^{123}I-CIT-SPECT examination performed within a maximum of 1 year before the enrollment visit. Semi-quantitative evaluation was performed with the assessment of specific Region of interests (ROI) and the determination of ratio caudate/occipital cortex and putamen/occipital cortex, both at level of affected side and contralateral. Presence and severity of motor symptoms were evaluated with the Non Motor Symptoms Scale (NMSS). Motor symptoms were also evaluated with UPDRS pars III and the analysis of different subtypes according to Williams and Lewis classifications.
Results: 52 patients (27 of male gender) were enrolled with age at observation equal to 67.5 ± 9.2 years. Analysis of the single items of NMSS showed a significant negative correlation between striatal uptake and item 28 (disturbances of smell and taste) both for the caudate ($r = 0.302$; $p = 0.030$) and the putamen ($r = -290$; $p = 0.037$). Regarding the correlation between uptake deficiency and non-motor symptoms a highly significant negative correlation with the putaminal deficit was highlighted both in relation to the UPDRS score-III [$r = -0.590$ ($p < 0.0001$)], both for what concerns the subscores of UPDRS III bradykinesia [$r = -0.565$ ($p < 0.0001$)], rigidity [$r = -0.640$ ($p < 0.0001$)] and posture/postural instability [$r = -0.399$;($p < 0.003$)].

Conclusions: We demostrated a clear correlation between loss of olfaction/taste and dopaminergic deficit releaved at ^{123}I-FP-CIT SPECT. Moreover, a further confirmation of previous study describing a correlation between dopaminergic impairment at ^{123I}-FP-CIT SPECT and severity of motor symptoms was observed.

OP6
Correlation among cortical thickness, depression and attention performance in early-stage Parkinson's disease

Stefano Zanigni[1,2], Luisa Sambati[2,3], Stefania Evangelisti[1,2], Giovanna Calandra-Buonaura[2,3], Raffaele Lodi[1,2], Pietro Cortelli[2,3], Caterina Tonon[1,2]

[1]Functional MR Unit, Policlinico S. Orsola–Malpighi, Bologna, Italy; [2]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy; [3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Introduction: Depression and attention deficits represent frequent early non-motor symptoms of Parkinson's Disease (PD) [1]. Gray matter alterations related to depression [2] and cognitive impairment [3] in PD have been reported, although studies investigating a correlation with cortical thickness (CT) in the early stages of the disease are lacking.
Objective: To evaluate the correlation between CT, depression and attention performance in early-stage PD.
Methods: we evaluated 16 non-demented possible PD patients (9 males; mean ± SD age: 61.2 ± 11.3 years; disease duration: 1.2 ± 0.8 years; Hoehn-Yahr scale: 43.7 % stage-1; 56.7 % stage-2; MMSE: 28.2 ± 1.3) with Beck's Depression Inventory (BDI), Barrage (BT) and immediate visual memory (IVM) tests. All patients underwent a 1.5T brain-MR protocol including high-resolution T1-w sequences. FreeSurfer's cortical reconstruction was performed to evaluate a vertex-wise correlation between CT and BDI, BT and IVM, controlling for age, sex and total intracranial volume.
Results: BDI score was 8.8 ± 6.4, with 6 patients presenting mild-moderate depression. No patients showed pathological BT and IVM test scores (0.04 ± 1.07 and 19.77 ± 2.18, respectively). At follow-up, all patients evolved to probable PD. CT was significantly increased ($p < 0.01$, uncorrected) in anterior-cingulate, medial-frontal, pre-cuneal, superior-parietal cortices in depressed PD patients vs non-depressed, with a direct correlation with BDI score ($p < 0.01$, uncorrected). Worse performances in BT and IVM were correlated to a CT reduction in posterior-cingulate, precuneal and parietal cortices and in superior-frontal, temporal-parietal and precuneal cortices, respectively ($p < 0.01$,uncorrected).
Conclusions: CT alterations in regions related to depression and attention performances may be evident also in the early stages of PD and may represent either a degenerative or an adaptive response to cortical network alterations [4].
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OP7
Polymorphisms of dopamine receptor genes are associated to increased risk of visual hallucinations in Parkinson's disease patients

Fabiola De Marchi[1], Marco Ferrari[2], Franca Marino[2], Gaia Oggioni[1], Luca Magistrelli[1], Silvia Rosa[1], Miryam Carecchio[1], Giulio Riboldazzi[3], Giorgio Bono[3], Marco Cosentino[2], Roberto Cantello[1], Cristoforo Comi[1]

[1]Department of Neurology, University of Eastern Piedmont, Novara, Italy; [2]Center of Research in Medical Pharmacology, University of Insubria, Varese, Italy; [3]Department of Neurology, University of Insubria, Varese, Italy

Background: Visual hallucinations (VHs) are a frequent non-motor complication of Parkinson's disease (PD). VHs are associated to a negative prognosis. Variations in the dopamine receptor (DRD) genes may have a role in predisposing to VHs; previous studies showed an association between DRD variations and Alzheimer's disease with psychosis, schizophrenia and bipolar disorder. Only one published study analyzed the relationship between DRD variations and VHs in PD, failing to detect a statistically significant association.
Objective: To determine whether single nucleotide polymorphisms (SNPs) of DRD genes are associated with VHs in PD patients.
Patients and methods: Case–control study of 84 PD subjects, 42 with and 42 without VHs matched for age, gender, disease duration and dopaminergic medication. Genomic DNA was analyzed by PCR for SNPs in both D1 (DRD1 A48G and C62T, DRD5 T798C) and D2-like receptor genes (DRD2 G2137A and C957T, DRD3 G25A and G712C, DRD4 C616G and nR VNTR 48 bp).
Results: We found that PD patients with, compared to those without VHs had a statistically increased frequency of allele G at DRD1 A48G (OR 3.7; $P = 0.0075$), allele T at DRD1 C62T (OR 10.7; $P = 0.0001$) and allele T at DRD2 C957T (OR 3.4; $P = 0.0286$). From a functional perspective, the detected variations may have a synergistic effect since they provide increase of D1 and decrease of D2 transmission.
Conclusions: Our study shows that PD patients with VHs display higher frequency of DRD SNPs that are known to increase cAMP intercellular levels. Our data are in line with associations published in psychiatric conditions. On a clinical level, our findings may provide valuable information for personalizing pharmacological therapy in PD patients.

OP8
Pain processing in de novo Parkinson's disease patients: an event-related fMRI study during nociceptive stimulation

Rosa De Micco[1], Antonio Russo[1], Fabrizio Esposito[2], Alfonso Giordano[1], Michele Fratello[2], Giuseppina Caiazzo[3], Gioacchino Tedeschi[1,3], Alessandro Tessitore[1]

[1]Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, Second University of Naples, Naples, Italy; [2]Department of Medicine and Surgery, University of Salerno, Baronissi (SA), Italy; [3]MRI Research Center SUN-FISM, Second University of Naples, Naples, Italy

Aims: To investigate, by means of functional MRI (fMRI), the brain reorganization of central nociceptive processing network in de-novo Parkinson's disease (DNPD) patients, during heat stimulation.

Introduction: Recent studies have demonstrated that PD patients show a reduced threshold and tolerance to pain stimulation, with or without pain symptoms. However, whether pain origin is principally central or peripheral has not been completely elucidated.
Methods: Twenty pain-free DNPD patients and 10 pain-free age and sex-matched healthy controls (HCs) were enrolled in the study. Contact heat evoked potential stimulation (CHEPS) inducing heat stimulation to the forearm was tested in all patients and HCs: 10 DNPD patients were tested on the more PD affected side and 10 on the less one. fMRI imaging were used to measure whole-brain activation in response to a severe (53 °C) and a control (41 °C) stimuli applied.
Results: When comparing the differential effects of the two stimuli (41 and 53 °C) on brain functional activation, DNPD patients showed significant clusters of greater activation in the pons and in the left post-central gyrus compared to HCs. This activation pattern did not correlate neither with the side nor with the severity of motor symptoms. Importantly, there were no significant differences in pain perception between DNPD patients and HCs.
Discussion: Our findings demonstrate an increased activation in brain regions known to be involved in pain processing in DNPD patients. This activation pattern may represent a compensatory reorganization to modulate pain perception at the same intensity of HCs. Since recent studies have shown that a peripheral deafferentation, possibly due to dopaminergic therapy, could play a role in the pathogenesis of pain in PD, we have demonstrated, studying DNPD, that an abnormal central pain processing may be a specific PD feature, likely related to dopaminergic system disregulation.
Conclusions: Our findings revealed an abnormal central pain processing in DNPD patients.

OP9
Primary motor cortex LTP/LTD-like plasticity in cortico-basal syndrome

Luca Marsili[1], Antonio Suppa[1,2]*, Flavio Di Stasio[1]*, Neeraj Upadhyay[1], Daniele Belvisi[1,2], Antonella Conte[1,2], Nicola Modugno[2], Carlo Colosimo[1], Giovanni Fabbrini[1,2], Alfredo Berardelli[1,2]

[1]Dipartimento di Neurologia e Psichiatria, Roma, Italy; [2]Istituto Neuromed, Pozzilli (IS), Italy; [3]"Sapienza" Università di Roma, Roma, Italy

Introduction: Whether the primary motor cortex contributes to the pathophysiology of motor and non-motor symptoms in cortico-basal syndrome remain largely unclear [1, 2].
Objectives: Given that the primary motor cortex long-term potentiation/depression-like plasticity is a crucial mechanism involved in motor execution and learning, in this study in cortico-basal syndrome, we tested primary motor cortex plasticity as reflected by long-term - changes in motor evoked potentials (after-effects) after theta-burst stimulation over the primary motor cortex contralateral to the limb manifesting "parkinsonian" and "parkinsonian plus" symptoms [3].
Methods: In 17 patients and 17 healthy subjects we applied intermittent and continuous theta-burst stimulation over the primary motor cortex contralateral to the limb manifesting "parkinsonian" and "parkinsonian plus" symptoms and measured theta-burst stimulation-induced after-effects.
Results: Theta-burst stimulation delivered over the primary motor cortex contralateral to the limb manifesting "parkinsonian" symptoms elicited fewer after-effects in patients than in healthy subjects. In a patient subgroup, transcranial magnetic stimulation applied to the primary motor cortex contralateral to the limb manifesting "parkinsonian plus" symptoms, elicited abnormally low-amplitude motor evoked potentials that prevented us from evaluating primary motor cortex plasticity. In the remaining patients, unlike healthy subjects, theta-burst stimulation elicited altered after-effects characterized by high inter-subject variability. A subsequent two-step cluster analysis, identified two patient clusters with different theta-burst stimulation-induced after-effects and clinical features.
Conclusions: By collecting plasticity changes over primary motor cortex contralateral to the limb manifesting "parkinsonian" and "parkinsonian plus" symptoms and clustering patients into specific subgroups, our study might help to explain the clinical and neurophysiological heterogeneity in cortico-basal syndrome.
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OP10
A four-year longitudinal study on restless legs syndrome in Parkinson's disease

Marcello Moccia[1], Roberto Erro[2,3], Marina Picillo[4–5], Gabriella Santangelo[6–7], Emanuele Spina[1], Roberto Allocca[1], Katia Longo[7], Marianna Amboni[7], Raffaele Palladino[8–9], Roberta Assante[10], Sabina Pappatà[11], Maria Teresa Pellecchia[4], Carmine Vitale[7,12], Paolo Barone[4]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, Federico II University, Naples, Italy; [2]Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, UK; [3]Department of Neurological and Movement Sciences, University of Verona, Policlinico Borgo Roma, Verona, Italy; [4]Center for Neurodegenerative Diseases (CEMAND), Neuroscience Section, Department of Medicine, University of Salerno, Salerno, Italy; [5]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Division of Neurology, Toronto Western Hospital, University of Toronto, Toronto, Canada; [6]Department of Psychology, Neuropsychology Laboratory, Second University of Naples, Caserta, Italy; [7]IDC Hermitage-Capodimonte, Naples, Italy; [8]Department of Primary Care and Public Health, Imperial College, London, UK; [9]Department of Public Health, Federico II University, Naples, Italy; [10]Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy; [11]Institute of Biostructure and Bioimaging, National Research Council, Naples, Italy; [12]Department of Motor Sciences, University Parthenope, Naples, Italy

Background and objectives: Restless legs syndrome (RLS) has a prevalence of 10–52 % in Parkinson's disease (PD). However, it is still debated whether RLS in PD is a premotor feature, a motor complication, or an association by chance. The present study aims to evaluate RLS prevalence in de novo PD subjects, and incidence during 4-year follow-up, together with laboratory, clinical and neuroradiological correlates.
Methods: This is a 4-year longitudinal study, with evaluations at the time of PD diagnosis, and after 2 and 4 years. One-hundred-nine newly diagnosed, drug naïve PD subjects were evaluated at the time of PD diagnosis, and after 2 and 4-year follow-ups at the

Movement Disorder Unit of Federico II University Hospital, Naples, Italy. Motor features, non-motor symptoms (NMS), concomitant dopaminergic and non-dopaminergic treatments were recorded. At baseline visit, 65 subjects were randomly selected to undergo a FP-CIT SPECT to study dopamine transporter availability. RLS diagnosis was performed with the RLS Diagnostic Index.

Results: RLS prevalence rose from 4.6 % (n = 5) at baseline evaluation, to 6.5 % after 2-year (n = 7), up to 16.3 % after 4-years (n = 16) (p = 0.007). A multinomial logistic stepwise regression model selected NMS Questionnaire items more likely to be associated with RLS at diagnosis: (insomnia, OR = 15.555; p = 0.040) and with occurrence of RLS during follow-up (dizziness, 1/2 OR = 1.153; p = 0.022; and daytime sleepiness; OR = 9.557; p = 0.001), as compared to patients without RLS. Older age was more likely associated to increased RLS occurrence during follow-up in a random effect logistic regression model (OR = 1.187; p = 0.036). A multinomial logistic stepwise model selected increased V3" values of affected caudate and putamen to be more likely associated with RLS presence at diagnosis (OR = 75.711; p = 0.077), and RLS occurrence during follow-up (OR = 12.004; p = 0.059), respectively, as compared to patients without RLS.

Conclusions: RLS is present since PD diagnosis, and increases in prevalence during the course of PD. PD subjects with RLS have higher age at PD onset, more preserved dopaminergic pathways, and worse sleep and cardiovascular disturbances.

OP11

Effects of cerebellar theta-burst stimulation on arm and neck movement kinematics in patients with primary dystonia

Giulia Paparella[1], Matteo Bologna[2], Andrea Fabbrini[1], Giorgio Leodori[1], Giovanni Fabbrini[1,2], Alfredo Berardelli[1,2]

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

Introduction: The pathophysiological mechanisms of dystonia are still not entirely clear. Dystonia is classically considered a disorder of basal ganglia but recent studies suggest a possible involvement of the cerebellum in this condition [1].

Objective: We aimed to investigate the cerebello-thalamo-cortical connectivity in primary focal dystonia using the cerebellar continuous theta burst stimulation-cTBS [2] and to evaluate its possible effects on arm and neck movement kinematics in patients.

Methods: Thirteen patients with focal hand dystonia, twelve patients with cervical dystonia and ten healthy subjects underwent two experimental sessions: (i) cTBS over the right cerebellar hemisphere (real cerebellar cTBS) and (ii) cTBS over the neck muscles (sham cerebellar cTBS). The two sessions were performed at least 1 week apart. The effects of real and sham cerebellar cTBS were quantified as excitability changes on contralateral primary motor cortex, as well as possible changes of dystonic movements, i.e. writing, fast neck movements and reaching movements on the ipsilateral arm in patients. Primary motor cortex excitability was assessed by recording the input/output curve of the motor evoked potentials from the right first dorsal interosseous muscle. Movement analysis was performed using kinematic techniques.

Results: Real cerebellar cTBS reduced the excitability in the controlateral primary motor cortex in healthy subjects and in patients with cervical dystonia, though not in patients with focal hand dystonia. There was no significant change in dystonic and reaching movements, as assessed by kinematic techniques, after real or sham cerebellar cTBS in patients.

Conclusions: The results suggest that the cerebello-thalamo-cortical connectivity tested by cTBS is not similarly involved in the pathophysiology of different types of dystonia and therefore this abnormality cannot be considered an endophenotipic trait of the disease.

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OP12

Advanced therapeutic options versus best medical treatment in Parkinson's disease: a long-term analysis of outcome

Alberto Romagnolo, Aristide Merola, Andrea Bernardini, Laura Rizzi, Elisa Montanaro, Serena Angrisano, Carlo Alberto Artusi, Francesca Dematteis, Mario Giorgio Rizzone, Maurizio Zibetti, Leonardo Lopiano

Department of Neuroscience, University of Turin, Turin, Italy

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) and levodopa/carbidopa intestinal gel infusion (LCIG) are established therapeutic options for Parkinson's disease (PD) with fluctuating symptoms unresponsive to conventional oral treatments (OT). Previous studies demonstrated a sustained improvement in activities of daily living (ADL) and motor fluctuations, but long-term comparative data among these therapeutic options still lack.

Objectives: To assess over a follow-up period of 5 years the effects of STN-DBS, LCIG and OT, comparing their efficacy on cardinal PD symptoms, motor fluctuations and ADL.

Methods: Thirty-six patients (12 STN-DBS, 12 LCIG and 12 OT) similar for demographic, clinical and neuropsychological characteristics were evaluated at baseline and after an average follow-up period of 5 years, by means of UPDRS.

Results: A progressive worsening of UPDRS-III in OFF-condition was present in all groups, while SNT-DBS and LCIG showed a better control of motor symptoms in ON-condition (p: 0.031). Regarding ADL impairment, the advanced therapies showed better outcomes, with a substantial stabilization of UPDRS-II Med-OFF in the LCIG group (−5 %), a significant improvement (−29.7 %) in STN-DBS group, and a significant worsening (+65.1 %) in OT group (p < 0.001). Motor fluctuation (UPDRS-IV) significantly improved both in STN-DBS (−65.5 %) and LCIG (−26.4 %), while OT patients reported a progressive worsening during follow-up (+55 %) (p < 0.001). Similarly, the percentage of waking day spent in OFF showed a sustained improvement in STN-DBS (−55 %) and LCIG (−52.3 %), with a worsening in OT patients (+79 %) (p < 0.001). On the contrary, only STN-DBS subjects reported a significant amelioration of the duration and severity of dyskinesias (−66.9 and −76.5 %; p < 0.01).

Conclusion: STN-DBS and LCIG confirmed a long-lasting superior clinical efficacy on motor fluctuations than oral medical therapy, lessening the severity of ADL impairment associated to the advanced PD phases. Moreover, STN-DBS seems to ensure a better control of duration and severity of dyskinesias.

VIDEO PRESENTATIONS

VP1
GPi-DBS in neuroacanthocytosis: a case report

Christian Lettieri, Sara Rinaldo, Grazia Devigili, Roberto Eleopra

Dipartimento di Neuroscienze, SOC di Neurologia, Azienda Ospedaliero-Universitaria "S. Maria della Misericordia", Udine, Italy

We describe the case of a 37 years old male patient affected by an oromandibular dystonia and facial dyskinesias associated with blepharospasm and involuntary movements of the trunk and limbs from January 2008. The complex diagnostic process has allowed us to make the diagnosis of neuroacanthocytosis. Because of the unresponsiveness to drug polytherapy/botulinum toxin injection, in September 2014 he underwent of bilateral GPi-DBS surgery under general anesthesia with significative benefit. We present the video documentation of preoperative baseline and follow-up 5 months after surgery, comparing the outcome with the recent data of the literature regarding DBS in the eredodegenerative forms.

VP2
Delirium induced by fever in an older patient with cognitive impairment: not always so simple

Damiano Baroncini, Mario Fichera, Vittorio Martinelli, Giancarlo Comi, Maria Antonietta Volontè

Università Vita-Salute San Raffaele Hospital, Neurology Department, INSPE, Milan, Italy

A 74 years old man with an unremarkable past history presented to emergency care with confusional state and fever. Careful recollection of clinical data with relatives undercovered a mild progressive decline in memory function over the last year. Routine blood exams showed only moderate hyponatremia and elevated CK. Chest and abdomen X-ray, as well as brain CT scan were unremarkable. He was admitted to medicine department, and started empiric antibiotic therapy and intravenous electrolytic therapy. As state of consciousness continued to worsen, leading to coma, a lumbar puncture was performed, showing increased proteins and cellularity. PCR for herpes viruses resulted negative. He was then transferred to our neurology ward. Clinical evaluation showed comatous state (GCS 9) with odd involuntary movements of the mimic musculature (video), midriasis with conserved response to light, neck and limbs paratonia, bilateral Babinski sign. Brain MRI resulted normal, except for atrophy of temporal lobes. A complete CT scan of the body showed no overt signs of infections as cause of the persisting fever and increased inflammatory state. EEG showed symmetrical slowing of cerebral activity without epileptiform abnormalities. A lumbar puncture was repeated, showing similar results to the previous, except for the presence of oligoclonal bands. Extensive research of onconeural antibodies showed positivity to anti NMDA-R on three different samples. He was started on intravenous immunoglobulins with no immediate clinical response and subsequently on steroids, with sustained improvement of clinical picture and disappearance of the involuntary facial movements. Anti NMDA-R encephalitis is becoming a frequent finding in the differential diagnosis of subacute confusional and psychiatric state, especially in young females [1]. Few cases of this entity were reported in older patient [2, 3], probably due to under-recognition. Progressive neurologic deterioration, orofacial dyskinesia and poor response to antiviral/antibiotic therapy should raise clinical suspicion.

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VP3
An atypical case of Pure Akinesia with gait freezing

Vincenzo Moschella[1], Maria Carla Massimetti[1], Enrica Olivola[2], Alessandro Stefanini[1], Paolo Stanzione[2], Alessandro Stefani[2]

[1]Neurological Service, San Camillo de Lellis General Hospital, AUSL of Rieti, Rieti, Italy; [2]Neurology Unit, University of Rome "Tor Vergata", Rome, Italy

Background: Pure Akinesia with Gait Freezing (PAGF) is a peculiar movement disorder, whose cardinal symptoms are freezing during walking, writing and speaking. Recently, several studies arranged it in the spectrum of tauopaties, particularly as a Progressive Supranuclear Palsy (PSP) variant with a low grade of pathological involvement [1, 2]. Since its nosology is still not completely defined, PAGF is often not or late diagnosed.

Aims: To describe a case of PAGF with asymmetrical involvement, whose diagnosis was performed with a complete clinical, neuropsychological and imaging evaluation.

Methods and results: A 77-years old woman, without relevant diseases a part of an episode of post-partum depression, came to our attention referring a 2 years history of gait disturbance, for whom she had done neurological evaluation, performed brain MRI (without relevant abnormalities) and received diagnosis of Parkinson disease. She had started treatment with low dose of levodopa, selegiline and a tricyclic drug, without improvement. During last months, gait difficulty has gradually worsened and at the moment of the visit patient was almost unable to walk alone. Neurological examination revealed severe freezing of gait, with asymmetry for marked right involvement. Supranuclear ophtalmoplegia, other parkinsonism features and any other neurological signs were absent. Discontinuation of therapy did not worse motor symptoms and an acute test with high dose of melevodopa failed to improve it. Patient underwent to a complete neuropsychological battery that revealed deficits in attention, executive functions and frontal-behaviours alterations, a profile significantly similar to PSP's. Finally, a ^{123}I-FP-CIT SPECT showed a decreased uptake in left putamen. According to literature [3, 4], these findings together allowed us to perform a diagnosis of PAGF.

Conclusions: A complete clinical, neuropsychological and neuroradiological analysis is essential to perform diagnosis of PAGF. Particularly, neuropsychological evaluation could give a significant contribution, especially in case of atypical presentation.

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POSTER PRESENTATIONS

YOUNG AND RESEARCH

PP1
Non-motor correlates of smoking habits in de novo Parkinson's disease

Roberto Allocca[1], Brit Mollenhauer[2,3,4], Marcello Moccia[1], Roberto Erro[5,6], Marina Picillo[7,8], Raffaele Palladino[9,10], Paolo Barone[7]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, Federico II University, Naples, Italy; [2]Paracelsus-Elena-Klinik, Kassel, Germany; [3]Department of Neurosurgery, University Medical Center Goettingen, Germany; [4]Department of Neuropathology, University Medical Center Goettingen, Germany; [5]Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, UK; [6]Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [7]Center for Neurodegenerative Diseases (CEMAND), Neuroscience Section, Department of Medicine, University of Salerno, Salerno, Italy; [8]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Division of Neurology, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada; [9]Department of Primary Care and Public Health, Imperial College, London, UK; [10]Department of Public Health, Federico II University, Naples, Italy

Background: Parkinson's disease (PD) subjects are less likely to ever smoke and are more prone to quit smoking, as compared to controls. Therefore, smoking habits can be considered part of the non-motor phenotype, preceding the onset of motor PD by several years.
Objectives: To explore non-motor symptom (NMS) correlates of smoking habits.
Methods: This cross-sectional study included 281 newly diagnosed, drug-naïve PD subjects, recruited in Naples (Italy) and in Kassel (Germany). All subjects completed the NMS Questionnaire (NMSQ), and were investigated for smoking status (never, current and former smokers) and intensity (pack-years).
Results: 140 PD subjects never smoked, 20 currently smoked, and 121 had quit smoking before PD diagnosis. NMSQ total score did not associate to smoking status, but to smoking intensity ($p = 0.028$; coefficient = 0.088). A multinomial logistic regression stepwise model presenting never smoking as reference, selected as NMSQ correlates of current smoking: sex difficulties ($p = 0.002$; OR = 5.254), daytime sleepiness ($p = 0.046$; OR = 0.085), insomnia ($p = 0.025$; OR = 0.135), and vivid dreams ($p = 0.040$; OR = 3.110); and of former smoking: swallowing ($p = 0.013$; OR = 0.311), nausea ($p = 0.027$; OR = 7.157), unexplained pains ($p = 0.002$; OR = 3.409), forgetfulness ($p = 0.005$; OR = 2.592), sex interest ($p = 0.007$; OR = 0.221), sex difficulties ($p = 0.038$; OR = 4.215), and daytime sleepiness ($p = 0.05$; OR = 0.372). An ordinal logistic regression stepwise model selected as NMSQ correlates of smoking intensity: nocturnal restlessness ($p = 0.027$; coefficient = 0.974), and leg swelling ($p = 0.004$; coefficient = 1.305).
Conclusions: Certain NMSs are associated with different smoking status and intensity, suggesting a variety of adaptive mechanisms to cigarette smoking, with heterogeneous changes in the release of dopamine and of other neurotransmitters.

PP2
Role of the cerebellum in the pathophysiology of tremor in dystonia

Elena Antelmi[1,2], Flavio Di Stasio[2,3], Roberto Erro[2], Lorenzo Rocchi[2], Rocco Liguori[1], Alfredo Berardelli[3], John Rothwell[2], Kailash Bhatia[2]

[1]Department of Biomedical and Neuromotor Sciences, Alma Mater Studiorum, University of Bologna, Bologna, Italy; [2]Sobell Department of Motor Neurosciences and Movement Disorders, University College of London, UK; [3]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome, Italy

Background: The pathophysiology of tremor in dystonia is still unclear. Functional and structural changes of the cerebellum have been reported in dystonia.
Aim: To assess if patients with dystonia with and without tremor may present with different degree of cerebellar impairment, by using the paradigm of the eyeblink classical conditioning (EBCC).
Methods: Twenty-four patients with cervical dystonia have been recruited and assessed at the wearing-off of the Botulinum toxin by means of history taking, neurological examination, video-recordings, and scales (Toronto Western Spasmodic Torticollis Rating Scale, -Fahn-Tolosa-Marin Tremor Rating Scale, and Scale for the Assessment and Rating of Ataxia). Neurophsyiological assessment comprised the blink reflex recovery cycle and EBCC, performed as detailed elsewhere [1]. Basing on clinical data patients have been divided into two groups: with tremor (#12) and without tremor (dystonic tremor and tremor associated with dystonia) (#12). Data have been compared with those collected in a group of 12 age and sex matched heathy voluntaries.
Results: Dystonic patients (16 F) had a mean age of 68 ± 11 year-old, a mean severity at the TWSTRS of 18 ± 7 and a mean disease duration of 14 ± 5 years. Statistical analysis did not disclose any significant difference in demographic and clinical data in patients with and without tremor. When comparing dystonic patients and healthy controls we found that patients had a significant increased brainstem excitability and a slightly decreased response to the paradigm of EBCC.When comparing patients with and without tremor, we found a significant more impaired EBBC in patients with tremor.
Conclusions: In patients with dystonia the abnormal conditioning seems to segreagate with tremor, in keeping with the hypothesis that

the cerebello-thalamo-cortical pathway may play a role in the pathophysiology of tremor in dystonia.

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PP3
Do Late-Stage Parkinson's Disease patients still respond to levodopa?

Margherita Fabbri[1], Miguel Coelho[1,2], Daisy Abreu[1], Nilza Costa[1], Mario M. Rosa[1,2,3], Leonor C. Guedes[1,2], Joaquim J. Ferreira[1,2,3]

[1]Clinical and Pharmacology Unit, Instituto de Medicina Molecular, Lisbon, Portugal; [2]Neurology Service, Department of Neurosciences, Hospital Santa Maria, Lisbon, Portugal; [3]Laboratory of Clinical and Pharmacology and Therapeutics, Faculty of Medicine, Lisbon, Portugal *Margherita Fabbri: Clinical and Pharmacology Unit, Instituto de Medicina Molecular, Lisbon, Portugal

Introduction: A subgroup of advanced Parkinson's disease (PD) patients reaches a late disease phase [late-stage PD (LSPD)], whose phenotype is dominated by complete dependence and levodopa-resistant symptoms [1]. Controversy still exists whether the apparent loss of benefit from levodopa is real or the result of down-titrating its dosage due to the occurrence or fear of adverse effects (AEs) [2].
Objective: Our aim was to study the response to levodopa in a LSPD population.
Methods: 20 LSPD patients, with Schwab and England ADL Scale (SE) < 50 or Hoehn Yahr (HY) Stage > 3 (MED ON), underwent a levodopa challenge test with a supra-maximal dose (150 %). MDS-UPDRS-III and the Abnormal Involuntary Movement Scale were evaluated before and after levodopa.
Results: Patients had a median age of 78.8 years (IRQ: 73.5–82) and median disease duration of 14 years (IQR: 10–19.75). Levodopa significantly improved the MDS-UPDRS-III score (14.9 %) with positive effect on tremor at rest, rigidity and bradykinesia, but had no effect on axial signs with exception of gait in a few cases. SE or HY slightly improve after levodopa. The response to levodopa positively correlated with the acute appearance of dyskinesias and the MDS-UPDRS-IV score. AEs occurred in 7 patients.
Conclusions: LSPD patients still show a slight response to a supra-maximal levodopa dose but frequently this is associated to AEs. Even in this late disease phase, a positive response to levodopa is associated with motor fluctuations and dyskinesias. A decrease in the response to a levodopa test is a potential marker of disease progression in the later stages.

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PP4
Subdural continuous theta burst stimulation of the motor cortex in essential tremor

Marina Picillo[1,2], Elena Moro[3], Mark Edwards[4], Vincenzo Di Lazzaro[5], Andres M. Lozano,[6] Alfonso Fasano[1]

[1]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital and Division of Neurology, University of Toronto, Toronto, Ontario, Canada; [2]Centre for Neurodegenerative diseases (CEMAND), Department of Medicine and Surgery, University of Salerno, Salerno, Italy; [3]Service de Neurologie, CHU Grenoble, Joseph Fourier University, INSERM U836, Grenoble, France; [4]UCL Institute of Neurology, Queen Square, London UK; [5]Institute of Neurology, Campus Bio Medico University Rome, Italy; [6]Division of Neurosurgery, Toronto Western Hospital—UHN, University of Toronto, Toronto,Ontario, Canada

Continuous theta-burst stimulation (cTBS) using short bursts of low-intensity, high-frequency (50 Hz), pulses repeated every 200 ms is a repetitive transcranial magnetic stimulation (rTMS) protocol with inhibitory effects on human cortex. Primary motor cortex (M1) plays a role within the central oscillatory network in generating Essential Tremor (ET). Accordingly, cTBS over M1 leads to a small and transient reduction of the tremor amplitude in ET. Invasive motor cortex stimulation (MCS) with subdural electrodes connected to an implantable pulse generator (IPG) has been successfully tested in six ET patients [1]. We applied a cTBS protocol to the first ET patient with subdural MCS enrolled in the original studyusing the implanted subdural electrodes (ScTBS) [1]. Detailed clinical assessments up to 5 years after surgery have been described elsewhere (Patient 1) [1]. Recently, the patient presented worsening of upper limbs tremor reporting a sort of habituation of tremor to continuous MCS. In order to obtain a stronger inhibitory effect on M1, we trialed the patient with stimulation parameters matching the cTBS protocol. By using the cyclic mode embedded in the IPG (Activa PC, by Medtronic, MN, USA), five 50-Hz pulses lasting 60 μsec were delivered every 200 ms (4·0 V/60 μsec/50 Hz, Cycling On/Off:0·1/0·2 s). This new stimulation protocol induced a definite improvement in hand tremor, greater than the one used at baseline. A double-blind evaluation of tremor during three different conditions was then performed over two different mornings. Bilateral ScTBS provided the most effective tremor control on both objective and subjective assessments. The patient is currently using ScTBS since 3 months with sustained benefit, no side effects and no evidence of habituation. This preliminary experience

suggests that the direct stimulation of the cortex with the cTBS paradigm can further enhance the ET improvement initially described with MCS. The exact mechanisms of action remain speculative, though a plasticity effect has been hypothesized. Interestingly, this 'patterned' form of stimulation appears to be more efficient in producing long term potentiation/depression effects in brain slice preparations compared to constant frequency stimulation. It is additionally possible that, similarly to other forms of non invasive brain stimulation techniques delivered at intensities below those needed for synaptic activation, like transcranial alternating current stimulation, ScTBS might induce subthreshold changes in the membrane potentials of affected neurons, thus altering their firing rate. Further studies are needed to fully understand the clinical utility of invasive chronic ScTBS in ET.

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PP5

Levodopa acute effect on kinematic parameters during Timed "Up and Go" tested by a portable inertial sensor

Valeria Dibilio, Simona Toscano, Giovanni Mostile, Antonina Luca, Loredana Raciti, Donatella Contrafatto, Calogero Edoardo Cicero, Rosario Vasta, Giorgia Sciacca, Giulia Donzuso, Cristina Rascunà, Giacomo Portaro, Paolo Cantavenera, Alessandra Nicoletti, Mario Zappia

Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy

Introduction: Gait deficits are common and debilitating signs of Parkinson's disease (PD) with consequent disability, falls and reduced quality of life. An instrumented version of Timed Up and Go test (iTUG) has been introduced in clinical practice to provide automatic and detailed analysis of each subcomponent (sit-to-stand, gait, turning, turn-to-sit, stand-to sit), detecting kinematic parameters in order to indicate dynamic disequilibrium and increased risk of falls. Despite levodopa (LD) has a predominant role in improving PD motor symptoms, there are no evidence about specific effects in kinematic variables during TUG.

Objectives: To assess the effect of LD therapy on different iTUG parameters in patients with PD.

Methods: Twenty-eight PD patients in LD treatment performed consecutively TUG test three times and a 24 meters walking trial. Tasks were recorded in OFF and ON state using the portable sensor BTS G-WALK. Kinematic measures were derived from iTUG subtasks sit-to-stand, mid-turning, turn-to-sit, stand-to-sit and from the walking phase.

Results: Speed and step length significantly differed in OFF and ON state (respectively $p = 0.05$; $p = 0.004$). Significant differences were detected between OFF and ON state in TUG total duration (20.18 ± 12.64 vs. 15.4 ± 5.23 s; $p = 0.021$), forward phase duration (5.03 ± 4.55 vs. 3.47 ± 1.83 s; $p = 0.037$), backward phase duration (3.23 ± 2.31 vs. 2.43 ± 1.43 s; $p = 0.011$). Significant decrement in duration as well as increment in angular speed and peak of angular speed was recorded during mid-turning and turning-before-sitting ($p < 0.05$).

Conclusions: Our results showed that several components of iTUG can reveal specific deficits of gait and turning in people with PD. Only certain aspects seem to be responsive to levodopa therapy. This knowledge could lead to pharmacological and rehabilitative individualized approaches for patients showing different kinematic features.

PP6

Aceruloplasminemia or hemochromatosis?

Valentina Fioravanti[1], Sara Contardi[1], Francesco Cavallieri[1], Elena Corradini[2], Massimo Fiorini[2], Franco Valzania[1]

[1]Department of Neuroscience, S. Agostino-Estense Hospital and University of Modena and Reggio Emilia, Modena, Italy; [2]Division of Internal Medicine and Center for Hemochromatosis, Mario Coppo Liver Research Center, University Hospital of Modena, Modena, Italy

Introduction: Aceruloplasminemia is classified as an inherited neurodegenerative disorder associated with systemic iron-overload syndrome. It's characterized by progressive neurodegeneration with brain iron accumulation due to complete lack of ceruloplasmin ferroxidase activity caused by mutations in ceruloplasmin gene. Neurological manifestations include ataxia, involuntary movements, cognitive dysfunction and parkinsonism. Accumulation of iron in the affected parenchymal tissues results in diabetes, cardiac failure and hypothyroidism.

Case report: A 40-year-old man, born to consanguineous parents, was admitted with a 2-year history of balance disorder, mental slowing and behavioral disorders. Previous history reveals: diabetes mellitus from the age 25, hypothyroidism and pontine minor ischemic stroke (good outcome). Neurological examination showed facial hypomimia, neck dystonia, oro-mandibular dyskinesias, marked bradikinesia, axial and limb rigidity, severe gait impairment with ataxia. Archaic reflexes were present; tendon reflexes were brisk. Hoffmann and Babinski signs were present at right limbs. Brain MRI showed overload of paramagnetic material (dentatus, putamen, posterior talamus, cortical grey matter) associated with brain atrophy. Neurophysiological studies reported no alterations. Laboratory findings revealed reduced blood iron level, hyperferritinemia (>2000 ng/ml), complete absence of serum ceruloplasmin with reduced blood and urinary copper levels. Genetic testing revealed the presence of heterozygous mutation for hemochromatosis and gene homozygosis for ceruloplasmin mutation. In last 6 months therapy with deferasirox caused decrement of ferritin level, and mild clinical improvement.

Discussion and conclusion: The great phenotypic heterogeneity of aceruloplasimemia has been widely described. We suggest that in patients with movement disorder as ataxia and distonia associated with cognitive dysfunction and internal diseases, extensive laboratory tests including iron and copper set are required. In case of detection of neuroradiological overload of ferromagnetic material in brain regions, the key element for differential diagnosis with neuroferritinopathy is the absence of signs outside the central nervous system (CNS); in Neuroferritinopathy, in fact, iron accumulates exclusively in the CNS.

PP7

Neuroimaging correlates of blinking abnormalities in patients with clinically probable progressive supranuclear palsy

Alessandra Formica, Matteo Bologna, Maria Cristina Piattella, Neeraj Upadhyay, Antonella Conte, Giovanni Fabbrini, Carlo Colosimo, Patrizia Pantano, Alfredo Berardelli

Department of Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy

Background: Progressive supranuclear palsy is a neurodegenerative disorder affecting cortical (mainly frontal) areas, subcortical and brainstem regions, as shown by neuropathological investigations and neuroimaging studies. Progressive supranuclear palsy is clinically characterized by parkinsonian signs, early falls and oculomotor abnormalities [1]. Patients with progressive supranuclear palsy often have abnormalities of voluntary, spontaneous and reflex blinking [2].
Objective: To identify the possible relationship between the blinking abnormalities that occur in patients with progressive supranuclear palsy and neurodegenerative changes in cortical, subcortical and brainstem structures that characterize this condition.
Methods: We studied 18 patients with clinically probable progressive supranuclear palsy and 13 healthy controls. Voluntary, spontaneous and reflex blinking abnormalities were detected using kinematic techniques. Changes in cortical, basal ganglia and brainstem structures were detected by T1-weighted magnetic resonance imaging.
Results: Kinematic analysis showed several abnormalities in voluntary blinking, a reduced spontaneous blinking rate and increased trigeminal blink reflex excitability in patients in comparison to healthy subjects. Neuroimaging also detected significantly smaller regional volumes in patients than healthy subjects in the supplementary motor area, thalamus, putamen, pallidum and brainstem (all $P < 0.05$). Correlation analysis between kinematic and neuroimaging abnormalities showed an inverse association between the inter-phase pause duration (the time elapsing between the closing and opening phases) during voluntary blinking and volumes in putamen ($r = -0.68$, $P = 0.002$) and thalamus ($r = -0.67$, $P = 0.002$).
Conclusion: Blinking abnormalities in progressive supranuclear plasy appear to be associated mainly with changes in subcortical structures. By providing further insight into the pathophysiological mechanisms underlying blinking abnormalities in progressive supranuclear palsy these findings might be useful in developing disease biomarkers.
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PP8
Potential disease-modifying effect of statins in Parkinson's disease: a pilot case–control retrospective study

Martina Giuntini, Daniela Frosini, Giovanni Palermo, Roberto Ceravolo, Ubaldo Bonuccelli

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

Background: In recent years, experimental and epidemiological studies suggested that statins possess anti-inflammatory properties by different mechanisms and their potential protective role against neurodegeneration.
Objective: Aim of our study was to compare, in a case control retrospective study, motor and non motor features in PD patients treated with statins (ST-PD) and without statins (nST-PD).
Methods: From the cohort of drug-naïve PD patients referred to our institute over a 3-years period, we identified 30 patients treated with statins before PD onset and during the follow-up and 30 control PD subjects never treated with statins, matched for sex, age at onset and disease duration. Cardiovascular disease, diabetes mellitus and macrovascular complications at brain MRI were exclusion criteria. Motor symptoms were evaluated by UPDRS, cognitive state by MMSE, at baseline and after 3 years-follow-up. Statistical analysis was performed by Chi-test for categorical variables, Mann–Whitney U for continuous variables and Wilcoxon test to compare the longitudinal progression of symptoms between groups.
Results: ST-PD patients were similar to nST-PD in terms of demographic and general medical features. No differences were found regarding motor scores at baseline, except for higher postural scores in the ST-PD group, and at follow-up, except for higher postural scores in the ST-PD group and rigidity scores in the nST-PD group. MMSE scores were similar both at T0 either at follow-up between groups. The group treated with statins did not show a significant progression in terms of UPDRS III, bradykinesia, rigidity and postural scores during the follow-up, ($p > 0.05$), in comparison with a significant progression of the same scores in the control group ($p < 0.05$).
Conclusion: The treatment with statins during the course of the disease could have an impact on PD progression, speculating a possible disease-modifying effect able to reduce cell degeneration. However, the mechanism of interplay with PD needs to be furtherly elucidated.

PP9
Kinematic analysis of repetitive finger tapping and the effects of selegiline in newly diagnosed patients with Parkinson disease

Giorgio Leodori[1], Matteo Bologna[2], Daniele Belvisi[2], Andrea Fabbrini[1], Giulia Paparella[1], Paola Stirpe[1], Alfonso Fasano[3], Giovanni Fabbrini[1,2] Alfredo Berardelli[1,2]

[1]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome, Italy; [2]IRCCS Neuromed, Pozzilli (IS), Italy; [3]Movement Disorders Center, TWH, UHN, Division of Neurology, Toronto Western Hospital and University of Toronto, Toronto, Ontario, Canada

Introduction: Motor impairment in Parkinson's disease includes slowness (bradykinesia), decreased amplitude (hypokinesia) and progressive reduction in speed and amplitude during repetition of finger movements, i.e. sequence effect [1]. The kinematic features of the sequence effects in the early stage of PD are unknown. Also, the pathophysiological mechanisms of the sequence effect in PD are still unclear and they are not entirely explained by dopaminergic loss [2].
Objective: To evaluate the kinematic features of the sequence effect in the early stage of PD and the response to selegiline administration. A selective irreversible MAO-B inhibitor. There is considerable evidence showing that selegiline has either dopaminergic and non-dopaminergic effects. We thus hypothesized that selegiline might improve the sequence effect in patients with PD.
Methods: Fifteen newly diagnosed and previously untreated patients with PD and ten healthy controls performed a repetitive finger tapping task in two separate sessions, performed at least 4 weeks apart: OFF and ON selegiline (10 mg taken daily). The analysis of repetitive finger movement was performed using kinematic techniques. The sequence effect was measured as decrements in speed and amplitude during movement.
Results: The amplitude of the repetitive finger movement was lower in patients than in healthy controls whereas the speed of the finger movement was similar in the two groups. Selegiline administration improved the overall amplitude but it did not influence the decrement

in amplitude during repetition of finger movements, i.e. the sequence effect.

Conclusion: Patients with newly diagnosed PD show a progressive reduction in amplitude during repetition of finger movements which differ from the pattern in patients with more advanced PD [3]. Selegiline does not ameliorate the sequence effect in de novo PD patients thus suggesting that this abnormality may result from a complex of pathophysiological mechanisms.

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PP10

Upper limb dystonia: beyond inkwell and pen (focusing on non task specific variants)

Daniele Liuzzi[1], Angelo Fabio Gigante[1], Roberta Pellicciari[1,2], Antonia Giordano[1], Marco Guido[1], Giovanni Defazio[1]

[1]Department of Basic Medical Sciences, Neuroscience and Sense Organs, University of Bari, Bari, Italy; [2]Department of Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy

Introduction: Upper limb dystonia (ULD) is a form of dystonia characterized by involuntary, sustained muscle contractions leading to abnormal limb movements and postures often interfering with motor performance. Task specificity is a peculiar feature of ULD. This means that task specific ULD (T-ULD) manifests only during a particular action, for instance writing, playing a musical instrument, typing etc. Although demographic clinical and patophysiological features of T-ULD have been well studied, information is lacking about clinical and demographic aspects of non task –specific upper limb dystonia (NT-ULD).

Objectives: To describe clinical and demographic features of NT-ULD.

Methods: 68 patients with a clinical diagnosis of idiopathic NT-ULD were included in the study. Demographic and clinical data were collected by a standardized interview and examination.

Results: Our sample included 29 men and 39 women. NT-ULD manifested as a spontaneous dystonia in 8.5 % of patients, was activated by a variety of movements in 44.7 % of patients, manifested at rest and during voluntary actions in 46.8 %. Only a few patients (4/68) reported a phase of task specificity preceding the appearance of NT-ULD. Upper limb was the site of dystonia onset in 33 patients, a site of dystonia spread in the remaining 35 patients. Age of ULD onset (58.6 ± 18.2 vs. 55.8 ± 12.7, $p = 0.25$) and frequency of family history of dystonia (about 30 %) were similar in the two groups. In the group presenting with NT-ULD, dystonia spread to other body sites in 51 % of patients.

Conclusions: Demographic and clinical features of NT-ULD are very different from the features of T-ULD (peack age of onset in the 3rd decade, male preponderance and low tendency to spread). This may reflect differences in risk factors.

PP11

Motor fluctuations predict the re-emergence of fatigue in Parkinson's disease

Davide Massucco, Tiziano Tamburini, Roberta Marchese, Giovanni Abbruzzese

Department of Neurology, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Genoa, Italy

Introduction: Fatigue is one of the most prevalent and disabling non motor symptoms in Parkinson's disease (PD) [1]. Despite much effort has been put in understanding fatigue in PD, its pathophysiology is still unclear [2] and studies show conflicting results about whether fatigue is correlated with the motor condition of patients, dopaminergic therapy or other comorbid issues such as sleep disturbances, depression and cognitive decline [3].

Objective: To evaluate whether the presence and severity of fatigue is correlated with motor fluctuations in a cohort of patients with H&Y stage II PD.

Methods: 40 patients with bilateral PD without postural instability taking L-DOPA were recruited in this study. Fatigue was assessed using the PFS-16 and the presence of wearing off by means of the WOQ-19. The motor state and the impact of motor fluctuations were evaluated with the MDS-UPDRS parts III and IV. Sleep was assessed using the Parkinson's Disease Sleep Scale and mood with the Beck Depression Inventory. Cognitive performances were also screened using the Montreal Cognitive Assessment.

Results: A logistic regression using the PFS-16 mean score as binary dependent variable (value 1 when mPFS ≥ 2.95) showed that only the presence of wearing off (WOQ-19 score ≥ 2) significantly increased the odds of having fatigue in our PD patients (OR = 19.06, $p = 0.022$). The severity of fatigue (mPFS) was correlated to the frequency (number of daily OFFs) and impact of motor fluctuations (UPDRS IV score), as respectively shown by Pearson coefficients $r = 0.7$ and $r = 0.56$, and associated with higher UPDRS III scores ($p = 0.0016$). No differences in the other considered variables were found between the fatigued and nonfatigued subgroups.

Conclusion: This study shows that only motor fluctuations are predictive of the presence of fatigue in PD patients within the same disease severity stage. Thus we can suggest that the suboptimal control of striatal dopaminergic level is related to the re-emergence of fatigue.

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PP12

Homovanillic acid in cerebrospinal fluid in Parkinson's disease patients after levodopa challenge: a new diagnostic tool?

Enrica Olivola[1], Mariangela Pierantozzi[1,2], Salvatore Galati[3], Gianluigi Lunardi[4], Domenicantonio Tropepi[4], Claudio Liguori[1], Valentina Saviozzi[1], Atticus Henry Hainsworth[5], Paolo Stanzione[1,2], Ernesto Fedele[6], Giacoma Angileri[1], Alessandro Stefani[1,2]

[1]Centro Parkinson, Dip. Medicina dei Sistemi, Università di Roma Tor Vergata, Rome, Italy; [2]IRCCS Fondazione Santa Lucia, European Centre for Brain Research CERC, Rome, Italy; [3]Neurocenter Svizzera Italiana, Lugano, Svizzera; [4]Ospedale Sacro Cuore Negrar, Verona, Italy; [5]Stroke & Dementia Research Centre, St Georges University of London, London, UK; [6]Department of Pharmacy, Università di Genova, Genoa, Italy

Introduction: In Parkinson's disease (PD) stage-specific biomarkers are elusive and clinical trials are dependent on clinical assessment. Predictive biochemical parameters as a reliable readout of disease-modifying therapies remain an unmet clinical need. The major metabolites of dopamine (DA) are 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA).
Objectives: Here we tested whether cerebrospinal fluid (CSF) concentrations of DA, HVA and DOPAC correlate with motor performance in a group of non-fluctuating PD patients.
Methods: CSF samples were acquired, after 2 days of washout, via lumbar puncture (LP), 130 min after administration of levodopa dose (200 mg oral), when CSF levodopa reaches a steady state concentration. DA, DOPAC and HVA were assayed by high performance liquid cromatography, in all patients who attained >30 % motor amelioration (n = 19 out of 21).
Results: In these *challenged* PD patients, the DOPAC and HVA both increased in parallel with the motor impairment in all subjects (n = 19). HVA correlated with pre-LP baseline Unified PD rating scale part III (UPDRS-III) scores (R = 0.61). HVA and DOPAC correlated with each other (R = 0.56), despite distinct kinetics.
Conclusions: Our data are consistent with early subtle alterations of the DA presynaptic machinery even before the advanced PD stages characterized by fluctuations and dyskinesia. CSF HVA concentration, might represent a biomarker for monitoring the effectiveness of PD-modifying pharmacological therapies.

PP13

Subthalamic Nucleus Activity at gait initiation in Parkinson disease: report of three cases

Nicolò Gabriele Pozzi[1,2,3], Gabriele Arnulfo[3,4], Frank Steigerwald[3], Virginia Maltese[3], Chiara Palmisano[3,5], Joachim Brumberg[6], Martin M. Reich[3], Esteban Pavan[5], Jens Volkmann[3], Claudio Pacchetti[1,2], Ioannis U. Isaias[3]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia, Italy; [2]Interdepartmental Research Center for Neurodegenerative Disease, National Institute of Neurology Foundation "C. Mondino", Pavia, Italy; [3]Department of Neurology, University Hospital and Julius-Maximilian-University, Würzburg, Germany; [4]Department of Informatics, Bioenginering, Robotics and System Engineering, University of Genoa, Genoa, Italy; [5]Movement Biomechanics and Motor Control, TBM Lab, DEIB-Politecnico di Milano, Milano, Italy; [6]Department of Nuclear Medicine, University Hospital and Julius-Maximilian-University, Würzburg, Germany

Background: Gait initiation (GI) is defined as the transient state between standing and walking. It is affected in Parkinson's disease (PD) and its impairment is a hallmark of disease progression. Despite Deep Brain Stimulation of the Subthalamic nucleus (STN DBS) has shown to remarkably improve PD symptoms, its effect on gait and posture is still debated. Actually, the physiological role of STN in gait and posture is largely unknown. For the first time in this study we were able to record STN activity (Local Field Potential, LFPs) during locomotion.
Methods: LFPs were recorded in three patients by means of the Activa PC + S® (Medtronic® Inc., Neuromodulation, Minneapolis, USA). We also measured striatal dopaminergic innervatino by means of [123I]FP-CIT and SPECT. GI was defined by kinematic (SIMI Motion System®, Muenchen, DE) and dynamic (Kistler force plates®, Kistler Holding AG) measurements in meds-ON and -OFF state. Subjects stood upright and started walking, at a natural (preferred) speed when receiving a visual clue. GI was identified through definition of four intervals: (i) *standing* (ST); (ii) *anticipatory postural adjustment* (*APA*): form ST to instant of heel-off of the leading foot (HOld); (iii) *gait initiation*: from HOld to toe-off trailing foot (TOtr); (iv) *walking*. Beta band was defined (±5 Hz to frequency peak) and data from each subject were normalized to their *standing* condition.
Results: The striking finding was a beta activity modulation (reduction) during *gait initiation* compared to *APA* (STNright: −93 % vs. *APA*, −1 % vs. *walking*; STNleft: −43 % vs. *APA*, −1 % vs. *walking*). No clear difference was observed with regards of the STN ipsi- or contralateral to the leading foot. Interestingly, the right STN, with greater beta activity reduction, happened to be—in all subjects—ipsilateral to the striatum with less dopaminergic innervation loss. Lastly, we confirmed the effect of L-Dopa in suppressing the beta over-activity in all the intervals.
Conclusion: Despite being preliminary and in a limited number of PD subjects, these data suggest a selective involvement of the STN in distinctive gait phases, in particular in the propulsive phase of gait initiation. Also of interest, we found a prevalent activity of the STN related to the less affected striatum, possible suggesting a compensatory role within the basal ganglia circuitry and output.

PP14

Risk of motor complications and clinical efficacy among different L-dopa administration modalities and dopamine agonists therapy in early Parkinson's disease

Giovanni Mostile, Cristina Rascunà, Valeria Dibilio, Antonina Luca, Loredana Raciti, Donatella Contrafatto, Calogero Edoardo Cicero, Rosario Vasta, Giorgia Sciacca, Giulia Donzuso, Simona Toscano, Giacomo Portaro, Roberta Bonomo, Alessandra Nicoletti, Mario Zappia

Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy

Background: It has been suggested that Pulse L-dopa (PLD) stimulation modality in early Parkinson's Disease (PD) may prevent the onset of motor complications compared to the conventional intermittent L-dopa (ILD) therapeutic regimen exploiting the Long-Duration Response to L-dopa.
Objectives: To evaluate risk of motor complications and clinical efficacy in early PD treated with different L-dopa administration modalities (PLD or ILD) and Dopamine Agonists (DAs) therapy.
Methods: We consecutively enrolled de novo PD patients who were stably treated with one of the following treatments: PLD (250 mg/die), ILD (125 mg TID), or DAs. Patients were followed-up every 5 ± 1.1 months for 20.1 ± 4.6 months. Study outcomes were: frequency of wearing-off and dyskinesia at the end of the follow-up, according to UPDRS-IV item 36 and 32, respectively; clinical efficacy expressed as the percent improvement in "practical-off" state scored using the UPDRS-ME from the first observation.
Results: Forty-one de novo PD patients were enrolled (27 men, age at onset: 59.7 ± 8.3 years). Twelve patients were treated with PLD modality, 14 with ILD, 15 with DAs. At the end of the follow-up, 8 (19.5 %) developed wearing-off and 10 (24.4 %) dyskinesia. Motor complications were less frequent among the DAs-treated patients (wearing off = 13.3 %; dyskinesia = 6.7 %) while there were no significant differences between PLD-treated and ILD-treated groups about the occurrence of wearing-off (25 vs 21.4 %, $p = 0.83$) and dyskinesia (41.7 vs 28.6 %, $p = 0.48$). Considering clinical efficacy, DAs-treated patients reached maximum motor improvement (−9.8 %) after 8.8 ± 1.3 months and declining soon after, returning to baseline after 20.1 ± 4.6 months. L-dopa groups reached a similar maximum improvement (−20.6 % among PLD vs −19.3 % among ILD), however PLD-treated group maintained such improvement for a longer period of time (14.8 ± 1.3 months) while the ILD-treated group reaches the maximum improvement after 8.8 ± 1.3 months to decline soon after.
Conclusions: PLD stimulation modality may guarantee a stable clinical benefit without adjunctive risk of motor complications in early PD.

PARKINSON - CLINICAL TRIALS

PP15

Preliminary data about correlation between Parkinson's disease and malignant tumors

Enrico Binaghi, Marcello Mario Mascia, Paolo Solla, Mario Meloni, Rita Farris, Daniela Ciaccio, Giovanni Orofino, Francesco Marrosu, Antonio Cannas

Clinica Neurologica, Policlininico Monserrato, Università di Cagliari, Cagliari, Italy

Introduction: Many hypotesis about low cancer rates in patients with Parkinson's disease (PD) have been studied in the literature, especially the reduction of cancer onsets related to smoking. On the other hand many researches shown, that in patients treated with levodopa, the risk of melanoma may be increased [1]. Further studies are needed to understand the true prevalence of cancers in PD.
Objective: We have done the research among the group of Sardinian patients with PD to evaluate the occurrence of malignant tumors in PD patients versus the general population. In particular the impact of treatment on the onset of Melanoma and Breast Cancer (BC) has been analysed.
Methods: We have collected currently data of 300 PD patients, in the mean age of 72 years (range max: 90 min: 44), which are currently receiving treatment at the Clinic of Neurology of the University Hospital of Cagliari and evaluated the frequency of occurrence of malignant tumors. PD patients are matched by age and sex to a general population free-PD, randomly selected, of Sardinia. The PD patients were divided according to gender and three main forms of onset of PD: classical type, rigidity-akinetic predominant and a tremor predominant.
Results: The frequency of cancers is lower in PD patients (5 %) than in free-PD (21 %).
Conclusions: In PD patients the risk of developing cancer in their lifetime is lower than in the free-PD population. The association between BC, Melanoma and PD must be sought in probable pathogenic pathways common to both diseases, and we are investigating which factors are involved in the low prevalence of tumors in PD patients.
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PP16

Measures of quality of life in Parkinson's disease patients and their caregivers: an observational study

Francesco Corallo[1], Viviana Lo Buono[1], Maria Cristina De Cola[1], Placido Bramanti[1], Giuseppe Di Lorenzo[1], Silvia Marino[1,2]

[1]IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy; [2]Department of biomedical Sciences and Morphological and Functional Imaging, University of Messina, Messina, Italy

Introduction: The concept of QoL is included and expands the definition of health given by the World Health Organization and comprises complete physical, mental, and social well-being. It expresses the degree of satisfaction in various areas as a result of the opportunities that arise during one's lifetime despite the restrictions and impediments that life itself puts forth [1]. Parkinson's disease (PD) influences quality of life (QoL) of the patients and in addition to creating a burden on the caregiver altering emotional, physical and financial demands [2].
Objective: We analyzed if the degree of cognitive disability of patient affected the quality of life of caregiver.
Methods: A total of 60 subjects with idiopathic PD were included, all had a primary caregiver. All patients were undergo to evaluation by using Quality of Life Questionnaire PDQ-39, Mini Mental State examination, Activities of daily living and Instrumental Activities of Daily Living. The SF-36 was used to assess QoL of the primary caregivers. Major demographic and clinical variables were also recorded.
Results: We found significant correlations between the MMSE scores and the subscales scores of the PDQ-39, especially with "mobility" ($r = -0.54$; $p < 0.0001$), "physical discomfort" ($r = -0.66$;

$p < 0.0001$); as well as the subscales scores of the SF-36, especially with the "emotional role functioning" ($r = 0.38$; $p < 0.01$). We also found a high correlation of "physical discomfort" of the PDQ-39 with "vitality" ($r = -0.47$; $p < 0.001$) and "social role functioning" ($r = -0.55$; $p < 0.0001$) of the SF-36.

Conclusion: The present study shows a relationship between quality of life of the subject with PD and the caregiver's perceived burden. Indeed, the cognitive impairment of the patients, is strictly related to lower QoL scores for both patients and caregivers.

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PP17

Accuracy of clinical diagnosis of Parkinson's disease: a systematic review and Bayesian meta-analysis

Giovanni Rizzo[1], Massimiliano Copetti[2], Simona Arcuti[1], Davide Martino[3,4], Andrea Fontana[2], Giancarlo Logroscino[1,5]

[1]Department of Clinical Research in Neurology, University of Bari, Tricase, Italy; [2]Unit of Biostatistics, IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy; [3]Department of Neurology, King's College NHS Foundation Trust, London, UK; [4]Department of Neurology, Queen Elizabeth Hospital, Lewisham and Greenwich NHS Trust, London, UK; [5]Department of Basic Medical Science, Neuroscience and Sense Organs, University of Bari, Bari, Italy

Background: The diagnosis of PD remains primarily clinical. A correct diagnosis of PD is important for clinical management and pharmacological and epidemiological studies.

Objective: To evaluate the diagnostic accuracy of the clinical diagnosis of Parkinson's disease (PD) reported in the last 25 years by a systematic review and meta-analysis.

Methods: PUBMED and EMBASE database were searched for papers published between 1988 and 25th August 2014. Studies were included if reporting diagnostic parameters regarding the clinical diagnosis of PD, as sensitivity, specificity, positive predictive value, negative predictive value and accuracy, or crude data. The selected studies were sub-classified based on the different study setting, type of test diagnosis and gold standard. Meta-analyses of the available data were performed using a Bayesian approach.

Results: We selected 21 studies reporting on 23 populations and 5260 patients. The pooled diagnostic accuracy was 79.8 % [95 % credible interval (CrI), 75.7–83.5 %]. The pooled diagnostic accuracy was 76.2 % (95 % CrI, 69.7–81.8 %) for clinical diagnosis performed mainly by non-experts. Accuracy of clinical diagnosis performed by movement disorders experts rising from 76.4 % (95 % CrI, 71.4–80.7 %) of initial assessment to 84.9 % (95 % CrI, 73.5–92.3 %) of refined diagnosis after follow-up. Using UKPDSBRC criteria the pooled diagnostic accuracy was 82.7 % [95 % CrI, 62–93 %].

Conclusion: The overall validity of clinical diagnosis of PD is not satisfying. The accuracy did not significantly improve in the last 25 years, particularly in the early stages of disease. Misclassification rate should be considered to calculate the sample size both in observational studies and RCT. Imaging and biomarkers are urgently needed to improve the accuracy of clinical diagnosis in vivo.

PP18

Diagnosing Parkinson's disease at the age of 80: a different phenotype?

Andrea Pilotto[1], Antonella Alberici[1], Rosanna Turrone[1], Valentina Dell'Era[1], Marta Bianchi[1], Loris Poli[1], Barbara Borroni[1], Enrico Premi[1,2], Barbara Bigni[1], Maura Cosseddu[1], Elisabetta Cottini[1], Alessandro Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy; [2]Neurovascular Unit, Brescia Hospital, Brescia, Italy

Background: Few studies suggested that Parkinson's disease patients with old age onset (PD-L) may present different motor and non-motor symptoms compared to patients with middle age onset (PD-M, onset between 60 and 70 years).

Objective: To evaluate the clinical presentation and progression of PD-L compared with matched PD-M patients.

Methods: We retrospectively analysed patients with a PD diagnosis, according to clinical criteria and with a first neurological evaluation at the age of 80 years or older. All patients underwent CT/MRI, neurological and neuropsychological assessment, with a clinical follow-up for 2–5 years. By using a case–control design, we assigned each PD-L to random chosen PD-M patients ($N = 2$ for each PD-L), matched for gender and disease duration at baseline.

Results: Out of 450 consecutive PD patients, 23 PD-L were identified (mean age 81.8 ± 2.6 years). At baseline the majority of PD-L presented tremor-dominant phenotype ($n = 11$), followed by pure akinetic-rigid ($n = 7$) and mixed phenotype ($n = 5$). Baseline UPDRS-III was significantly higher ($p = 0.03$) in PD-L vs PD-M (21.5 ± 7.4 vs 15.7 ± 6.9 respectively). Changes in L-dopa equivalent daily dose (LEDD) and motor scores were similar during the first 2–5 years of follow-up. The majority of PD-L patients presented mild to moderate cognitive dysfunction ($n = 13$) and comparable depressive symptoms to PD-M.

Conclusion: PD-L is a relative rare condition in movement disorder outpatient clinic. Our results confirmed only slightly higher motor and cognitive involvement in PD-L compared to PD-M during early disease stages.

PP19

Four copies of *SNCA* responsible of autosomal dominant Parkinson disease in two Italian siblings

Nicola Modugno[1], Rosangela Ferese[1], Rosa Campopiano[1], Marco Santilli[1], Stefania Zampatti[1,3], Emiliano Giardina[2,3], Annamaria Nardone[4], Diana Postorivo[4], Francesco Fornai[5], Giuseppe Novelli[1,2], Edoardo Romoli[1], Stefano Ruggieri[1], Stefano Gambardella[1]

[1]IRCCS Neuromed, Pozzilli (IS), Italy; [2]Department of Biomedicine and Prevention, School of Medicine, University of Rome 'Tor Vergata', Rome, Italy; [3]Molecular Genetics Laboratory UILDM, Santa Lucia Foundation, Rome, Italy; [4]Fondazione Policlinico Tor Vergata, Rome, Italy; [5]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Background: The α-synuclein gene (*SNCA*) multiplication has been implicated in autosomal dominant forms of Parkinson's disease (PD).

Methods: We performed genetic testing on two PD siblings with a family history compatible with dominant inheritance of PD.
Results: Molecular analysis together with anamnestic interview showed an *in-cis* mechanism with a 351 Kb triplication containing *SNCA* and 5 exons of *MMRN1* gene in 4q22.1 (90,500–90,851 Mb), inside a duplicated region of 1.29 Mb (90,013–91,310 Mb). Clinical phenotypes of the siblings are different. In both brothers the clinical response to levodopa was significant but with a different extent. In the brother parkinsonism had an early-onset, a rapid progression with a progressive slow degeneration of levodopa response, appearance of cognitive impairment and psychiatric symptoms dopamino-agonists induced, sleep and speech disturbances without dysautonomia. The sister, with a shorter duration of the disease, showed a later age at onset of parkinsonism, a better treatment response without deterioration of the clinical effect up to now, slight camptocormia, but not other significant motor and not motor symptoms a part a slight depression.
Conclusions: The identification of another family with *SNCA* multiplication confirm a genomic instability in this region and add information to the complex genotype-phenotype correlation of PD patients. The clinical differences between the two brothers confirm the complexity of this correlation.

PP20
Clinical phenotype of parkinsonian patients with α-synuclein mutation: our case report and review of the literature

Pasquale Nigro[1], Nicola Tambasco[1], Michele Romoli[1], Simone Simoni[1], Elisa Sacchini[1], Erica Marsili[1], Francesco Ripandelli[1], Elona Brahimi[1], Paolo Prontera[2], Paolo Calabresi[1,3]

[1]Clinica Neurologica, Azienda Ospedaliera-Università di Perugia, S. Andrea delle Fratte, Perugia, Italy; [2]Centro di Riferimento Regionale di Genetica Medica, Azienda Ospedaliera-Università di Perugia, S. Andrea delle Fratte, Perugia, Italy; [3]IRCCS Fondazione S. Lucia, Roma, Italy

Background: The first mutation associated with familial Parkinson disease was found in the SNCA gene in 1997 [1]. Although α-synuclein protein appears to play a central role in the pathogenesis of PD, mutations in the SNCA gene have been identified very rarely [2]. Duplications are detected in ~1–2 % of the PD families compatible with autosomal dominant inheritance. Triplications and point mutations are exceedingly rare.
Aim: To improve the knowledge of clinical aspects of this hereditary condition, especially focusing on non-motor features.
Methods: All analogous cases, recovered through a search of the MEDLINE (National Library of Medicine, Bethesda, MD) data base or referenced by other authors during a wide bibliographic research, have been studied. Furthermore we report a case of A53T point mutation in a women of greek origin.
Results: The clinical phenotype of PD patients with SNCA mutations (including multiplications) has certain characteristics. Most patients have earlier onset than in sporadic PD and a faster decline of motor symptoms. In the early stages, levodopa usually improves those PD symptoms that commonly respond. Early occurrence of motor fluctuations (often within 2 years of disease beginning) and the presence of prominent nonmotor features, such as severe autonomic dysfunction- behavioral changes- cognitive decline, are reported.
Discussion and conclusions: The findings of this study show that SNCA mutations exhibit specific effects on the phenotype of PD and support the hypothesis that frequency of non motor features (in our case hyposmia and orthostatic hypotension) appears to be less striking than their severity [3].
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PP21
Frequency and clinical features of GBA mutations in Italian patients with Parkinson disease

Simona Petrucci [1,2], Monia Ginevrino[1], Maria Teresa Pellecchia[3], Maria Concetta Altavista[4], Francesco Bove[5], Carlo Colosimo[2], Autilia Cozzolino[6], Chiara Criscuolo[7], Anna De Rosa[7], Giovanni Fabbrini[2], Francesca Morgante[8], Martina Petracca[5], Massimo Squillante[6], Giampiero Volpe[6], Anna Rita Bentivoglio[5], Alfredo Berardelli[2], Paolo Barone[3], Enza Maria Valente[1,3]

[1]Unità di Neurogenetica, Laboratorio CSS-Mendel, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [2]Dipartimento di Neurologia e Psichiatria, "Sapienza" Università di Roma, Roma; [3]Dipartimento di Medicina e Chirurgia, Università di Salerno, Salerno, Italy; [4]U.O. Neurologia, ACO San Filippo Neri, Roma, Italy; [5]Dipartimento di Neurologia, Università Cattolica del Sacro Cuore, Ospedale A. Gemelli, Roma, Italy; [6]Dipartimento di Neuroscienze, AOU San Giovanni di Dio e Ruggi d'Aragona, Salerno, Italy; [7]Dipartimento di Neuroscienze e di Scienze Riproduttive e Odontostomatologiche, Università Federico II, Napoli, Italy; [8]Dipartimento di Medicina Clinica e Sperimentale, Università di Messina, Messina, Italy

Biallelic mutations in the Glucocerebrosidase gene (GBA) cause autosomal recessive Gaucher Disease. More recently, heterozygous rare variants of GBA have been consistently associated with increased risk to develop Parkinson disease (PD) and Lewy Body Dementia (LBD). All exons and exon/intron boundaries of GBA gene were sequenced in familial and sporadic patients with early onset parkinsonism (EOP, 130), PD (408) and LBD (70) from Central-Southern Italy. GBA mutations were detected in 71/608 probands (11.68 %; 27 EOP, 39 PD and 5 LBD), all but five in heterozygous state. Among homozygous patients (2 EOP, 1 PD and 1 LBD), none had features of Gaucher features. Overall, 27 distinct mutations were identified. The two recurrent mutations L444P and N370S overall accounted only for less than 40 % of mutated cases (15/71, 21 %, and 13/71, 18 % respectively). A third mutation, E326 K, was also common (10/71, 14 %), while three mutations (p.G232R, p.C381F and p.M400Lfs*2) were novel. No specific genotype-phenotype correlations emerged. Frequencies of mutation carriers were 7.1 % among LBD, 9.6 % among PD and up to 20.8 % among

EOP patients. In fact, 38 % of GBA mutation carriers had a diagnosis of EOP. Among PD and EOP patients, non-motor signs, such as cognitive impairment, psychiatric and autonomic dysfunctions were more frequently reported in mutated than not mutated cases, although this difference did not reach statistical significance. GBA mutations were significantly more frequent in patients with positive family history (15.9 %) than sporadic cases (9 %). About half mutated cases (34/71) originated from Campania, while the others came mostly from Lazio, Abruzzo and Sicily. These findings suggest that sequencing of the whole GBA gene should be considered in patients with PD, LBD and especially EOP if other monogenic forms have been excluded, even more in case of positive family history and if coming from high prevalence regions such as Campania.

PP22

Cholinergic dysfunction: a common substrate for gait disturbances among fallers in older adults and people affected by Parkinson's disease

Giovanna Lagravinese[1], Elisa Pelosin[1], Carla Ogliastro[1], Andrea Ravaschio[1], Anat Mirelman[2], Jeffrey M. Hausdorff[2], Giovanni Abbruzzese[1], Laura Avanzino[3]

[1]Department of Neurosciences (DINOGMI), University of Genoa, Genoa, Italy; [2]Movement Disorders Unit, Department of Neurology, Tel-Aviv Medical Center, Department of Neurology, Tel Aviv, Israel; [3]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy

Background: Older adults and patients with Parkinson's disease (PD) share a heightened risk of falls and a reduced ability to allocate attention. Deficits in the cholinergic system may contribute to both of these common problems.
Aim: To assess cortical cholinergic activity in elderly and patients with PD who reported at least 2 falls in the previous 6 months.
Methods: This study involved 50 participants (33 PD and 17 elderly) with a history of falls recruited for the V-TIME study. Cholinergic activity was estimated with short latency afferent inhibition (SAI), measured by conditioning TMS stimulus on the motor cortex with electrical stimuli delivered to the contralateral median nerve from 18 to 26 ms before and expressed as conditioned/test response. Cognitive functions were assessed with the Montreal Cognitive Assessment (MoCA) and the Trail Making Test (TMTA-B). Gait speed (GS) and stride time variability (STV) under single and dual-task conditions were measured using an electronic walkway. In PD patients, disease severity was evaluated with the UPDRS part III.
Results: The mean value of SAI was significantly higher in PD than in elderly. In both groups, GS was significantly reduced and STV significantly increased during the dual task condition, compared to single task. The dual task change in GS was significantly correlated with the mean value of SAI. This significant association remained significant when adjusting for TMT-A, TMT-B and MOCA. In PD subjects, this association remained significant after adjusting for UPDRS III.
Conclusions: Cortical cholinergic activity was an independent predictor of change in gait characteristics under dual task in these two populations of fallers. Interestingly, this association was independent of cognitive status and was not influenced by disease severity in the PD subjects. These findings suggest cortical cholinergic dysfunction plays a pivotal pathophysiological role in gait deficits among elderly fallers and patients with PD.

PP23

Does the Pisa syndrome affect postural control, balance, and gait in patients with Parkinson's disease? An observational cross-sectional study

Federica Bombieri[1], Christian Geroin[2], Nicola Smania[2,3], Federico Schena[4], Eleonora Dimitrova[2], Elisabetta Verzini[4], Francesca Nardello[1], Michele Tinazzi[5], Marialuisa Gandolfi[2]

[1]School of Sport and Exercise Sciences, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [2]Neuromotor and Cognitive Rehabilitation Research Center (CRRNC), Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [3]Neurological Rehabilitation Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [4]School of Specialization in Physical Medicine and Rehabilitation, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [5]Neurology Unit, Movement Disorders Division, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy

Introduction: An altered sense of verticality, associated with impaired proprioception and somatosensory integration deficits, has been reported in patients with Parkinson's disease (PD) but it has not been characterized in patients with Pisa syndrome (PS). Therefore, we investigated postural control, balance, and gait disturbances in patients with PD and PS, patients with PD but without PS, and aged-matched normal controls.
Methods: This observational cross-sectional study involved patients with PD and PS ($n = 10$, Hoehn and Yahr score <4), patients with PD but without PS ($n = 10$), and age-matched healthy controls ($n = 10$). The primary outcome measure was the velocity of CoP displacement (VEL_MED_AP/ML) assessed by static stabilometry in eyes open (EO) and eyes closed (EC) conditions. The secondary outcomes were other stabilometric parameters, the Sensory Organization Balance Test (SOT), and gait analysis (GA).
Results: There were no significant differences in demographic and clinical data and Berg Balance Scale scores between the groups. There was a significant main effect in the VEL_MED_AP/ML between the groups and eye conditions ($p = 0.016$). A significant main effect was found in the EO ($p = 0.01$) and EC ($p = 0.04$) conditions. Post-hoc comparisons showed a significant increase in VEL_CoP in both the EO and EC conditions only in the patients with PD and PS. No significant main effects on SOT and GA were found.
Conclusion: Patients with PD and PS had more difficulty achieving good postural alignment with gravity and greater velocity of body sway than the other groups. Rehabilitation programs for patients with PD and PS should include spine alignment and dynamic postural training.

PP24

A prospective study of the cumulative incidence and course of restless legs syndrome in de novo patients with Parkinson's disease during chronic dopaminergic therapy

Elena Marchesi[1], Anna Negrotti[1], Monica Angelini[1], Matteo Goldoni[3], Giorgia Abrignani[1], Stefano Calzetti[1,2]

[1]Department of Emergency and Medical Speciality Area, Neurology Unit, Azienda Ospedaliero-Universitaria of Parma, Parma, Italy; [2]Department of Clinical and Experimental Medicine, Headache, Movement Disorders and Cerebrovascular Diseases Unit, University of Parma, Parma, Italy; [3]Department of Clinical and Experimental Medicine, Laboratory of Industrial Toxicology, University of Parma, Parma, Italy

The authors report the cumulative incidence of Restless Legs Syndrome over a 3 years follow-up period in 92 de novo Parkinson's disease patients under chronic dopaminergic therapy and the clinical course of the sensory-motor disorder over 12 months as from its onset. The overall cumulative incidence of Restless Legs Syndrome was found by 15.3 %, i.e. 14 incident cases, and by 11.9 %, i.e. 11 incident cases after the exclusion of possible "secondary" forms of the disorder. These figures are higher than those reported in general population in Germany (Study of Health in Pomerania), confirming our previous findings of incidence rate of the disorder. At the end of the 3 years follow-up period the prevalence of "current" restless legs syndrome was significantly greater than that previously found in drug naïve Parkinson's disease patients and in controls, supporting the view that restless legs syndrome emerging in the course of chronic dopaminergic therapy is the main determinant of the co-morbid association with Parkinson's disease. During the 12 months period of observation the restless legs syndrome showed a frequency of occurrence of 6.08 episodes per months on average and a remittent clinical course was preminent in the 11 incident cases, with a significant frequency decrease in the second as compared to the first 6 months, i.e. 3.26 vs. 8.9 episodes per months. It is hypothesized that the remittent course observed in these patients could be due to long-term adaptation (downregulation) of the hypersensitive post-synaptic dopamine receptors in the spinal cord to a continuous dopaminergic stimulation, possibly coupled with compensatory up-regulation of pre-synaptic dopaminne re-uptake mechanism, in the patients in which the hypothalamic A11 area, site of origin of the dopamine-mediated diencephalo-spinal pathway, is involved in the neurodegenerative process.

PP25

Coffee consumption and the risk of levodopa-induced dyskinesia in Parkinson's disease: the FRAGAMP Study

Giovanni Mostile[1], Alessandra Nicoletti[1], Giuseppe Nicoletti[2], Gennarina Arabia[3], Giovanni Iliceto[4], Paolo Lamberti[4], Roberto Marconi[5], Letterio Morgante[6], Paolo Barone[7], Aldo Quattrone[2,3], Mario Zappia[1]

[1]Dipartimento G.F. Ingrassia, Sezione di Neuroscienze, Università degli Studi di Catania, Catania, Italy; [2]Istituto di Bioimmagini e Fisiologia Molecolare, Consiglio Nazionale delle Ricerche, Catanzaro, Italy; [3]Clinica Neurologica, Università "Magna Græcia", Catanzaro, Italy; [4]Dipartimento di Scienze Mediche di Base, Neuroscienze e Organi di Senso, Università di Bari, Bari, Italy; [5]Divisione di Neurologia, Ospedale Misericordia, Grosseto, Italy; [6]Dipartimento di Neuroscienze, Università di Messina, Messina, Italy; [7]Dipartimento di Medicina e Chirurgia, Università degli Studi di Salerno, Salerno, Italy

Introduction: It is unclear whether caffeine intake may reduce the risk of levodopa induced dyskinesia among patients affected by Parkinson's disease (PD).
Objectives: To determine the possible association between coffee consumption and risk levodopa-induced dyskinesia in PD patients.
Materials and methods: The FRAGAMP study is a large Italian multicenter case–control study. Patients affected by PD diagnosed according to the Gelb's criteria were enrolled and underwent a face-to-face interview. Clinical and pharmacological history, as well as data on environmental exposures were collected using a standardized questionnaire. Clinical scales were used to evaluate motor and cognitive impairment. Presence of levodopa-induced dyskinesia according to the item 32 of the UPDRS section IV was considered as main outcome measure. The possible association between coffee consumption and the risk of dyskinesia was evaluated using unconditional logistic regression.
Results: 485 PD patients (292 men; mean age 65.6 ± 9.8) were enrolled in the study of whom 128 (26.4 %) presented levodopa-induced dyskinesia. Presence of dyskinesia was significantly associated with age at onset, disease duration, Hoehn–Yahr stage and UPDRS-ME score, duration and levodopa equivalent dose. Multivariate analysis showed a significant negative association between presence of dyskinesia and coffee drinking with an adjusted OR of 0.50 (95 %CI 0.26–0.97; *p* value 0.04) with a trend dose–effect (test for trend p value <0.05).
Conclusions: Our findings provide evidence that chronic administration of caffeine may reduce the long-term risk of levodopa-induced dyskinesia in PD patients.

PP26

Transcranial sonography and autonomic failure in idiopathic REM behaviour disorders and Parkinson's disease: preliminary data

Elena Guaschino[1], Natascia Ghiotto[1], Roberta Zangaglia[2], Brigida Minafra[2], Michele Terzaghi[3], Gabriella Capone[1], Alessandra Spiritelli[1], Ilaria de Cillis[1], Daniele Bosone[1], Claudio Pacchetti[2]

[1]National Neurological Institute "C. Mondino", Clinical Neurophysiology Unit, Neurovascular and Autonomic Nervous System Ambulatory, Pavia, Italy; [2]National Neurological Institute "C. Mondino", Parkinson's Disease and Movement Disorders Unit, Pavia, Italy; [3]National Neurological Institute "C. Mondino", Sleep Medicine Unit, Pavia, Italy

In prospective longitudinal study subjects with idiopathic REM behaviour disorders (iRBD) may convert in PD or other synucleinopathies. PD-specific pathologic hallmarks antedate the onset of motor clinical features, even years before. Substantia nigra (SN) hyperechogenicity detected by Transcranial Sonography (TCS), is considered as a biomarkers of neurodegeneration in PD as well as in patients with iRBD. Many of the non-motor symptoms that occur in PD also occur in iRBD, moreover PD patients can also show the loss of circadian rhythm of arterial blood pressure (CRPB). The aim of our study is to correlate the cardiovascular failure with TCS findings

using tilt table test for orthostatic hypotension–(OH) and some vagal tests and the 24-hours ambulatory blood pressure monitoring. We enrolled 14 patients having videoPSGc diagnosis of iRBD. They were compared with PD patients. All these patients underwent tilt table test, 24-hours blood pressure monitoring, Valsalva and deep breathing maneuver and cerebral ecography. 5 iRBD patients presented with TCS findings of SN hyperechogencity (iRBD/SN + group); whilst the other 9 without hyperechogencity (iRBD/SN- group). The two groups of iRBD were compared with 10 PD patients in early stage (PD "de novo" group) and 10 in late stage (PD "advanced" group). All PD subjects showed SN hyperechogenicity. iRBD/SN + and PD "advanced" showed similar alterations in the CRPB. This result, however, is not present in PD "de novo" as well as in iRBD/SN- group. OH was present in all groups except in PD "de novo" group. iRBD patients, especially those with SN hyperechogenicity, present comparable burden of autonomic dysfunction of advanced PD patients. Interestingly, PD "de novo" group did not show cardiovascular autonomic failure in similar extent. If these preliminary findings will be confirmed, iRBD/SN + manifested a greater autonomic impairment than observed in early stage of PD. This could suggest an iRBD/SN + conversion in a synucleinopathies dissimilar from PD.

PP27
Parkinson Disease and sexual dysfunction

Marilena Gubbiotti[1], Jacopo Adolfo Rossi De Vermandois[1], Silvia Proietti[2], Antonella Conte[3], Alfredo Berardelli[3], Antonella Giannantoni[1]

[1]Dip. di Scienze Chirurgiche e Biomediche, Università di Perugia, Perugia, Italy; [2]Dip. di Urologia Humanitas Clinical and Research Center, Rozzano, Milano, Italy; [3]Dip. di Neurologia e Psichiatria, Università di Roma "La Sapienza", Roma, Italy

Introduction and aim: Parkinson's Disease (PD) is the second most common chronic neurodegenerative disease in older people and lower urinary tract (LUTS) dysfunction is a common condition (38–71 %). Epidemiological data on the incidence of sexual dysfunction (SD) in patients affected by PD are limited. Aim of the study was to evaluate the incidence of SD, LUTS, anxiety and depression and their relationships.
Materials and methods: Twenty-one males and 13 females were enrolled. At baseline, patients underwent clinical neurological and urological assessment (3-day voiding diary) and standardized "Hamilton Anxiety Scale" (HAM- A), "Hamilton Depression Scale" (HAM- D), "Incontinence Quality of Life" (I-QoL), "Female Sexual Function Index" (FSFI) and "International Index of Erectile Function" (IIEF) questionnaires. Pharmacological treatments were also investigated.
Results: Mean age was 74.7 ± 8.7 years and mean disease's duration was 10.3 ± 6.6 years. The mean ± SD Hoehn and Yahr stage of the disease was 3 ± 0.2; 22 and 29 patients had increased day-time and night-time urinary frequency, respectively; 31 complained of urinary urgency and 23 were affected by urge urinary incontinence. Six females and 13 males were not sexually active. Mean ± SD HAM- D total score was 17 ± 8.04 and 31 patients had depression; mean ± SD HAM- A total score was 18.1 ± 8.3 and 19 patients had anxiety. 31 patients were under neurologic treatment, 32 assumed urologic therapies and 20 antidepressant (in 4 patients combination therapy). Night-time urinary frequency was significantly associated with increased age ($p > 0.001$). In women, mean FSFI total score decreased with age's increase ($p > 0.01$); desire, arousal, lubrication and orgasm were significantly correlated with pain during sexual intercourse ($p > 0.002$). In both gender, SD was related with the severity of the disease.
Conclusion: SD is present in a high proportion of PD patients, together with LUTS and deterioration of psychological status. SD in PD patients is significantly associated with old age and more severe disease's clinical stage.

PARKINSON - PSYCHIATRIC AND COGNITIVE DISORDERS

PP28
Neuropsychological correlates of "punding" and ICDs in Parkinson's disease

Carmine Vitale[1,2], Fabrizia Falco[2,3,4], Marianna Vicidomini[2,3], Marianna Amboni[2,5], Katia Longo[2,5], Roberto Erro[5], Marcello Moccia[6], Roberto Allocca[6], Emanuele Spina[6], Paolo Barone[5], Gabriella Santangelo[2,3]

[1]Dipartimento di Scienze Motorie e del Benessere, Università degli Studi di Napoli Parthenope, Napoli, Italy; [2]Istituto di Diagnosi e Cura (IDC), Hermitage-Capodimonte, Napoli, Italy; [3]Dipartimento di Psicologia, Seconda Università degli Studi di Napoli, Caserta, Italy; [4]Dipartimento di Studi Umanistici, Università degli Studi di Napoli Federico II, Napoli, Italy; [5]Centro per le Malattie Neurodegenerative (CEMAND), Università degli Studi di Salerno, Salerno, Italy; [6]Dipartimento di Scienze Neurologiche, Università degli Studi di Napoli Federico II, Napoli, Italy

Background: Punding is defined as a costellation of complex and stereotyped behaviours including an intense fascination with repetitive manipulations of technical equipment, excessive grooming or gardening. The punding was associated with high doses of dopamine replacement therapy in patients with Parkinson's Disease (PD). However, until now, no study has investigated the neuropsychological correlates underpinning punding in non-demented PD patients.
Objective: To explore the possible relationship between neuropsychological dysfunctions and punding in PD.
Methods: We enrolled 32 PD patients with both punding and other Impulse Control Disorders (P + ICDs), 32 PD patients with ICDs alone (ICDs), and 20 PD patients without ICDs or punding (controls). All PD patients underwent neurological scales and a comprehensive neuropsychological battery tapping memory, attention, frontal/executive functions, visuospatial functions and behavioural disorders.
Results: Statistical analysis showed significant differences among the three groups on age, educational level, age at PD onset, UPDRS-Part III, disease duration and levodopa equivalent daily dose. MANCOVA with abovementioned clinical variable as covariates revealed significant differences on copy task of Rey complex figure, attentive matrices and on total, cortical and subcortical tasks of Parkinson's Disease-Cognitive Rating Scale among the three groups. The post hoc Bonferroni test showed that ICDs patients with and without punding had worse performances than controls. As for behavioral variables, while ICDs patients without punding were more depressed, those patients with punding were more apathetic, and have more severe sleep and appetite disturbances than controls.
Conclusions: The findings revealed that occurrence of ICDs and Punding is related to alteration of both frontal-striatal circuitries and posterior cortical areas. Moreover, our results suggested that these patients might be more at risk of developing Dementia associated with PD.

PP29

A 2-year non-interventional study to assess the prevalence of impulsive-compulsive behaviors (ICBs) in an outpatient Italian Parkinson's Disease (PD) population (ICARUS)

Paolo Stanzione[1], Angelo Antonini[2], Ubaldo Bonuccelli[3], Karin Annoni[4], Mahnaz Asgharnejad[5], Andreas Fichtner[6], Paolo Barone[7]

[1]Neurology Clinic, University Roma Tor Vergata, Rome, Italy; [2]IRCCS San Camillo Venice and First Neurology Clinic, University of Padua, Padua, Italy; [3]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [4]UCB Pharma, Milan, Italy; [5]UCB Pharma, Raleigh, NC, USA; [6]UCB Pharma, Monheim am Rhein, Germany; [7]University of Salerno, Fisciano, Italy

Introduction: ICBs occur in patients with PD, but the relationship with disease characteristics and therapy has not been fully investigated.
Methods: ICARUS (SP0990), a prospective non-interventional multicenter study, included an Italian outpatient PD population, treated for 6 months. Study visits occurred at Baseline, Year 1 and 2. The primary variable was the presence of ICBs by means of the modified Minnesota Impulsive Disorder Interview (mMIDI). Prevalence is reported at Baseline, Year 1 and 2.
Results: 1069 of 1095 pts (97.6 %) patients were included in the FAS (patients who completed the mMIDI, H&Y, and UPDRS at Baseline). Prevalence of ICBs at Baseline was 28.6 % (306/1069 patients). In general, at Baseline ICB + patients were younger (mean ± SD age: 63.6 ± 9.5 vs 66.6 ± 9.3 years), younger at diagnosis (mean ± SD age: 56.6 ± 10.5 vs 60.8 ± 10.5 years), and had longer disease duration (mean ± SD: 6.9 ± 5.2 vs 5.8 ± 4.9 years). Baseline ICB + Patients reported more severe non-motor symptoms (NMSS), worse sleep impairment (PDSS-2), lower Quality of Life (PDQ-8), and more depressive symptoms (BDI-II). Prevalence rates of ICBs were similar at Baseline, Year 1 and 2. However individual patients could have switched their ICB status. The most prevalent ICB subtype was compulsive eating, followed by punding behavior, hypersexuality, compulsive gambling, and buying disorder. The prevalence of subtypes generally remained stable across the 3 visits.
Conclusions: The results of this 2-Year non-interventional study suggest that specific demographic features, disease characteristics, and PD symptoms are associated with the presence of ICBs in patients with PD. The prevalence of ICBs was stable over the 2-Year observation period.

PP30

Compulsive stereotyped behaviours triggered by dopaminergic therapy in two cases of pure akinesia

Alberto Lerario[1,2], Federico Verde[1,2], Andrea Ciammola[1], Floriano Girotti[1], Vincenzo Silani[1,2]

[1]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milan, Italy; [2]Department of Pathophysiology and Transplantation, 'Dino Ferrari' Center, University of Milan, Milan, Italy

Pure akinesia (PA) is a clinical diagnosis based on the presence of freezing during walking, writing, and speaking, with paradoxical kinesia in the absence of tremor, rigidity, or bradykinesia; levodopa has little or no beneficial effect. Pathological findings in cases of PA are most often consistent with progressive supranuclear palsy (PSP), making PA one of the possible clinical phenotypes of this tauopathy, while a minority of PA cases display pathological features of Parkinson's disease or other rarer entities. We describe two patients with a clinical diagnosis of pure akinesia: a 55-year old man and a 60-year-old woman. The first one showed a hypokinetic gait disturbance with freezing associated with tachyphemia and micrographia, while the second patient displayed gait imbalance with falls, hypophonia, and tachyfemia. In both cases bradykinesia, rigidity, and tremor were remarkably absent and cognitive function was not impaired. Brain MRI did not reveal any significant alterations, whereas presynaptic dopamine transporter nuclear imaging with 123Ioflupane disclosed bilateral nigrostriatal dysfunction in both cases. Notably, in both patients a hyperthymic personality trait was reported during their premorbid life. In the male patient, initiation of therapy with levodopa (150 mg daily) and the dopamine agonist ropinirole (titrated to a daily dose of 8 mg) was followed by onset of agitation, confusion, and compulsive stereotyped behaviours which regressed after discontinuation of treatment. Similarly, in the female patient introduction of levodopa (150 mg daily) was followed by similar neuropsychiatric symptoms as well as visual hallucinations, which both subsided after stopping treatment. Motor symptoms were not significantly ameliorated by these drugs in either patient. Based on these two cases, we hypothesize that in PA dopaminergic treatment, while being of no benefit on the motor disturbances, can cause pathologic dopaminergic overactivity leading to the above-mentioned neuropsychiatric manifestations, especially in patients with a possible psychiatric predisposition.

PP31

Improvement of ICDs and sleep disorders in PD patients treated with rotigotine patch switching from other dopamine-agonists

Giulio Riboldazzi[1,2], Antonios Maras[1,2,3], Maria Laura Ester Bianchi[1], Roberto Giani[2], Giorgio Bono[1,3], Marco Mauri[1,3]

[1]Centro Parkinson e Disordini del Movimento, Ospedale di Circolo, Varese, Italy; [2]Unità Semplice Riabilitazione Disordini del Movimento Fondazione Gaetano e Piera Borghi, Brebbia, Italy; [3]Università degli Studi dell'Insubria, Varese, Italy

Parkinson's disease (PD) is characterized by motor and non-motor symptoms including nocturnal akinesia, sleep disorders and impulse control disorders (ICD). These disorders may be directly related to the underlying disease pathology but may also be a consequence of medication use and pharmacological management. Rotigotine is a non ergoline dopamine agonist (DA) applied once a day using a transdermal continuous delivery patch. Several studies demonstrated significant treatment benefit of rotigotine on motor and non-motor symptoms. Objective of this study is to evaluate the benefit on ICD and sleep disorders on PD patients swithching from other dopamine agonist to rotigotine. We collected data from 59 subjects with PD treated with DA except from rotigotine in stable management for at least 3 months. Motor functions were assessed using Unified Parkinson's Disease Rating scale (UPDRS) part III. Sleep disorders and ICDs were assessed with Parkinson's Disease Sleep Scale (PDSS), Epworth Sleepiness Scale (ESS) and modified Minnesota Impulse Disorders Inventory (mMIDI). DA was shifted after baseline evaluation and titrated to optimal dose without any

other pharmacological modification. Each patients was evaluated after 3 month from baseline. UPDRS Part III score had decreased -1 point from baseline ($P = 0.0073$). Greater improvement was obtained in PDSS score (−2.9 points; $p < 0.0001$), ESS score (−203 points; $p < 0.0001$) and mMIDI score (−3.3 points; $p < 0.0001$). This represent a significant improvement in sleep disorders and ICD with rotigotine compared with other DA resulting in improved quality of life for PD patients.

PP32
Reversible dopaminergic drug-induced delusional and hallucinatory psychosis: differential susceptibility among different subtypes of Parkinson-Plus Syndromes

Mario Meloni, Antonino Cannas, Paolo Solla,
Marcello Mario Mascia, Gianni Orofino, Rita Farris, Daniela Ciaccio, Enrico Binaghi, Noemi Murdeu, Francesco Marrosu

Department of Neurological and Cardiovascular Sciences, University of Cagliari, Cagliari, Italy

Introduction: Dopaminergic therapy with levodopa and dopamine agonists is a key component in the medical management of Parkinson's disease (PD). The clinical use of dopaminergic drugs is associated with non-motor complications including impulse control disorders, psychosis and hallucinations, as well as hypomania and mania. Overstimulation of dopaminergic receptors, particularly in the mesocorticolimbic region, may occur in the context of chronic dopaminergic therapy, leading to aberrant cortical and brainstem activation patterns, sleep disturbances, abnormal attentional and cognitive functioning.
Objective: To describe reversible dopaminergic drug-induced neuropsychiatric symptoms in a small cohort of patients with Parkinson-Plus Syndromes (PPS).
Methods: We collected a series of seven clinical cases previously classified as having idiopathic PD that evolved rapidly into a diagnosis of PPS. All cases were assessed using Unified Parkinson's disease rating scale (UPDRS) and Hoehn & Yahr (H&Y) stage. Cognitive and behavioral screening was performed before starting the dopaminergic therapy. All patients had received early levodopa treatment with modest benefit for the motor symptoms.
Results: Within 3–4 months from the initiation of the treatment all patients developed subacute psychosis with persecutory and jealous delusions as well as confusion and structured hallucinations. Several precipitating factors were excluded, including medication noncompliance, stressful life events and general medical conditions. Sustained remission of psychosis after dopaminergic drugs suspension was obtained in all patients.
Conclusions: All medications currently used to treat PD carry some risk of causing confusion, hallucinations, or disruption of such higher-order mental operations as problem-solving and learning. In this contest, we suppose that the more widespread brain pathology characterizing PPS is related to higher susceptibility in developing dopaminergic drug-induced psychiatric complications. Appropriate management remains challenging, indeed, doses required for control of motor symptoms, especially for atypical parkinsonian conditions, induce subacute behavioral changes. In conclusion, before initiating antipsychotic drugs, we recommend gradual discontinuation of dopaminergic treatment until remission of psychiatric complications.

PP33
Effects of DM2 on cognition in a cohort of PD patients

Emanuele Spina[1], Gabriella Santangelo[2], Roberto Erro[3], Paolo Barone[4]

[1]Department of Neurological Sciences, University Federico II, Naples, Italy; [2]Deparment of Psychology, Second University of Naples, Naples, Italy; [3]Sobell Department of Motor Neuroscience and Movement Disorders, University College London (UCL) Institute of Neurology, London, UK and Dipartimento di Scienze Neurologiche e del Movimento, Università di Verona, Verona, Italy; [4]Department of Medicine and Surgery, Neurodegenerative Diseases Center, University of Salerno, Salerno, Italy

Background: Cognitive impairment is relatively common in Parkinson's disease (PD) and has been linked to a number of risk factors including the motor phenotype and disease duration. Diabetes mellitus type (DM2) is an independent risk factor for dementia. No studies have evaluated whether PD patients with DM2 have an increased likelihood to develop cognitive impairment compared to those without.
Aim: To assess the effect of DM2 on cognition in a large cohort of PD patients.
Patients and methods: Fifty-one consecutive patients with PD were enrolled at the Movement Disorders Centre of Federico II University of Naples. All underwent a comprehensive neuropsychological battery tapping attention, frontal, memory and visuospatial functions.
Statistical analysis: Demographic, clinical and neuropsychological features were compared between diabetic and non diabetic PD patients by means of the Mann–Whitney U test.
Results: No differences were found between groups as to sex, age and disease duration. Patients with DM performed significantly worse on the Trail Making Test part B ($p = 0.03$) and Trail Making test part B-A ($p = 0.017$). No other differences were observed on the remaining neuropsychological battery.
Conclusions: Our data suggest that DM2 could represent an indipendent role in cognitive impairment in PD patients, especially with regards of executive functions. Further studies are needed to evaluate the neurophysiopathological implications of diabetes in PD.

PP34
Parkinson's disease: what relationship is there between disease progression and executive dysfunction?

Elisa Montanaro, Barbara Svevi, Maurizio Zibetti, Leonardo Lopiano

Department of Neuroscience, Turin University, Turin, Italy

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder. Non-motor features have been recently considered as part of the clinical symptomatology. Specifically, cognitive impairment is a major non-motor feature of PD that can occur at all stages of the disease. Although there is heterogeneity in the clinical presentation of cognitive impairment in PD, generally cognitive impairment involves executive function, attention

and working memory. To date, few studies have investigated the relationship between executive dysfunction and clinical progression of PD.
Objective: Our study is a preliminary exploration of executive-cognitive profile in idiopathic PD patients referring to three stages of the disease: initial (G1), intermediate (with initial motor fluctuations-G2) and advanced (patients eligible for complex therapy-G3). We will focus attention on changes in superior frontal cortical functions in relation to the phases of the disease and will consider the role of clinical and neuropsychological features on the risk of developing dementia.
Methods: Patients, divided into three groups corresponding to disease stage, underwent a motor evaluation and an extensive neuropsychological assessment. Frontal-executive functions were investigated by: FAB, M-WCST, TMT-A and B, Digit Cancellation Test. Descriptive statistics and nonparametric test were used to compare groups.
Results: Referring to the disease stage, our preliminary data on eighteen patients (men/women = 10/8; mean age: 60.44 ± 11.39), suggest a progressive impairment in attentional-executive functions with a specific involvement of performance on the following neuropsychological tests: FAB (G1:16.5 ± 1.22; G2:13 ± 1.67; G3:10.66 ± 2.06; $p = 0.002$), M-WCST Categories (G1:5.83 ± 0.40; G2:4.5 ± 1.37; G3:2.5 ± 0.54; $p = 0.002$) and TMT-B (G1:118 ± 74.82; G2:314.66 ± 137.81; G3:445 ± 73.49; $p = 0.004$). G1 and G2 differ for FAB-$p = 0.009$, M-WCTS-$p = 0.041$ and TMT-B-$p = 0.026$ scores, whereas G2 and G3 differ only for M-WCTS-$p = 0.026$.
Conclusion: This preliminary report is the basis of an ongoing study focused on the specific cognitive profile associated to the different phases of the disease, exploring whether early executive dysfunctions are predictors of a future global cognitive impairment in PD.

PP35
Experience of an UVA: 15 years data

Cristina Paci, Sara Tiberi, Anna Rita Caiazzo, Fabio Di Marzio, Giordano D'Andreamatteo, Antonio Cinti, Terenzio Carboni, Sandro Sanguigni, Roberto Gobbato, Michele Ragno

UOC Neurologia, Area Vasta 5 San Benedetto del Tronto-Ascoli Piceno, Ospedale Civile "Madonna del Soccorso", San Benedetto del Tronto (AP), Italy

Introduction: Since the month of September, 15 years ago (2000), we started to work in a out-patients of Dementia. We prescribed cholinesterase inhibitors (donepezil or rivastgmine or galantamine) and memantine to 710 patients affected by Alzheimer's disease (AD). The aim of our study is to assess if in the last period (2008–2015) there is an early diagnosis compared with the first one (2000-2007) and if patients have a significant MMSE score in the two evaluated periods.
Materials and methods: Totally patients were 710. We eliminated 130 patients for incomplete data. So we studied 580 patients that were divided into 5 categories: (1) adverse events, (2) decease, (3) worsening, (4) abandon, (5) fulfilment. We revealed the different sex, moreover we calculated the MMSE media score and media age at the beginning of their disease in two different periods: 2000–2007 (period 1) and 2008–2015 (period 2).
Results: Number of females was 392 and males number was 188. MMSE media score, at the beginning of AD, in period 1 was 15.82 ± 4.67 while was 17.47 ± 4.44 in period 2 (statistically not significant, $p = 0.000$). Media age of period 1 was 79.24 ± 6.35 and media age of period 2 was 77.53 ± 6.80 (statistically low significant $p = 0.002$).
Conclusions: Our study confirm data literature that Alzheimer disease is more prevalent in females compared to males. There was not significant different of MMSE score at the beginning of the disease in the two studied periods while probably is possible to suppose that in period 2 (last period), the diagnosis of AD is quite more early.

PP36
Anxiety in Parkinson's disease: the Italian version of Parkinson Anxiety Scale

Fabrizia Falco[1,5], Carla Caterino[1], Sofia Cuoco[1], Simona Raimo[1], Marianna Amboni[2,3], Katia Longo[2], Paolo Barone[3], Carmine Vitale[2,4], Gabriella Santangelo[1]

[1]Dipartimento di Psicologia, Seconda Università degli Studi di Napoli, Caserta, Italy; [2]Istituto di Diagnosi e Cura (IDC), Hermitage-Capodimonte, Napoli, Italy; [3]Dipartimento di Scienze Neurologiche, Università degli Studi di Napoli Federico II, Napoli, Italy; [4]Dipartimento di Scienze Motorie e del Benessere, Università degli Studi di Napoli Parthenope, Napoli, Italy; [5]Dipartimento di Studi Umanistici, Università degli Studi di Napoli Federico II, Napoli, Italy

Background: Anxiety is a non-motor symptom of Parkinson's Disease (PD) and has a negative impact on quality of life. Recently, the Parkinson Anxiety Scale (PAS) has been created to measure anxiety in PD patients, thus overcoming the limitations of scales non-specific for PD. The PAS consists of three subscales assessing persistent, episodic anxiety and avoidance behaviors, respectively; its original version (English) was found to be a reliable and valid anxiety measure for use in PD patients.
Objectives: The aim of the present study was to investigate psychometric properties of Italian version of the PAS (I-PAS) in non-demented PD patients.
Methods: The original version of the PAS was translated into Italian. The I-PAS was administered to 90 Italian healthy subjects to assess its comprehension. One examiner interviewed 104 consecutive PD patients by observer-rated I-PAS to explore internal consistency. All patients underwent to Beck Anxiety Inventory (BAI), Beck Depression Inventory, Apathy Evaluation Scale, in order to explore convergent and divergent validity of the I-PAS. The Mini-International Neuropsychiatric Interview (MINI) was used to identify patients with clinically significant anxiety and to propose a screening cut-off score for anxiety.
Results: The I-PAS revealed good internal consistency with Cronbach's alpha total of 0.894. As for the convergent and divergent validity, we found: (1) a strong correlation between I-PAS and BAI (Spearman's rho = 0.895; $P < 0.001$); (2) a modest correlation between I-PAS and BDI (Spearman's rho = 0.574); (3) and a low correlation between I-PAS and AES. The analysis of the ROC curve (receiver operating characteristic) revealed a value of 13/14 as cut-off score to identify clinically significant anxiety.
Conclusions: The results indicated that I-PAS had good clinicometric properties; it is a valid, reliable tool for measurement of anxiety in PD patients. We proposed as screening cut-off score to identify patients with clinically significant anxiety disorder.

PP37

Theory of Mind in early drug-naïve Parkinson's disease patients: role of dopaminergic therapy

Eleonora Del Prete, Elisa Unti, Daniela Frosini, Pierpaolo Turcano, Ubaldo Bonuccelli, Roberto Ceravolo

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

Introduction: Theory of Mind (ToM) refers to ability to infer other persons' thoughts, intentions or emotions in social situations; recently a dissociation between "cognitive" and "affective" ToM has been proposed. Impairment of cognitive component has been described since early stages of Parkinson's disease (PD) and the role of therapy is not completely clarified.
Objective: To investigate ToM in early drug-naïve PD patients and the role of dopaminergic therapy in social cognition.
Methods: Participants included 18 drug-naïve PD patients, tested before (PD-T0) and after 3 months of dopaminergic therapy (PD-T1) and 11 healthy controls (HC). ToM abilities were evaluated using 5 different tasks: Perception of faces expression (KDEF) and Verbal Emotion test (affective tasks), Faux Pas (cognitive and affective task), Picture Sequencing Capture Story test and Strange Stories (cognitive tasks). All the subjects underwent an extensive neuropsychological battery and a screening for mood disorders.
Results: Comparing PD-T0 and HC, PD-T0 patients performed worse in some cognitive Faux Pas' sub-items (Correct Hits score $p = 0.022$, answer to question: "Why should not s/he have said it or why was it awkward?" $p = 0.047$; Explanation Score $p = 0.019$). Comparing PD-T0/T1 we found an improvement after therapy in some cognitive Faux Pas' sub-items (Correct Hits score $p = 0.006$, answer to question: "Why should not s/he have said it or why was it awkward?" $p = 0.009$, answer to question "Why do you think s/he said it?" $p = 0.010$, Intention Attribution Score $p = 0.018$ and Explanation score $p = 0.006$) and in an affective Faux Pas' sub-item (Emotion attribution score $p = 0.035$). There was also an improvement in PD-T1 compared to PD-T0 in Picture Sequencing Task Capture Story $p = 0.029$ and in Verbal Emotion test $p = 0.011$.
Conclusion: Our results confirm an impairment of ToM in PD patients in cognitive tasks since early stages and indicate an improvement in some ToM tasks after therapy suggesting an involvement of dopaminergic pathway.

PP38

Unawareness of dyskinesias in Parkinson's disease: is there a relationship with Theory of Mind dysfunctions?

Sara Palermo[1], Martina Amanzio[2], Maurizio Zibetti[1], Leonardo Lopiano[1]

[1]Department of Neuroscience, University of Turin, Turin, Italy; [2]Department of Psychology, University of Turin, Turin, Italy

Introduction: The presence of dyskinesias-reduced-self-awareness (DRSA) in patients suffering from Parkinson's disease (PD) was previously related with metacognitive executive functions. As the association with Theory of Mind (ToM) dysfunction is a matter of debate in PD patients and we hypothesize it could play an important role in DRSA, we analyzed the role of dopaminergic treatment on the medial-prefrontal-ventral-striatal circuitry causing DRSA using a neurocognitive approach. ToM has been recently studied in PD patients suggesting that not only cognitive but also affective ToM may be impaired. However, to our knowledge, there are no studies investigating deficits on awareness of movement disorder and ToM all together.
Objective: The purpose of the current study is to analyze the existence of a relationship between DRSA and abilities related to mentalizing and perspective-taking (affective and cognitive ToM, respectively) that may represent a novel explanation of the phenomenon.
Methods: 48 idiopathic PD receiving levodopa treatment and presenting motor fluctuations (M/F = 26/22; age (mean ± SD) = 65.79 ± 6.52, MMSE (mean ± SD) = 27.65 ± 2.08) were assessed using the MDS-UPDRS scale and the Global Awareness Movement scale (GAM) to measure the presence of DRSA subdividing patients into aware and unaware groups. Patients underwent a first level neuropsychological assessment and questionnaires on behavioral mood changes. Differences between aware and unaware patients with respect to affective (RME) and cognitive ToM (TOM1 and TOM2) were evaluated by means of an independent sample *t*-test.
Results: We found a significant difference between the two groups for the RME ($t = 5.224$ $p = 0.001$) but not for TOM1 and TOM2 ($t = -1.269$ $p = 0.211$; $t = 0.335$ $p = 0.739$, respectively).
Conclusions: Our data support the notion that dyskinesias-reduced-self-awareness impaired the affective component but not the cognitive component of ToM, thus supporting the idea that DRSA is caused by a complex interplay between motor, neuropsychological and affective factors, rather than being a pure neurological-motor problem.

PARKINSON - EXPERIMENTAL

PP39

Fatigue is associated with performance on a demanding finger motor task in Parkinson's disease

Laura Avanzino[1], Tiziano Tamburini[2], Panagiotis Zis[3], Elisa Pelosin[2], Anna Sauerbier[3], Giovanni Abbruzzese[2], K. Ray Chaudhuri[3], Davide Martino[3]

[1]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy; [2]Department of Neurosciences (DINOGMI), University of Genoa, Genoa, Italy; [3]King's College, London, UK

Background: Central fatigue occurs in 33–58 % of PD patients, contributing substantially to quality of life impairment. The dependency of fatigue in PD on central mechanisms is suggested by motor cortex excitability and functional imaging studies. However, investigation of attention-demanding repetitive motor tasks in this condition is limited.
Aim: To compare Parkinson's disease (PD) patients with and without fatigue (PD + F, PD-F) on a demanding finger motor task (DMFT) designed to capture the dual (cognitive-motor) nature of central fatigue.
Methods: Forty-two right-handed non-demented patients with PD were consecutively enrolled, divided into 21 PD + F and 21 PD-F (screened using the Parkinson's Fatigue Scale-16 scale). Wearing a sensor-engineered glove (Glove Analyzer System) on their dominant hand, patients performed sequential opposition digital movements following an acoustic cue paced at 2 Hz for 5 min (5 min-SEQ), and for an additional minute (1 min-SEQ) following a 2-minute rest period. Kinematic measures on the DMFT (movement time, contact time, movement rate, and percentage of correct sequences) and clinical scores of bradykinesia, depression and sleep impairment were obtained in all participants.
Results: PD + F patients showed significantly increased movement time (expressed as inter-tapping interval) and decreased movement

rate at MIN3 ($p = 0.001$ for both time and rate) and MIN5 of the 5 min-SEQ ($p = 0.003$ and $p = 0.04$, respectively) with full recovery after the 1 min-SEQ; PD-F patients maintained stable movement time and rate throughout all the sequences. Deterioration and recovery indices of movement time differed significantly between the two groups. PD + F patients performed also a lower number of correct sequences than PD-F stably throughout the whole DMFT. Bradykinesia, depression and sleep disruption scores did not correlate significantly with any of the DMFT measures.
Conclusions: Performance on a repetitive motor task requiring sustained attention differs significantly between PD patients with and without fatigue. This task could be explored as behavioural measure of central fatigue in PD in future research.

PP40
Interoception and subjective emotional perception in Parkinson's disease

Gina Ferrazzano[1], Lucia Ricciardi[2], Benedetta Demartini[3], Francesca Morgante[4], Roberto Erro[2], Christos Ganos[2], Kailash P. Bhatia[2], Alfredo Berardelli[1,5], Mark Edwards[2]

[1]Department of Neurology and Psychiatry, "Sapienza" University of Rome; [2]Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, London, UK; [3]Department of Psychiatry, San Paolo Hospital and University of Milan, Milan, Italy; [4]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [5]IRCCS Neuromed Institute, Pozzilli, Italy

Background: Although Parkinson's disease (PD) is defined by its motor symptoms, it is now well recognized that cognitive, affective and emotion domains are also impaired. The pathophysiology of these disabling non-motor symptoms (NMS) remains unclear; recently the involvement of limbic areas, in particular the insula, in the neurodegenerative process has been suggested to have a key role. These areas, and the insula in particular, are also been suggested as key regions for interoception; interoceptive sensitivity (IS) is a measure of the veracity of perception of sensations from inside the body related to the function of internal organs.
Aim: To evaluate IS in PD patients and healthy subjects, matched for demographic characteristics by means of a well established task for assessing IS: heartbeat detection. Moreover, we evaluated possible correlations between IS and psychological, affective and disease-related characteristics as well as fatigue perception in PD patients.
Methods: Twenty PD patients and 20 HS were included and underwent the heartbeat detection task: they were asked to mentally count their heartbeats during rest, while their heart rate was objectively measured. The level of concordance between the two measures is considered as a relatively stable trait of IS. An extensive evaluation of motor, non-motor, affective and emotion domains was carried out.
Results: PD patients showed lower IS than HS (0.58 ± 0.2 vs 0.72 ± 0.1; $p = 0.04$). PD patients reported higher scores than HS in scales assessing depression (Hamilton depression scale: 8.7 ± 5.8 vs 6.2 ± 7.5; $p = 0.04$); anhedonia (Snaith–Hamilton Pleasure Scale: 26.8 ± 9.7 vs 15.4 ± 2.9; $p = <0.001$) and apathy (Apathy Evaluation Scale: 35.8 ± 8.6 vs 27.8 ± 6.8; $p = 0.008$). No significant correlations were detected between IS and motor, non-motor, affective and emotion symptoms.
Conclusions: PD patients have reduced interoceptive sensitivity. Future studies are encouraged to evaluate the importance of interoception in understanding the pathophysiology of affective/emotional symptoms in PD.

PP41
Enhanced homeostatic regulation of primary motor cortex plasticity in Parkinson's disease

Daniele Belvisi[1], Flavio Di Stasio[2], Anna La Torre[2], Antonella Conte[1,2], Giovanni Fabbrini[1,2], Alfredo Berardelli[1,2]

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

Introduction: A number of transcranial magnetic studies (TMS) have shown that cortical plasticity is abnormal in Parkinson's Disease (PD) [1]. Cortical plasticity is regulated by homeostatic mechanisms that intervene to maintain plasticity in a physiologic range [1, 3]. No studies have investigated cortical homeostatic plasticity mechanisms in PD and whether these mechanisms have a role in abnormal cortical plasticity.
Objective: To investigate cortical homeostatic-like plasticity in patients with PD, by coupling two TMS plasticity-inducing protocols: intermittent theta burst stimulation (iTBS) and low frequency repetitive TMS (1 Hz-rTMS).
Methods: Fifteen PD patients and 13 age- and sex- matched healthy controls participated. The diagnosis of PD was based on the United Kingdom Parkinson's Disease Society Brain Bank criteria. The neurophysiological assessment consisted of two sessions. Firstly, we evaluated iTBS effects on primary motor cortex (M1) by recording 20 motor evoked potentials (MEPs) before and after iTBS. In the second session, we evaluated whether iTBS effects on M1 were modified by the prior 1 Hz rTMS administration. 1 Hz rTMS was delivered on M1 for 15 min (900 stimuli). Twenty MEPs were recorded before and after the combined stimulation (1 Hz rTMS + iTBS). In both sessions MEPs were recorded from the left first dorsal interosseous muscle. PD patients were studied on and off therapy.
Results: iTBS induced a MEPs amplitude facilitation in healthy subjects but not in PD patients. When 1 Hz rTMS preceded iTBS, MEPs increased in size to a greater extent in PD than in healthy subjects. Dopaminergic treatment left 1 Hz rTMS +iTBS-induced MEPs amplitude facilitation unchanged in PD.
Conclusions: Our findings demonstrate that M1 homeostatic-like plasticity is enhanced in PD. The increase of homeostatic-like plasticity could reflect a compensatory mechanism to the reduced M1 cortical plasticity.
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PP42
Defective glucocerebrosidase in GBA mutant Parkinson's disease fibroblasts is rescued by chemical chaperone ambroxol through modulation of lysosomal factors

Giulia Ambrosi, Cristina Ghezzi, Roberta Zangaglia, Giovanna Levandis, Claudio Pacchetti, Fabio Blandini

Center for Research in Neurodegenerative Diseases, C. Mondino National Neurological Institute, Pavia, Italy

Introduction: Heterozygous mutations in *GBA* gene, encoding for lysosomal enzyme glucocerebrosidase (GCase), are a major risk factor for sporadic Parkinson's disease (PD). Defective GCase has been recently reported in fibroblasts of *GBA*-mutant PD patients and pharmacological chaperone ambroxol has been shown to correct such defect. A number of endogenous elements support GCase activity, especially transporter and lysosomal receptor LIMP2 and activator saposin (Sap) C, which have been suggested as possible disease modifiers in PD.
Objective: Our aim was to further investigate GCase activity, associated lysosomal and proteasomal factors at baseline and after ambroxol administration in fibroblasts from sporadic PD patients, with or without heterozygous *GBA* mutations, and healthy subjects.
Methods: We assessed protein levels of GCase, LIMP2, Sap C and parkin – a central element in PD and cellular proteostasis – by western blotting. We measured activities of GCase and cathepsin D, responsible for Sap C cleavage from precursor prosaposin, using ELISA assays. All analyses were carried out in basal conditions and following exposure to ambroxol.
Results: GCase activity was reduced in fibroblasts from *GBA*-mutant patients and ambroxol corrected this defect, thereby confirming previous results. Ambroxol increased cathepsin D activity, GCase and Sap C protein levels in all groups and LIMP2 protein levels in *GBA*-mutant PD fibroblasts. Parkin levels were slightly increased only in the PD group without *GBA* mutations and were not significantly modified by ambroxol.
Conclusion: Our study confirms that GCase activity is deficient in *GBA*-mutant PD patients—further indicating that fibroblasts are a good model to investigate proteolytic dysfunction—and that ambroxol corrects this defect. We show that ambroxol-induced rescue of GCase activity is associated with enhanced expression of LIMP2 and Sap C, but not parkin. Therefore, chemical chaperone ambroxol selectively modulates lysosomal pathways that may be targeted for the development of innovative therapeutic strategies.

PP43
Parkin regulates kainate receptors by interacting with the GluK2 subunit

Andrea Ciammola[1], Anna Maria Maraschi[1], Alessandra Folci[2], Francesca Sassone[1], Giuseppe Ronzitti[3], Graziella Cappelletti[4], Vincenzo Silani[1,5], Shigeto Sato[6], Nobutaka Hattori[6], Michele Mazzanti[4], Evelina Chieregatti[3], Christophe Mulle[7], Maria Passafaro[2], Jenny Sassone[1]*

[1]IRCCS Istituto Auxologico Italiano, Department of Neurology and Laboratory of Neuroscience, Cusano Milanino, Milan, Italy; [2]CNR Institute of Neuroscience, Department of BIOMETRA, University of Milan, Milan, Italy; [3]Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genova, Italy; [4]Department of Biosciences, Università degli Studi di Milano, Milano, Italy; [5]"Dino Ferrari" Center, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy; [6]Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan; [7]Interdisciplinary Institute for Neuroscience, CNRS UMR 5297, University of Bordeaux, Bordeaux, France * Present address: 3rd Neurology Unit, IRCCS Foundation, 'Carlo Besta' Neurological Institute, Milan, Italy (J.S.)

Introduction: Loss of function mutations in the PARK2 gene, which encodes the ubiquitin E3 ligase named parkin, cause autosomal recessive juvenile parkinsonism. Parkin is an E3 ubiquitin-ligase that targets proteins for degradation and modulates mitochondria turnover. Besides these widely recognized functions, a new potential parkin function comes from evidence showing that parkin localizes at synapses, modulates synaptic protein functions and that loss of endogenous parkin makes neurons highly vulnerable to excitotoxic stimuli.
Objectives: We tested the hypothesis that parkin regulates glutamate ionotropic receptors and that neurodegeneration induced by PARK2 mutations may stem from excitatory synapse vulnerability.
Methods: Glutamate receptor subunit levels were analyzed in vitro and in vivo PARK2 models and in post-mortem human brain tissues. We investigated the molecular mechanism by which parkin modulates Kainate receptors, cell death and excitotoxicity in primary hippocampal neurons.
Results: We found significantly increased levels of GluK2 subunit of kainate receptors (KARs) in brain lysates from patients with the PARK2 mutation as compared to healthy controls. We showed that parkin interacts with the Gluk2 subunit of KARs and identified the interaction domains. We also showed that parkin can ubiquitinate GluK2 and regulate GluK2 surface levels. Finally, we demonstrated that pharmacological antagonism of the Gluk2 subunits protects PARK2 silenced primary neurons from KA-induced cell death.
Conclusion: Our results support the hypothesis that a loss of neuronal parkin increases vulnerability to excitotoxicity and suggest KAR as a new target for neuroprotective therapy in patients with the PARK2 mutation.

PP44
Identification of new genomic variations in protein coding and RNA genes by NGS in Parkinson's disease

Marialuisa Valente[1,2], Roberta Zangaglia[3,2], Stella Gagliardi[1,2], Ivana Ricca[1,2], Susanna Zucca[1,2], Fabio Blandini[2], Claudio Pacchetti[3,2], Cristina Cereda[1,2]

[1]Laboratory of Experimental Neurobiology, C. Mondino National Institute of Neurological Foundation, Pavia, Italy; [2]Center for Research in Neurodegenerative Diseases, C. Mondino National Institute of Neurological Foundation, Pavia, Italy; [3]Parkinson's Disease and Movement Disorders Unit, C. Mondino National Institute of Neurological Foundation, Pavia, Italy

Background: The introduction of deep sequencing technologies has revolutionized genetic studies, prompting the development of innovative theories for Parkinson's Disease (PD) pathogenesis. In addition to canonical protein genes associated with PD, potentially relevant antisense genes (AS) have been recently discovered, for example the PINK1 antisense gene (PINK1-AS) [1]. This new class of genes transcribed in endogenous RNA molecules of natural antisense transcripts (NATs) that exhibit partial or complete complementarity to mRNAs. NATs contribute to the regulation of sense genes and molecular functions at various levels. Variations in AS genes may interfere with protein gene regulation, influencing PD phenotype expression.
Objectives: Identification of new genomic variants in either protein and AS genes in a cohort of PD patients.
Methods: Next Generation Sequencing analysis has been performed in a cohort of 65 Italian PD patients. True Seq Custom Amplicon platform was composed by PARK2, PINK1, DJ-1, LRRK2, SNCA, UCHL1, EIF4G1, ATP13A2, VPS35 and GBA genes.
Results: Regarding protein genes, the data analysis showed the presence of new non-synonymous mutations in PARK2, LRRK2, PINK1 and ATP13A2. For the mutations in PARK2 (p.W447G,

p.R191Q), LRRK2 (p.I178F, p.L2425 V) and PINK1 (p.A124 V) the in silico prediction (PolyPhen2 and Mutation Tester) supported its pathological implication, while the mutation in ATP13A2 (p.N1091S) resulted neutral. The most interesting data concerned a new AS gene: we found a not yet described SNCA-AS, aside from PINK1-AS. Moreover, several mutations were detected in the SNCA-AS and PINK1-AS, whose functional relevance is currently under investigation.

Discussion: Our NGS data indicated variations in either protein and AS genes, opening intriguing perspectives in PD genetics. Further studies will be needed to investigate the functional role of AS gene variations, but it is clear that the classic genotype-phenotype vision may no longer be able to explain the complexity of PD molecular mechanisms.

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PP45

Dopamine receptors polymorphisms are a risk factor for developing dyskinesias in Parkinson's disease

Luca Magistrelli[1], Marco Ferrari[2], Silvia Rosa[1], Fabiola De Marchi[1], Franca Marino[2], Gaia Oggioni[1], Myriam Carecchio[4,5], Giulio Riboldazzi[3], Giorgio Bono[3]; Marco Cosentino[2], Roberto Cantello[1], Cristoforo Comi[1]

[1]Department of Neurology, University of Eastern Piedmont, Novara, Italy; [2]Center of Research in Medical Pharmacology, University of Insubria,Varese, Italy; [3]Department of Neurology, University of Insubria,Varese, Italy; [4]Department of Paediatric Neurology, IRCCS "C. Besta", Milan, Italy; [5]Molecular Neurogenetics Unit, IRCCS "C.Besta" Milano, Italy

Introduction: Dyskinesias are one of the most frequent motor complications of advanced Parkinson's disease (PD) and are strictly related to levodopa therapy. While female sex, earlier disease onset and longer disease duration are well known risk factors, preliminary evidence suggests that also dopamine receptor (DRD) single nucleotide polymorphysms (SNPs) play a role in dyskinesias development.

Objective: To establish whether DRD SNPs influence dyskinesias development in PD.

Methods: We enrolled 72 PD patients, divided in two equal and age-gender matched groups (36 subjects each), defined by the presence/absence of dyskinesias. The two groups were also matched for disease duration and pharmacological treatment. The following SNPs were analyzed: DRD1 (rs 4532, rs686), DRD5 (rs6283), DRD2 (rs1800497, rs6277), DRD3 (rs6280, rs1800828), DRD4 (rs747302, 7 48-base pair).

Results: We found that frequencies of haplotype A at DRD2 rs1800497 and at DRD3 rs6280 were significantly increased in dyskinetic compared to non-dyskinetic PD patients ($p = 0.02$ and $p = 0.04$ respectively). On the contrary, we failed to demonstrate a statistically significant difference for the other SNPs.

Discussion: Our preliminary findings show that DRD2 and DRD3 variations increase the risk of diskinesias in PD. On a functional level, D2 like receptors (DR2 and DR3) regulate dopamine release through an intracellular signaling pathway that leads to a decrease of ATP release and calcium concentrations. Haplotype A at DRD3 rs6280 is more frequent in patients with tardive dyskinesias, and was found to favor dopaminergic release. On the other hand, haplotype A at DRD2 rs1800497 was shown to increase PD risk and cause a reduction of dopamine binding affinity and D2 density in brain. The identification of the genetic determinants of dyskinesias has important implications on both the knowledge of the molecular mechanisms of PD and on practical management of the pharmacological treatment.

PP46

Cortical sources of resting-state EEG rhythms in Parkinson's disease (PD) and Alzheimer's disease (AD) may reflect specific and common network pathological processes

Maria Francesca De Pandis[1], Claudio Babiloni[2], Susanna Lopez[2], Fabiola Sorpresi[1], Lucia Fraioli[1], Doriana Vallone[1], Giovanni Battista Frisoni[3,4], Fabrizio Stocchi[5], Ute Gschwandtner[6], Peter Fuhr[6]

[1]San Raffaele Cassino, Cassino, Italy; [2]Sapienza University of Rome, Rome, Italy; [3]IRCCS Fatebenefratelli, Brescia, Italy; [4]Neuroscience, University of Geneve, Geneve, Switzerland; [5]IRCCS San Raffaele Pisana, Rome, Italy; [6]Neurology, University of Basel, Basel, Switzerland

Introduction: Neurodegenerative disorders characterized by cognitive impairment include Parkinson's disease (PD) and Alzheimer's disease (AD). Even at early stages of PD, cognitive deficits are found in the majority of patients even if without any impact on their global abilities within the cognitive spectrum [1]. Main cognitive deficits of PD related dementia (PDD) include typically executive dysfunction, memory complaints, attentional deficits and fluctuating cognition [2]. Neuropathological mechanisms underlying PDD and AD are still insufficiently understood, limiting the power of prognosis and drug discovery. Previous evidence [3] showed that theta and alpha rhythms differ in AD and PDD subjects with dementia.

Objective: Here we test the hypothesis that cortical source mapping of resting-state electroencephalographic (EEG) rhythms could characterize the early stage of Mild Cognitive Impairment in Parkinson's disease (PD-MCI) and Alzheimer's disease (AD-MCI) subjects.

Methods: To address this issue, eyes-closed resting state EEG rhythms were recorded in 29 AD-MCI, 29 AD, 16 PDD and 29 PD-MCI subjects. Age, gender, and education were carefully matched across the three groups. Mini Mental State Evaluation (MMSE) score probed subjects' global cognitive status, and was matched between all groups. EEG rhythms of interest were delta (2–4 Hz), theta (4–8 Hz), alpha1 (8–10.5 Hz), alpha2 (10.5–13 Hz), beta1 (13–20 Hz), and beta2 (20–30 Hz). EEG cortical sources were estimated by low resolution brain electromagnetic source tomography (LORETA).

Results: With respect to the AD and AD-MCI groups, the PDD and PD-MCI groups were characterized by peculiar abnormalities of

central delta sources and posterior cortical sources of theta and alpha1 rhythms.
Conclusions: Cortical sources of resting-state EEG rhythms may be useful to specifically characterize the Mild Cognitive Impairment and the Dementia stages in AD and PD subjects.
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PP47
Retinal electrophysiology in Parkinson disease: oscillatory potentials abnormalities reveal abnormal visual processing to luminance variations

Alberto Polo, Laura Ferigo, Lorenzo Bevacqua

UO Neurologia, Ospedale Mater Salutis, Legnago (VR), Italy

Introduction: Several circuits including lateral connections provided by horizontal and amacrine cells modulate vertical pathway from sensory to output neurons in the retina. They represent the generator source in the inner plexiform layer of the oscillatory potentials (OPs), having a functional significance as feed back inhibitory circuits. Pharmacological tests revealed a chemical sensitivity to GABA, dopamine and glycine of individual OPs. We have analyzed amplitude and latency of OPs in PD.
Method: Electrophysiology: Fifteen patients affected by PD, and normal aged matched individuals, have been studied (9 males—6 females) ranging in age between 42 and 63. Have also been dark adapted eyes were simultaneously stimulated by brief light flash; a Ganzfeld cupola has been used for providing uniform retinal illumination (30 cd/m2). Surface electrodes were placed in outer canthus. Five responses were averaged off line: single trials were re-checked for final averaging. Fast ERG OPs were amplified and filtered at 100 Hz–2 kHz. Paired flashes were used to test the inter stimulus interval producing perception of single flash.
Results: Individual peaks (O1-O2-O3-O4) were analyzed in latency and amplitude. The mean latency in ms and (SD) in patients were: O1 17.15 (0.71); O2 23.8 (0.74); O3 31.54 (1.48); O4 40.25 (2.4). The mean amplitude in μV and (SD) in patients were: O1 7.1 (1.7); O2 12.5 (4.4); O3 9,1 (4.6); O4 4.4 (1.8). The mean latency in patients and controls are not statistically different ($P > 0.05$) for all wavelets. The mean amplitude is higher in controls than in PD : the significance was larger for O1-O2 values ($p < 0.001$) than for O3-O4 values ($p < 0.02$). The mean inter stimulus interval for "perception of fusion" in paired flash was longer ($p < 0.03$) in patients (mean value 110 ms) than in controls (mean value 57 ms).
Discussion: Low amplitude oscillatory potentials in PD are suggestive of a defective lateral inhibitory processes, in which probably dopamine may play a role at retinal level. This fact can partly correlate with impaired perception of paired flashes in most PD patients. The brain itself by means of corticofugal pathways may control retinal output by manipulating the membrane potentials of the amacryne cells: OPs may be therefore regarded as a whole expression of rapid neural adaptive mechanism in CNS.

PP48
Adapted motor activity with pleasant music in Parkinson's disease: a comparative study

Stefano Tugnoli, Angela Abbasciano, Sara Marin, Giulia Brugnoli, Ilaria Casetta, Stefano Caracciolo, Enrico Granieri

Section of Neurological Psychiatric and Psychological Sciences School of Medicine, University of Ferrara, Ferrara, Italy

Introduction: Adapted motor activity with pleasant music (AMAPM) may improve the motor performances, may activate positive emotions and enhance the quality of life of patients with Parkinson's disease (PD) [1].
Objective: The main goal of the study is to highlight some clinical differences between two groups of patients affected by Parkinson's disease, by comparing 30 subjects (mean age: 71.9 ± 6.8) following a program of AMAPM (Group 1) with 30 subjects (mean age: 70.6 ± 7.4) who do not participate in such activity (Group 2). Psychiatric symptoms, quality of life and caregiver burden were measured in order to investigate correlations with disease duration.
Methods: All the subjects were patients with idiopatic PD with mild to moderate motor impairment, without cognitive impairment and not very dependent (Schwab and England >50 %), evaluated in "ON" condition, not treated with Apomorphine or PEG. The patients were tested with MMSE, UPDRS, GHQ-28, GDS, PDSS-2, PDQ-39 and CBI.
Results: The two groups are homogeneous in the activities of daily life (UPDRS II) and in motor performance (UPDRS III). We found significant differences between the two groups for almost all the other variables. Group 2 shows higher prevalence of psychiatric symptoms (67 vs. 20 %; $p < 0.00001$), depressive symptoms (43 vs. 7 %; $p < 0.0001$) and sleep disorders ($p < 0.01$). In Group 2 the quality of life is more impaired ($p < 0.001$) and the impact of the disease on caregivers is greater ($p < 0.01$). Finally, the severity of psychiatric symptoms (GHQ-28 total score) correlates positively with disease duration only in Group 2 ($p < 0.05$).
Conclusion: The subjects participating to the AMAPM show better psychological condition and better quality of life, and their disease causes lower burden on the caregivers than those who do not perform such activity. The duration of the disease has a negative effect on psychopathological symptoms only in PD patients not participating in AMAPM.
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PP49
Motor imagery and cognitive assessment in de novo Parkinson's: a preliminary study

Viviana Lo Buono[1], Lilla Bonanno[1], Francesco Corallo[1], Placido Bramanti[1], Giuseppe Di Lorenzo[1], Silvia Marino[1,2]

[1]IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy; [2]Department of Biomedical Sciences and Morphological and Functional Imaging, University of Messina, Messina, Italy

Introduction: Motor imagery (MI) is the mental representation of an action without engaging in its actual execution [1]. MI is a therapeutic approach that make use of cognitive function to study and understand the movement disorder in Parkinson's disease (PD) [2].
Objective: We investigated whether functional connectivity by using a fMRI motor imagery task is present in de novo PD and if it correlated with the cognitive assessment.
Methods: 13 de novo drug-naïve PD with mean age of 68.93 ± 6.02 years were consecutively enrolled. The neuropsychological evaluation consisted of Montreal Cognitive Assessment (MOCA) for global assessment and Wisconsin Card Sorting Test (WCST) to evaluate executive functions. Each subject was undergo to a fMRI 3.0T examination by using a motor imagery task. The data were analyzed by using Brain Voyager software. Fixed Effects (FFX) group analysis was used to integrate the data from multiple subjects into a single General Linear Model analysis.
Results: The clinical score highlight an impairment cognitive assessment (MOCA: 19.8 ± 4.83; WSCT: 107.8 ± 28.02). Imagery motor task functional changes were identified in motor cortical regions in both patients and healthy controls. Intra-group comparisons revealed relatively increased BOLD fMRI responses in left sensorimotor cortex, lateral premotor area, supplementary motor area and right posterior parietal cortex and occipital cortex ($p < 0.001$ uncorrected) and relatively decreased responses in the right occipital cortex and the left temporal ($p < 0.05$ corrected) in PD patients. Importantly, there were no significant differences in performance of the motor task between PD de novo patients and controls.
Conclusion: Our results showed activation of sensory-motor networks strictly connected with execution and imagination of movement. Our patients, in fact, had not high motor impairment, even if they presented a mild cognitive impairment. These findings could suggest that in a very early stage, the cognitive impairment could preexist the neuromotor symptoms.
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PP50
Resting state functional connectivity in olfactory network in de novo Parkinson's disease

Silvia Marino[1,2], Lilla Bonanno[1], Fabrizia Caminiti[1], Viviana Lo Buono[1], Francesco Corallo[1], Placido Bramanti[1], Giuseppe Di Lorenzo[1]

[1]IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy; [2]Dipartimento di Scienze Biomediche e delle Immagini Morfologiche e Funzionali, Università degli Studi di Messina, Messina, Italy

Introduction: Olfactory dysfunction often manifests years before the development of parkinsonian motor symptoms. Resting-state fMRI has been used to investigate brain function. It is known that PD patients exhibit impairments of functional network connectivity within cortico-striatal networks, as well as decreased functional integration across neuronal loops that involve striatum, mesolimbic cortex, sensorimotor regions.
Objectives: To assess the pattern of RS functional connectivity in PD de novo patients, related to olfactory psychometric test, to further elucidate olfactory-dependent cortical-subcortical functional networks.
Methods: We enrolled 10 de novo drug-naïve PD patients (UPDRS median motor subscores was 26, median disease duration was 2.1 ± 1.3 years) and 10 sex-aged normal controls (NC). All subjects were not cognitively impaired. None of the patients took anti-parkinsonian drugs. Olfactory function was studied with the Sniffin' Sticks Test. The study was performed with a 3T MRI scanner.
Results: PD patients were hyposmic (TDI scores 20.2 ± 2.1), if compared with NC ($P < 0.05$). At MRI examination, all subjects did not present structural abnormalities. The caudate was the ROI defined to study olfactory-dependent RS functional networks in PD patients. It had been known to be an important subcortical area in the cognitive cortico-striatal function. The PD patients showed increased positive striato-cortical connectivity in the left frontal areas and decreased connectivity in the right occipital area. The cortical functional connectivity with the caudate was negatively correlated with the TDI scores in the bilateral frontal areas, left occipital area and precuneus.
Conclusions: This study showed that the patterns of RS functional connectivity differ according to olfactory performance in de novo and drug-naïve PD patients and NC. A correlation analysis revealed that olfactory performance was negatively associated with cortical connectivity with the caudate. These data suggest that RS functional connectivity should be closely correlated with the level of olfactory performance in de novo PD patients.

PARKINSON - THERAPY 1

PP51
Sialorrhea and ultrasound-guided botulinum toxin-A: a 2-year prospective study

Carlo Alberto Artusi[1], Stefania De Mercanti[1], Marco Busso[2], Marco Tinivella[3], Marinella Clerico[1], Luca Durelli[1], Pierangelo Barbero[1]

[1]Clinical and Biological Sciences Department, Neurology Unit, University of Torino, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy; [2]Oncology Department, Radiology Unit, University of Torino, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy; [3]Clinical and Biological Sciences Department, Dietologic and Nutrition Unit, University of Torino, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy

Introduction: Botulinum toxin-A (BoNT-A) is an emerging treatment option for sialorrhea. There are limited studies investigating BoNT-A in large and diverse neurological populations of severe sialorrhea, especially with ultrasound-guidance.
Objective: To evaluate sialorrhea reduction, therapeutic effect duration, and caregiver satisfaction of ultrasound-guided BoNT-A injections in patients with severe sialorrhea secondary to neurological diseases.
Methods: Thirty-four severe adult sialorrhea patients (7 amyotrophic lateral sclerosis, 5 Parkinson's disease, 8 multiple sclerosis, 8 stroke, 6 Alzheimer's disease) referring consecutively to S.Luigi Gonzaga Hospital Neurology Unit were treated with BoNT-A injections in bilateral parotid and submandibular gland under ultrasound-guidance. Seventy-five IU were injected in each parotid gland (4–6 sites) and 50 IU in each submandibular gland (2 sites). Questionnaire-based scoring for drooling severity (score 1–5) and frequency (score 1–4), caregiver self-evaluation of the symptom improvement with a visual-analogue scale and adverse events were collected before treatment

and after every administration (Month 1 and 3). Thirty-three patients received 3 therapy sessions.
Results: We observed significant decrease from baseline in mean number of daily aspirations and significant improvement in *questionnaire-based scoring for drooling severity* and *frequency* and in *visual-analogue scale* following ultrasound-guided BoNT-A injections ($p < 0.001$ vs. baseline for all comparisons). No major treatment-related adverse events (AEs) and a low incidence of minor AEs (local pain, dry mouth, local bleeding, facial palsy and chewing muscle weakness) were reported. The mean onset of improvement was about 10 days and the mean duration of improvement was about 5.5 months after each treatment.
Conclusions: Ultrasound-guided BoNT-A injection for sialorrhea secondary to neurological disorders demonstrated sustained efficacy, prevention of major AEs and low rate of minor AEs. This study confirms the long-lasting efficacy and safety of ultrasound-guided BoNT-A injections for sialorrhea, regardless the causative neurological disorder, encouraging the use of ultrasound-guidance to obtain optimal results in terms of safety and reproducible outcomes.

PP52
Dynamic electromyography to symbiotic use of botulinum toxin and rehabilitation program in Pisa syndrome in Parkinson's disease

Massimo Bacchini[1], Vincenza Fetoni[2], Floriano Girotti[3], Manfredi Saginario[4], Augusto Scaglioni[5], Michele Rossi[1]

[1]Don Carlo Gnocchi Foundation Onlus, S. Maria ai Servi Center, Parma, Italy; [2]S.S. Neurologia, Azienda Ospedaliera Fatebenefratelli e Oftalmico, Milano, Italy; [3]S.S. Neurologia, Istituto Auxologico, Milano, Italy; [4]Sportello Parkinson, Don Carlo Gnocchi Foundation Onlus, S. Maria ai Servi Center, Parma, Italy; [5]S.S. Neurologia, Azienda Ospedaliera Vaio, Fidenza (PR), Italy

Introduction: Botulinum toxin injections are the first line option for the treatment of Pisa syndrome in Parkinson's disease, however is no consensus guiding the muscle selection.
Objective: Identifying affected muscles with dynamic electromyography for the use of botulinum toxin, it may be possible to get meaningful clinical improvement in Pisa syndrome (PS).
Methods: 11 patients with PS (6 males and 5 female; the average age was 61 years) participated in this study. All patients underwent clinical investigation (Trunk Dystonia Disability Scale: TDDS), X-rays and gait analysis with dynamic electromyography on two occasions: at inclusion and 1 month after botulinum toxin injection. The rules of engagement with dynamic EMG of the muscles to inject was a pattern of abnormal tonic hyperactivity at rest and during movements with potential of more than 100 μVolts/sec for more than 500 ms of the paraspinal muscles on the bending side, whereas activity was markedly reduced in both muscles on the opposite side. Were always also examined the abdominal muscles, to rule out any forms combined with camptocormia. Electromyography static needle excluded potential myopathic primary.Using electromyographic guidance, we injected botulinum toxin into the paravertebral muscles ipsilateral the bending side in four sites using 125 U per site. Patients underwent a rehabilitation programme consisting of individual 90-minute daily sessions, 5 days a week for 4 weeks.
Results: After the treatment, TDDS score showed a mean improvement of 6 points. Significant decrease of X-ray degree of trunk lateral bending ($26.9° \pm 5.6°$ vs. $15.3° \pm 4.2°$) and of mean axial rotation along the spine ($12.5° \pm 3.7°$ vs. $8.9° \pm 2.6°$) was observed. Kinematic: resumption of the pelvic sinusoidal trend in sagittal plane and pelvic lateral tilt in frontal plane. Dynamic EMG: reduction of abnormal tonic hyperactivity of the paraspinal muscles on the bending side, whereas activity was increased in muscles on the opposite side.
Conclusion: Here we show that dynamic electromyography can lead a significant change of standardized protocol for management Pisa syndrome in Parkinson's disease.

PP53
Efficacy of selegiline in the treatment of daytime sleepiness in patients affected by Idiopathic Parkinson's disease treated by dopamine agonists

Maria Laura Ester Bianchi[1], Giulio Riboldazzi[1,2], Antonios Maras[1,2,3], Marco Mauri[1,3], Giorgio Giovanni Bono[1,3]

[1]Centro Parkinson e Disordini del Movimento, Ospedale di Circolo, Varese, Italy; [2]Unità Semplice Riabilitazione Disordini del Movimento, Fondazione Gaetano e Piera Borghi, Brebbia (VA), Italy; [3]Università degli Studi dell'Insubria, Varese, Italy

Introduction: Excessive daytime sleepiness (EDS) affects up to 50 % of Parkinson's disease (PD) patients: it presents a multifactorial pathophysiology including age and disturbances of sleep-wake regulation, but dopamine agonists also contribute to EDS. The most potent first-line agents in the treatment of PD are dopamine agonists and levodopa, while monoamine oxidase B (MAO-B) inhibitors are useful as first-line therapy and to lessen the degree of "wearing off" in advanced PD. The MAO-B inhibitors approved for use in PD include selegiline and rasagiline. Selegiline is metabolized to desmethylselegiline and L-methamphetamine, both of which can be further metabolized to L-amphetamine as well as other minor metabolites. Previous studies have suggested the efficacy of selegiline in the treatment of narcolepsy and EDS in various neurological diseases.
Objectives: Aim of this study was to assess the efficacy of selegiline in the treatment of EDS in PD patients treated by dopamine agonists.
Methods: We enrolled 16 patients affected by idiopathic PD with a diagnosis of EDS, developed after the introduction of dopamine agonists and documented by Parkinson's Disease Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS). Among these patients 10 were treated by pramipexol, 4 patients by ropinirol and 2 patients by rotigotine as first-line or add-on therapy to levodopa. Among these patients thirteen introduced in their therapy selegiline, while in the remaining 3 patients we withdrew rasagiline and introduced selegiline as well.
Results: After 3 months of treatment with selegiline we found a statistical significant improvement of EDS in 12 patients ($p < 0.001$), 3 patients did not show any change, 1 patient presented a worsening of the EDS.
Conclusion: Based on these findings and accordingly with literature data we can hypothesize that selegiline is effective in the treatment of EDS induced by dopaminagonists in PD patients, although further studies are needed to confirm such results.

PP54
CBT vs psychoeducational intervention in Parkinson's disease

Maria Carmela Bloise[1], Isabella Berardelli[1], Massimo Pasquini[1], Massimo Biondi[1], Alfredo Berardelli1[1,2], Giovanni Fabbrini[1,2]

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

Background: To date, little attention has been paid to cognitive behavioural therapy (CBT) for the treatment of psychiatric disorders in Parkinson's disease (PD). Promising results have emerged from studies that have assessed the efficacy of individual CBT for depression and anxiety in PD. Only one open label trial has evaluated the utility of group CBT for psychiatric disorders and motor symptoms in PD. The aim of this study was to evaluate whether group CBT has a positive impact on both psychiatric and motor symptoms in patients affected by PD.
Methods: The study was conducted by comparing two patient groups, one of which was treated with CBT and the other by means of a psychoeducational protocol.The severity of PD was scored according to the Hoehn and Yahr (HY) Scale, the severity of motor symptoms was assessed by means of the UPDRS-III and the quality of life was assessed using the Parkinson's Disease Quality of Life Questionnaire. Non-motor symptoms (NMS) were assessed by means of the Non-Motor Symptom Scale. Cognitive function was measured using the Montreal Cognitive Assessment Scale (MoCA) and the Frontal Assessment Battery Scale (FAB) The psychiatric diagnosis was based on the SCID-I, while the severity of psychiatric symptoms was assessed by means of the Hamilton Depressive Scale, the Hamilton Anxiety Scale, the Brief Psychiatric Rating Scale and the Clinical Global Impressions. The neurological and psychiatric evaluations were performed at the baseline and at the end of the group intervention (12 weeks) in the CBT group and in the Psychoeducational group.
Results: The results suggest that group CBT is effective in treating depression and anxiety symptoms and in reducing the severity of motor symptoms in patients suffering from PD.

PP55
Rotigotine objectively improves sleep in Parkinson's disease: a pilot study with actigraphic recording

Giovanna Calandra-Buonaura[1,2], Pietro Guaraldi[3], Andrea Doria[2], Stefania Nassetti[1], Valentina Favoni[1,2], Sabina Cevoli[1], Federica Provini[1,2], Pietro Cortelli[1,2]

[1]IRCCS, Institute of Neurological Sciences of Bologna, Bologna, Italy; [2]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy; [3]Neurology Outpatient Clinic, Department of Primary Care, Local Health Authority of Modena, Modena, Italy

Introduction: Sleep disturbances represent important predictors of poor quality of life (QoL) in Parkinson's disease (PD). Rotigotine transdermal patch, a dopamine agonist used for treatment of motor symptoms in PD patients, demonstrated to subjectively improve sleep disturbances. However an objective evaluation of its effect on sleep is lacking.
Objective: To objectively evaluate the effect of rotigotine on sleep through actigraphic recording in PD patients with self-reported sleep complaints (PD Sleep Scale-2 $\geq$ 10).
Methods: Patients underwent wrist actigraphic recording for 1 week at enrolment (T0) and while on rotigotine (T1) which was titrated to the dose improving motor symptoms (4–8 mg per day). We evaluated sleep efficiency (SE), activity mean and median and wake minutes after sleep onset (WASO). We also assessed, by means of scales and questionnaires, changes in motor impairment, cognitive performance, sleep disturbances, daytime sleepiness, QoL and depression.
Results: 15 patients (12 males, mean age $\pm$ SD 67 $\pm$ 9 years) were evaluated. At T1 compared to T0 a significant improvement of motor performance, self-reported sleep complaints and QoL was observed. Four pts reported RLS at T0 and a significant improvement in RLS symptoms at T1. Actigraphic recording did not show change in SE and WASO at T1 compared to T0 while a reduction in activity mean and activity median, reaching significance only for activity mean, was observed. However, when considering only the ten patients who presented pathological SE (<85 %) at T0, we observed a significant improvement in SE and a significant reduction in WASO, activity mean and activity median at T1.
Conclusions: This study suggests that rotigotine subjectively improves sleep quality and QoL in PD patients with self-reported sleep complaints and induces a significant reduction in nighttime activity, which could contribute to compromise sleep. Further in patients with reduced SE, rotigotine objectively improves all sleep parameters.

PP56
Treadmill training frequency influences walking improvement in subjects with Parkinson's disease

Cecilia Cerulli[1], Elisa Pelosin[1], Laura Avanzino[2], Roberta Barella[3], Cristina Bet[3], Elisabetta Magioncalda[3], Carlo Trompetto[1], Mauro Casaleggio[3], Giovanni Abbruzzese[1]

[1]Department of Neurosciences (DINOGMI), University of Genoa, Genoa, Italy; [2]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy; [3]Polo Riabilitativo Levante, ASL3, Genoa, Italy

Background: Treadmill training (TT) has been indicated as a potential therapeutic tool for improving balance and gait in patients with Parkinson Disease (PD).
Aim: To provide novel information on the modality of TT program (i.e., frequency of sessions) that could be more effective for PD patients.
Methods: Three groups of PD subjects (10 participants for group) underwent a similar TT program (10 sessions lasting 45 min each), but with a different frequency of sessions throughout a week: (i) low-frequency (LF) group: 2 times a week, (ii) intermediate-frequency (IF) group: 3 times a week and (iii) high-frequency (HF) group: five times a week. Patients were evaluated by the Timed Up and Go (TUG) test, 10 meter walking test (10 MWT), the Berg Balance Scale (BBS), the Falls Efficacy Scale (FES) and a fall's diary before TT, within 1 week, and at 2 and 4 months after TT.
Results: Demographic characteristics and disease severity were not significantly different between groups. Immediately after the end of

the TT, TUG test, 10 MWT, FES and fall's diary scores significantly improved only in the LF and IF groups, whereas they did not no change in the HF group. Improvements were maintained till to 2 months in the LF and IF groups. At 4 months, outcome measures were either comparable or sometimes even better than baseline data in the LF and IF groups, whereas in the HF group, 10 MWT and FES score worsened.
Conclusions: Our results suggest that the frequency of TT influences short and long-lasting effects on walking performance and falls.

PP57
Prescribing pattern and resource utilization of Mono-Amino-Oxidasi-B inhibitors in Parkinson treatment: comparison between rasagiline and selegiline

Luca Degli Esposti[1], Carlo Piccinni[2], Diego Sangiorgi[1], Flavio Nobili[3], Stefano Buda[1]

[1]CliCon Srl, Health, Economics and Outcomes Research, Ravenna, Italy; [2]Department of Medical and Surgical Sciences-Pharmacology Unit, University of Bologna, Bologna, Italy; [3]Clinical Neurology, Department of Neuroscience (DINOGMI), University of Genoa, Genoa, Italy

Introduction: Difference between selegiline and rasagiline for effectiveness in Parkinson's Disease (PD) is uncertain, nevertheless their costs highly differ: rasagiline expenditure is 15-fold than selegiline.
Objective: To compare prescribing pattern and resource utilization in PD patients treated with rasagiline or selegiline.
Methods: Historic cohort study, based on databases of 3 Italian Local-Health-Authorities (Lecce, Frosinone and Pavia, covering 1,865,000 of inhabitants) was performed. Patients with PD and receiving rasagiline or selegiline between July 2009 and December 2011 were selected and followed-up for 12 months. The following outcomes, and relevant costs, were evaluated: (a) anti-parkinson drug prescriptions; (b) hospitalisation for PD and for fracture; (c) antiinflammatory and antirheumatic drugs prescriptions; (d) antipsychotic prescriptions; (e) hospitalisation for cardiovascular diseases; (f) cardiovascular drug prescriptions; (g) ambulatory visits or diagnostic tests. Average annual cost per patient was considered for both PD-related expenditure (a+b+c) and overall cost (a+b+c+d+e+f+g). Differences between rasagiline and selegiline were analysed by generalized linear model.
Results: 1607 patients were selected: 63.7 % under selegiline and 36.2 % under rasagiline. Hospitalisations for PD occurred more in rasagiline group than in selegiline one (13.6 vs. 8.0 %, $p < 0.001$), whereas hospitalisations for fractures occurred less in rasagiline group than in selegiline one (1.4 vs. 3.8 %, $p = 0.005$). Dopamine agonists (66.0 vs. 31.0 %, $p < 0.001$) and levodopa (73.9 vs. 49.0 %, $p < 0.001$) were prescribed more frequently in rasagiline group than in selegiline one. All costs, except for those related to cardiovascular diseases, appeared higher for rasagiline rather than for selegiline. The choice to prescribe rasagiline produced a cost increase statistically significant, for both the overall cost (+2404€, $p < 0.001$) and PD-related one (+2363€, $p < 0.001$).
Conclusion: Prescribing patterns and costs highly differ between patients with PD under rasagiline compared with those under selegiline. Since patients under rasagiline received more frequently either levodopa or dopamine agonists, it is possible to assume that rasagiline is preferred in more severe PD, this attitude is not based on evidences coming from direct comparison of the two molecules.

PP58
The effects of different gait training techniques for improving walking performance in patients in the early stages of Parkinson's Disease: a pilot randomized clinical trial

Christian Geroin[1], Federica Bombieri[2], Francesca Nardello[2], Barbara Pellegrini[2], Nicola Smania[1,3], Marialuisa Gandolfi[1], Michele Tinazzi[4], Federico Schena[2]

[1]Neuromotor and Cognitive Rehabilitation Research Center (CRRNC), Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [2]School of Sport and Exercise Sciences, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [3]Neurological Rehabilitation Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [4]Neurology Unit, Movement Disorders Division, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy

Background: Gait disorders, along with turning and balance disturbances, are the most important determinants of falls, which are recognized to be a major problem among people with Parkinson's Disease (PD). The physical exercise as an adjunct to pharmacological therapy is becoming an optimal procedure to optimize the gait performance expecially in the early stages of PD.
Objectives: The aim of this study is to compare the effect of different gait training procedures in patients with PD.
Methods: This is a single blind, randomized, controlled trial involving 35 outpatients with PD. Patients underwent to one of the 4 treatment groups: whole body exercises ($n = 7$), nordic walking ($n = 8$), treadmill training ($n = 10$), and overground walking training ($n = 10$). All patients received twelve, 40-minute treatment session, three times a week for 4 consecutive weeks. Patients were assessed before (T1), immediately after (T2), and 1 month of follow-up (T3) with the following clinical scales: 6 Minute Walking Test (6MWT), 10 Meter Walking Test (10MWT), and the Timed Up and Go Test (TUG).
Results: At T2, significant improvements ($p < 0.01$) were observed in all training groups, in the 6MWT and TUG. An increased of speed were observed only in patients who underwent to nordic walking ($p < 0.01$) and treadmill group ($p < 0.01$). All training effects persist at T3 ($p < 0.05$). Between group comparisons, treadmill training appears to be superior in improving gait performance assessed TUG ($p < 0.01$). The overground walking training could not be applied to train aerobic conditions whereas only generic and time-related effects have been appreciated.
Conclusion: These preliminary findings suggest that locomotor training could play a crucial role in treating this complex illness by reducing/preventing physical inactivity and in improving the quality of life.

PP59
Proprioceptive Focal Stimulation (Equistasi®) may improve gait in severe Parkinson's disease patients. Preliminary study

Antonella Peppe[1], Fabio Marchetti[1], Stefano Paravati[2], Marco Tramontano[1]

[1]IRCCS Santa Lucia Foundation, Roma, Italy; [2]Physical and Rehabilitation Medicine, University of Rome "Tor Vergata", Roma, Italy

Introduction: The efficacy of Gait Analysis (GA) on evaluating gait modification on Parkinson's Disease (PD) Patients [1] is already well known. On the other hand, several studies have shown that Proprioceptive Focal Stimulation seems to be useful in symptoms amelioration in several neurological disease. Unfortunately, just a few studies have been performed in this fiel in Parkinson's disease. GA was performed in a group of severe PD patients before and after the use of Equistasi® device.
Subjects and methods: Six PD patients (mean age 68 years, mean disease duration 9.1 years, mean UPDRS Part III 32.5) at the best pharmacological therapy were enrolled in the study. GA was performed during the morning in which they started using Equistasi® and at after 4 conescutive weeks of its use. Equistasi® is a nanotechnological device of the dimension of a plaster which generates High Frequency segmental vibration. Volpe et coll. [2] have tested a protocol of application of this device in PD disposing three plaques on the skin: one at C7, one at the right and at the left leg, over the confluence of gastrocnemius bellies. GA was performed as follows: six straight gaits were recorded and Spatial Temporal variables were studied before and after the use Equistasi®. Clinical state was monitored with the recording of UPDRS part III. Parametric (One-way ANOVA and paired t-Student) and not-parametric statistic (Freidman ANOVA and Wilcoxon test) Free tests were used.
Results: Statistical difference was found in mean velocity, which increased ($p < 0.019$), in stride right and Left, which increased as well ($p < 0.02$ and 0.016 respectively). The analisys of the Stride Phase Percentage showed a relevant reduction only in the double stance phase ($p < 0.028$).
Conclusion: Although the group of patients is small, preliminary data encourage to continue to investigate the mechanical segmental vibration as a stimulation of proprioceptive system in Parkinson's disease patients.
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PARKINSON - THERAPY 2

PP60
Increasing placebo response in Parkinson's disease through apomorphine pre-conditioning

Elisa Frisaldi[1,2], Elisa Carlino[1,2], Lucia Giudetti[3], Alan Pampallona[3], Maurizio Zibetti[1], Michele Lanotte[1], Leonardo Lopiano[1], Fabrizio Benedetti[1,2]

[1]Department of Neuroscience, University of Turin Medical School, Turin, Italy; [2]National Institute of Neuroscience, Turin, Italy; [3]Giancarlo Quarta Foundation, Milan, Italy

Introduction: Placebos have been found to affect the patient's brain in a number of conditions, such as pain and motor disorders [1,2]. For example, in Parkinson's disease, a placebo treatment induces a release of dopamine in the striatum and changes the activity of neurons in both thalamic and subthalamic nuclei [3,4].
Objectives: To see whether a placebo response requires pharmacological pre-conditioning with apomorphine.
Methods: We recorded from the motor thalamus during the implantation of electrodes for deep brain stimulation and analyzed the placebo response at the level of single neurons and from a clinical point of view.
Results: We found that placebo administration for the first time induces neither clinical nor neuronal improvement. However, this lack of placebo responsiveness could be turned into substantial placebo responses following previous exposure to repeated administrations of apomorphine. In fact, as the number of apomorphine administrations increased from 1 through 4, both the clinical response and the neuronal activity in the ventral anterior and anterior ventrolateral thalamus increased. After 4 apomorphine exposures, placebo administration induced clinical responses that were as large as those to apomorphine, along with long-lasting neuronal changes. These placebo responses following 4 apomorphine administrations lasted for at least 24 h, but they disappeared completely after 48 h.
Conclusions: These data indicate that learning plays a crucial role in placebo responsiveness, turning placebo nonresponders into responders, and suggest that these effects can be exploited in the clinical setting.
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PP61
Polysomnographic modifications following intraduodenal levodopa/carbidopa gel infusion in advanced Parkinson's disease

Maurizio Zibetti, Elisa Fattori, Serena Angrisano, Elisa Montanaro, Alessandro Cicolin, Leonardo Lopiano

Department of Neuroscience, University of Turin, Turin, Italy

Background: Sleep disorders are common in patients with advanced Parkinson's disease (PD). Levodopa-carbidopa intestinal gel (LCIG) infusion has been shown to improve motor complications in advanced PD, and evidences from questionnaire-based studies suggest that - sleep might improve following LCIG infusion.
Objective: To evaluate the impact of LCIG infusion on sleep symptoms and polysomnographic (PSG) measures in advanced PD patients.
Methods: Eleven consecutive PD patients were studied with in-laboratory PSG on two separate nights, at baseline before LCIG implementation and after 3–6 months of LCIG treatment. Patients also completed the PD-Sleep-Scale version-2 (PDSS-2). Activities of daily living, motor symptoms and complications were assessed with the Unified-PD-rating-Scale section II, III, and IV.
Results: Subjectively reported nocturnal sleep symptoms improved substantially in all patients with LCIG infusion (PDSS-2 total score was significantly reduced). PSG measures showed a reduction of the arousal index and a stability of sleep latency, total sleep time,

sleep efficiency and wakefulness after sleep onset. Motor complications and activities of daily living improved significantly with LCIG. **Conclusion:** Subjective measures of sleep quality and PSG measures improve in patients with advanced PD undergoing LCIG infusion.

PP62
Duodenal levodopa infusion: safety and efficacy in a 6-years outpatient follow-up

Simone Simoni[1], Nicola Tambasco[1], Pasquale Nigro[1], Erica Marsili[1], Elisa Sacchini[1], Francesco Ripandelli[1], Elona Brahimi[1], Michele Romoli[1], Paolo Calabresi[1,2]

[1]Clinica Neurologica, Azienda Ospedaliera, Università di Perugia, S.Andrea delle Fratte, Perugia, Italy; [2]IRCCS Fondazione S. Lucia, Roma, Italy

Background: Duodenal levodopa infusion (DLI) is used for the treatment of advanced Parkinson's disease (PD) in patients with motor fluctuations and dyskinesias. DLI efficacy and safety has been proved [1,2] and risks for its withdrawal are due to procedure and device or therapy related causes. To minimize procedure and device related risk of withdrawal is crucial.
Aim: To outline the determinants leading to a better organization of the outpatient follow-up, in order to reduce the risk of adverse events and dropout rate [1,3,4].
Methods: Clinical data on eleven PD patients treated with DLI at our centre over a 6-year period were retrieved and analysed to determine duration of treatment, number of adverse events reported, neurological interventions and PEG substitutions performed.
Results: Mean DLI duration was 24.27 ± 18.59 months (min 0–max 62), neurological evaluations have been performed every 1.26 ± 1.42 months (min 0–max 8) on each patient. Most common causes of PEG-J replacement interventions (tot. 27), were: normal tear and wear (6) and internal bumper deterioration (5); every patient had his PEG-J replaced 2.36 ± 1.96 times (min 0–max 6). Mean PEG-J duration was 9.04 ± 7.18 months (0 min–max 27). Peristomal skin infections (4 cases) and malnutrition (4 cases) were the most common adverse events. No serious adverse events have been reported. Of the 11 patients, 3 subjects died of causes unrelated to DLI infusion and none discontinued therapy.
Conclusion: Our study, has shown that a short term multidisciplinar follow-up with prompt clinical evaluations is helpful to lower adverse events severity and dropout rate. In line with previous studies, DLI is confirmed to be safe and effective [1, 2].

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PP63
Long-term prospective assessment of peripheral neuropathies associated with levodopa-carbidopa intestinal gel infusion

Andrea Bernardini, Alberto Romagnolo, Aristide Merola, Maurizio Zibetti, Dario Cocito, Leonardo Lopiano

Department of Neuroscience, University of Turin, Turin, Italy

Introduction: Levodopa-carbidopa intestinal gel infusion (LCIG) is an effective treatment for advanced Parkinson's disease (PD). Peripheral neuropathy (PN) is a complication of LCIG infusion, and both subacute and chronic forms have been reported. Although prospective analyses are required to investigate the role of LCIG in the pathogenesis of PN, only few data are currently available.
Objectives: To prospectively evaluate the incidence of PN during LCIG treatment.
Methods: 33 consecutive PD patients underwent a battery of PN-specific scales (ONLS, INCAT-SSS, MRCSS), nerve conduction studies and a serum work-up. The assessment was performed before starting LCIG infusion and regularly thereafter. Only subjects with normal clinical-electrophysiological (EP) features at baseline were included in the long-term analysis.
Results: At baseline 9 % patients showed a symptomatic sensory-motor PN and 21 % showed asymptomatic EP alterations (Subclinical-PN). Over a follow-up of 24.36 ± 12.18 months, 8.7 % subjects developed a subacute PN, 8.7 % a chronic PN and 30.4 % a Subclinical-PN. The onset of subacute PN was significantly more precocious compared to other PN phenotypes ($p = 0.001$). Only subacute PN patients required LCIG suspension. Patients with subacute or Subclinical-PN showed no significant differences in B12, folate, homocysteine or levodopa-equivalent daily dose (LEDD) variations over time compared to patients without clinical-EP alterations. On the contrary, patients who developed chronic PN showed a higher increase in homocysteine ($p = 0.024$) and LEDD ($p = 0.041$) compared to normal patients, while no differences were observed in vitamin B12 or folate levels. Both chronic PN subjects and normal patients showed a progressive BMI decrease ($p < 0.05$) compared to baseline.
Conclusion: PN is a relevant complication among PD patients undergoing LCIG. The pathogenesis of subacute PN might be related to immunological triggers on predisposed subjects. On the contrary, higher LEDD and homocysteine-mediated neurotoxicity could be implicated in chronic forms. Weight does not seem to represent a primary causative factor of PN.

PP64
Programming Deep Brain Stimulation for Parkinson's disease: the algorithms of Toronto Western Hospital

Marina Picillo[1,2], Renato Puppi Munhoz[1], Alfonso Fasano[1]

[1]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital and Division of Neurology, University of Toronto, Toronto, Canada; [2]Centre for Neurodegenerative Diseases (CEMAND), Department of Medicine and Surgery, University of Salerno, Salerno, Italy

Introduction: Deep brain stimulation (DBS) is an established and effective treatment for Parkinson's disease (PD). After surgery, a number of extensive programming sessions are performed in order to define the best stimulation parameters. No programming guidelines have been provided so far, with the exception of an algorithm proposed by experts for the initial programming [1,2]. Thus, programming sessions procedures mainly rely on neurologist's personal experience. As a result, patients often undergo inconsistent, repetitive and inefficient stimulation changes, as well as numerous or unnecessary visits.
Objective: Aim of this quality improvement project was to create algorithms guiding the initial programming and follow-up stimulation adjustments for common post-surgical issues (focus on: speech difficulties, stimulation-induced dyskinesia, freezing and festination and postural instability).
Methods: An extensive search of the literature on Medline until July 2014 was undertaken using keywords. Additional articles were also recovered from other sources, such as recent reviews and reference lists of relevant publications.
Results: Six hundred and sixty papers were retrieved. In total, seventy papers were taken into account. Data extracted from the selected articles for each topic were summarized in Tables. Algorithms and recommendations on troubleshooting were produced and are currently applied in our clinical practice.
Conclusion: Based on both the available literature and on our long-standing experience at TWH, we propose standardized protocols with algorithms to overcome current limits and gaps on common clinical issues during DBS programming of PD patients. Next steps include implementation of our algorithms and quality evaluation as compared to previous practice.

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PP65
Continuous dopaminergic stimulation in a patient treated with daytime levodopa-carbidopa intestinal gel and overnight rotigotine: a case report

Paola Imbriani[1], Tommaso Schirinzi[1], Enrica Olivola[1], Alessandro Stefani[1,2], Antonio Pisani[1,2]

[1]Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy; [2]IRCCS Santa Lucia Foundation, Rome, Italy

Introduction: Patients with Parkinson's disease (PD) receiving long-term L-Dopa therapy eventually develop motor complications with unpredictable "on–off" response fluctuations and involuntary movements, leading to progressive disability. Hence, the search for alternative therapeutic choices based on continuous dopaminergic stimulation (CDS) becomes crucial for the treatment of advanced PD.
Objective: To describe the case of a 70-year-old man with a 9-year history of PD, who received daytime levodopa-carbidopa intestinal gel treatment (LCIG, Duodopa®) and overnight rotigotine transdermal patch.
Methods: 5 years after onset of PD, the patient started to present motor fluctuations with wearing-off symptoms, progressively worsened by the appearance of unpredictable off periods, moderate camptocormia and paroxysmal freezing of gait with frequent fallings. He also complained about insomnia secondary to nocturnal hypokinesia with difficulty in turning in bed and morning akinesia. His daily oral dopaminergic medication consisted of levodopa (750 mg/day), rotigotine (4 mg/day, administered from 8:00 a.m. to 8:00 p.m.) and rasagiline (1 mg/day). He received treatment with LCIG via percutaneous endoscopic gastrostomy and jejunal tube (PEG/J). Duodopa was administered from 7:00 a.m. to 10:00 p.m (total daily dose 1080 mg). Moreover, the administration of rotigotine was shifted from daytime to overnight (from 10:00 p.m. to 7:00 a.m.). The assessments, performed at baseline and at follow-up visits, included: UPDRS parts I-IV, 24-hour diaries, PDQ-39 Questionnaire, PD Sleep Scale-2 (PDSS-2) and Epworth Sleepiness Scale (ESS).
Results: LCIG monotherapy significantly reduced motor fluctuations and akinesia, allowing the patient to walk longer distances, but only moderately affected paroxysmal freezing and camptocormia. Furthermore, improvements of night's sleep with better movement fluency and of morning akinesia were reported.
Discussion: Both LCIG and rotigotine induce CDS, which conceptually mimics physiologic striatal dopamine receptor function, clarifying the efficacy of both treatments respectively on motor fluctuations and sleep quality. Hence, they both represent a good therapeutic option for the treatment of advanced PD.

PP66
Impulse control disorders in Parkinson's disease before and after STN-DBS

Laura Rizzi, Mario Giorgio Rizzone, Maurizio Zibetti, Francesca Gentile, Elisa Montanaro, Serena Angrisano, Francesca Dematteis, Alberto Romagnolo, Leonardo Lopiano

Department of Neuroscience, University of Turin, Italy

Introduction: Impulse control disorders (ICDs) and related behaviours are a serious and increasingly recognized psychiatric complication in Parkinson's disease (PD). Although subthalamic deep brain stimulation (STN-DBS) might be a therapeutic option for those patients with ICDs, cases of new ICDs emerging after DBS have been described. Available studies show that STN-DBS is associated both with a favorable and negative outcome in terms of ICDs. Symptoms of ICDs present before surgery may be resolved or improve following STN-DBS, but they can also remain stable or even worsen after surgery.
Objective: The aim of the study is to analyze modifications of ICD following STN-DBS in advanced PD patients.
Methods: Symptoms of ICD were identified by reviewing medical records and through a clinical interview in 150 PD patients implanted for STN-DBS at our center between 2004 and 2013. Based on the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP-RS), we explored pathological gambling, compulsive shopping, binge eating, punding and the Dopamine Dysregulation Syndrome (DDS).

Results: Pre-operatory, 124 (82.6 %) patients did not show any ICD symptom, while 26 (17.4 %) had a history of behaviors compatible with ICD. In the follow-up period ranging from 2 to 10 years, 18 (69.2 %) patients showed a decrease in ICD symptoms, while 8 (30.8 %) patients had persistent ICD symptoms and 11/124 (8.9 %) patients developed new ICD symptoms after STN-DBS.
Conclusion: The behavioral disorders related to ICD, seem to be closely linked to drug therapy. Increased knowledge, allows to identify those symptoms quickly; however the impact on life quality of patients and their families is dramatic. The relationship between ICD and STN-DBS, at present, is still not clear; however, STN-DBS would seem to influence the control of symptoms.

PP67
A long-term assessment of early versus late deep brain stimulated patients in Parkinson's disease

Aristide Merola, Alberto Romagnolo, Andrea Bernardini, Laura Rizzi, Elisa Montanaro, Serena Angrisano, Carlo Alberto Artusi, Francesca Dematteis, Michele Lanotte, Mario Giorgio Rizzone, Maurizio Zibetti, Leonardo Lopiano

Department of Neuroscience, University of Turin, Turin, Italy

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) has been recently compared to a possible "second therapeutic honeymoon" for Parkinson's disease, as it might prevent the development of severe motor complications typical of the advanced disease phase, lessen the social adjustment associated to disease progression and provide a better quality of life.
Objectives: To evaluate whether an early surgical treatment could result in a better long-term outcome, comparing the follow-up evolution of 203 parkinsonian patients, treated at different stages of the disease course.
Methods: We retrospectively allocated patients to Early- or Late-Stimulated groups in accordance to disease severity at the time of surgery and motor fluctuations duration. Then, the clinical outcomes were compared after more than 8 years of follow-up, reporting the overall disability experienced by patients during the entire observational period.
Results: Long-term data were available for 15 Early-Stimulated and 25 Late-Stimulated patients. Early-Stimulated group reported a sustained improvement in the activities of daily living (ADL), showing even after $\geq$8 years of follow-up a 28.7 % lower UPDRS-II Med OFF score compared to baseline values ($p = 0.028$). On the contrary, Late-Stimulated subjects showed, after an initial improvement, a progressive re-alignment to the baseline scores during follow-up. Concerning motor complications, both groups reported a significant long-lasting decrease of UPDRS-IV, as well as severity of dyskinesias; on the other hand, only Early-Stimulated patients reported a significant lower duration of waking day spent in OFF (43.8 %; $p = 0.042$) compared to their pre-surgical basal scores. Interestingly, Early-Stimulated subjects never reached, even after $\geq$8 years, the severe levels of disability reported by Late-Stimulated patients at the time of surgical selection.
Conclusion: This long-term study suggests that an earlier STN-DBS treatment might prevent the development of severe motor complications, with positive long-term effects on the ADL, preserving the patient's social and professional life autonomy.

PP68
Subthalamic nucleus subterritories stimulation in Parkinson disease: a single centre experience

Nicolò Gabriele Pozzi[1,2,3], Brigida Minafra[1,2], Marta Piacascia[1,2], Roberta Zangaglia[1,2], Domenico Servello[4], Claudio Pacchetti[1,2]

[1]Parkinson's Disease and Movement Disorders Unit, National Institute of Neurology Foundation "C. Mondino", Pavia, Italy; [2]Interdepartmental Research Center for Neurodegenerative Disease, National Institute of Neurology Foundation "C. Mondino", Pavia, Italy; [3]Department of Neurology, University Hospital and Julius-Maximilian-University, Würzburg, Germany; [4]Departments of Neurosurgery and Neurology, IRCCS Galeazzi, Milan, Italy

Background: Parkinson's Disease (PD) is the most common movement disorders. Dopamine replacement therapy dramatically improved patient well-being, but get complicated with L-Dopa induced dyskinesia (LID) and, in a minority of patients, with Impulse Control Disorders (ICD). Subthalamic Nucleus Deep Brain Stimulation (STN-DBS) leads to a stable amelioration of patient's motor conditions, also improving LID and allowing a treatment reduction. In keeping, DBS was proposed as second line treatment for ICD in PD patients with motor complications. Here we review our experience in this hard-to-treat group of patients.
Methods: 174 with STN stimulation were retrospectively evaluated for presence of ICD symptoms in their previous medical history. Patients with suboptimal lead placement were excluded. For the two identified groups (1-with ICD and, 2-without ICD history) motor symptoms (MDS-UPDRS-III and -IV) and treatment dosage (calculated as levodopa equivalent daily dosage, LEDD), were collected. Stimulation parameters were schematically divided in two patterns: (a) dorso-lateral contacts (DLcs) and (b) ventral contacts (Vcs). Groups were compared, for each variable, at baseline and 1 year after surgery.
Results: ICD patients were younger and with higher LEDD. STN-DBS led to MDS-UPDRS amelioration and LEDD reduction in both groups. ICD improved after DBS. LID were reduced in both groups, but the stimulation pattern was locked for group 1. DLcs was mandatory in this group. Vcs wasn't tolerated because of dyskinesia re-appearance or due to the development of mood changes (e.g. Hypomania).
Conclusion: We retrospectively analysed our experience in the management of STN-DBS stimulation of PD patients with ICD. STN-DBS improves ICD and motor symptoms, with reduction of treatments dosage, in almost all patients. However, stimulation parameters were less flexible for those who suffered from ICD. Indeed, when ventral contacts were selected (e.g. gait problems), the recurrence of dyskinesia or the development of mood alteration led to the re-selection of DLcs.

PP69
Aleman in treatment of constipation in Parkinson's disease

Sara Mazza[1,2,3], Cesira Imondi[2,4], Maria Rao[2,4], Fabiola Sorpresi[2,4], Giovanni Di Sarno[3], Fabrizio Stocchi[5], Maria Francesca De Pandis[2,4,5]

[1]Extensive Rehabilitation Ex art 26 San Raffaele Cassino, Cassino; Italy; [2]Clinical Trial Center Parkinson San Raffaele, Cassino, Italy; [3]DH Neuromotor Rehabilitation San Raffaele Cassino, Cassino, Italy; [4]UO Neuromotor Rehabilitation San Raffaele Cassino, Cassino, Italy; [5]IRCCS San Raffale Pisana, Roma, Italy

Introduction: Gastrointestinal(GI) dysfunction cause important non motor symptom in PD. Enteric nervous system is affected from the early stages of disease [1] and dopaminergic drugs can also exacerbate some GI symptoms.
Aim: The aim of this study is to assess the effects of probiotic osmotic fructooligosaccharides (FOS) in association with D-mannitol on constipation in PD.
Methods: Our clinical observation of 6 week, included 20 patients, 8 females and 12 males, with constipation in PD (Rome II criteria) and all taking oral or rectal laxatives. After baseline, patients stopped their abitual laxative and started FOS 1 g plus D-mannitol 5 g daily. The dose could be modified (one to three sachets daily). As rescue therapy they could only use rectal laxatives. The patients completed, at baseline and after 6 week, a questionnaire in four items: (1) presence of excessive strain during defecation, (2) sensation of incomplete evacuation, (3) tenesmus, (4) hard stools. Each item was scored with the presence or not of the symptom (0 = absent, 1 = present) and severity (1 = mild, 2 = moderate, 3 = severe). The overall score was calculated by presence and severity. Patient was considered responder in improved stool frequency, decreased questionnary score and number of used rectal laxative.
Results: Daily stool frequency increased from 1.5 (IC95 % 1.2–1.7) a 2.9 (IC95 % 2.5–3.2) [$p < 0.001$]. The number of daily rectal laxative use is decreased from 1.1 (IC95 % 0.7–1.6) to 0.5 (IC95 % 0.1–0.8) [$p = 0.004$]. The questionnary score is decreased from 6.5 (IC95 % 5.2–7.8) to 3.0 (IC95 % 2.1–4.0, $p < 0.001$).
Conclusion: Constipation in PD causes significant impairment in quality of life [2], including peripheral absorption failure of farmacological therapy. Mechanism underlying are multifactorial as anorectal disfunction, intestinal bacterial overgrowth [3]. Treatment includes non pharmacological options. This study showed how FOS with D-mannitol (Aleman) can significantly improve stool frequency and bowel symptoms related to constipation in PD.
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PARKINSON - MOVEMENTS DISORDERS 1

PP70
Movement induced by focal transcranial magnetic stimulation (TMS) in normal subjects and focal dystonia

Roberta Arca[1,2], Christopher Cabib[1], Merce Morales[1], Josep Valls-Solè[1]

[1]EMG, Motor Control and Neuropathic Pain Unit, Neurology Department, Hospital Clinic, Institut d'Investigació August Pi i Sunyer (IDIBAPS), Barcelona, Spain; [2]Department of Neurology, AOU Cagliari, University of Cagliari, Cagliari, Italy

A suprathreshold single pulse focal transcranial magnetic stimulation (TMS) induces focal movements in the contralateral side. The characteristics of such movements are mostly unknown but it is reasonable to expect a correlation between movement and size of the motor evoked potentials (MEPs) recorded in the agonist muscles. However, this may not be the case in patients with cocontraction as in dystonia. We hypothesized that study the relationship between MEPs in the wrist extensors (WE) and the wrist flexors (WF) and the movement induced in the wrist by TMS would help in the pathophysiological characterization of arm dystonia.
Methods: 19 healthy subjects and 5 patients with writer's cramp were sitting with their right forearm and hand fixed on a two-pieces metallic platform joined with a hinge allowing only for flexo/extension wrist movements.TMS was applied over the contralateral motor area. Movements induced in the wrist were recorded with a signal transducer and entered, together with the EMG activity from the WE and WF muscles, into a polygraphic recording system. Subjects were studied at rest (baseline and 30° passive flexion and extension) and during sustained contraction to hold either a light or a heavy weight.
Results: At rest, MEPs were larger in the WE than in the WF, but movements were induced more frequently towards flexion. During WE contraction, healthy subjects showed a late movement towards flexion, as a rebound from TMS-induced WE silent period. In dystonia TMS-induced movements were similar to healthy subjects at rest but less prevalent and of lower amplitude than in healthy subjects during contraction. The silent period was shorter and no rebound movement was produced.
Conclusions: TMS-induced movements may be generated by the MEP or by the silent period that follows during contraction. Muscle elastic properties may also contribute to break or to induce movement. Patients with dystonia have less movement during muscle activation, consistent with cocontraction.

PP71
Clinical assessment of task specificity in tremor of SWEDD patients

Tommaso Schirinzi, Paola Imbriani, Alessio D'Elia, Antonio Pisani

Department of Systems Medicine, University of Rome Tor Vergata, Roma, Italy

Introduction: An asymmetric rest tremor poorly responsive to levodopa is one of the main features of patients without evidence of dopaminergic deficit (SWEDD). Although it has been previously suggested that these patients may have dystonic tremor, the clinical distinction between SWEDD and PD remains still difficult in some cases. Task specificity is consistently considered as a clinical marker of dystonia and also task-specific tremors, as writing tremor (WT), have been basically regarded as a form of dystonic tremor.
Objective: Here we assessed the task specificity of tremor in SWEDD patients aimed to better clarify their clinical phenomenology.
Materials and methods: Task specificity has been evaluated in terms of occurrence and severity of WT in SWEDD patients with asymmetric rest tremor compared to a sample of tremor-dominant PD patients with asymmetric rest tremor. Patients underwent MMSE, UPDRS III and Fahn–Tolosa–Marin Tremor Rating Scale (TRS). WT has been assessed by part B of TRS, calculating 3 subscores (item 10, writing with dominant hand; items 11–13, drawing with each hand separately). The Wilcoxon-Mann–Whitney test was used to compare the scores between the groups.
Results: No differences between the two groups were found in MMSE and TRS total score. As expected PD patients had higher UPDRS III score, while SWEDD patients showed greater presence of WT regardless of the side most affected by motor disturbances

(handwriting $p < 0.01$; right hand drawing $p = 0.01$; left hand drawing $p < 0.05$).
Conclusions: SWEDD patients clearly present a condition of task specific tremor in terms of WT. This finding may thus further support the dystonic origin of SWEDD tremor. Moreover it also provides an helpful tool which may assist in clinical assessment of patients with asymmetric rest tremor and uncertain diagnosis.

PP72
Primary writing tremor: escaping from dystonia?

Pierluigi Tocco[1], Domenicantonio Tropepi[2], Maria Chiara Tozzi[1], Laura Bertolasi[1]

[1]Neurology Unit, Department of Neurological and Movement Sciences, University of Verona, Verona, Italy; [2]Neurology Unit, "Don Calabria" Sacro Cuore Hospital, Negrar, Verona, Italy

Primary writing tremor (PWT) is a task-specific tremor that occurs and interferes with handwriting. Clinically, it can be classified into isolated writing tremor (type A) or both writing and positionally sensitive tremor (type B). PWT pathophysiology is still unknown, and there is some controversy on its nosological classification. Here we present a case of PWT and its management. A 50-year-old right-handed African woman complained of a 6-year history of shaking of her right hand while writing and performing some motor tasks by pronation of the forearm, that interfered with her work. She also referred slowness while writing since childhood. On examination, the writing speed was markedly improved using her preferred hand (27 letters per minute vs 60 letters per minute with the left hand), and mild abnormal pen handgrip was present. Electromyographic recording showed 7–8 Hz rhythmic activity predominantly in wrist flexor and abductor brevis pollicis muscles during writing with the right hand. There was no evidence overflow of this activity. The neurophysiological investigations including the H-reflex from the forearm flexor muscles, the brainstem and motor cortex excitability were normal. Levodopa, Propranolol, Biperiden and Clonazepam were not effective. Low-dose botulinum toxin type-A injection of the flexor digitorum profundus muscle improved symptoms. Although our case has clinical and neurophysiological features of PWT, there are some hints to suggest that this task-specific condition may represent a distinct entity with mixed dystonic characteristics.

PP73
Anticipatory behaviour and motor adaption during catching a ball in patients with cervical dystonia

Gaia Bonassi[1], Andrea Ravaschio[2], Elisa Pelosin[2], Giovanna Lagravinese[2], Roberta Marchese[2], Giovanni Abbruzzese[2], Laura Avanzino[1]

[1]Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy; [2]Department of Neurosciences (DINOGMI), University of Genoa, Genoa, Italy

Background: Dystonia has long been considered to be a manifestation of basal ganglia dysfunction, however the cerebellum may play a role in the pathogenesis of this disease. Among different functions, the cerebellum is needed to acquire the appropriate anticipatory adjustments for environmental changes by means of motor adaptation.
Aim: To evaluate the ability to adapt an arm movement to novel loads in patients with cervical dystonia (CD).
Methods: Fifteen patients with CD and 17 healthy controls were required to catch balls of different weight: the baseline phase consisted of 10 trials with a light ball, the adaptation phase of 25 trials with an heavy ball, and the post-adaptation phase of 15 trials with the light ball. Arm movements were recorded using the QUALYSIS motion capture system. We determined the impact (time of ball contact with the hand) using the vertical velocity of the wrist. The following parameters were evaluated: (i) the value of anticipatory displacement (the vertical distance travelled by the wrist up, towards the ball just before the impact); (ii) the value of impact displacement (the vertical distance travelled by the wrist from the impact to the first reversal in direction) and (iii) the extent of the adaptation by the end of the adaptation phase.
Results: The value of the anticipatory displacement increased during adaptation in controls (as expectable for a feed-forward control), whereas it did not change in CD patients. The value of impact displacement did not differ between groups. However, the extent of adaptation was lower in CD than controls and significantly correlated with the change in anticipatory displacement during adaptation.
Conclusion: The extent of adaptation was lower in CD patients than controls and this behaviour was correlated with the inability to act out an anticipatory behaviour in order to adapt to changing loads.

PP74
Unexpected acquired hand dystonia in Parkinson's disease

Roberta Di Giacomo, Francesca Anzellotti, Iole Borrelli, Holta Zhuzhuni, Aurelio D'Amico, Valerio Frazzini, Maria Chiara D'Amico, Luca Mancinelli, Valeria Di Tommaso, Laura Bonanni, Astrid Thomas, Marco Onofrj

Department of Neuroscience, Imaging and Medical Science, University G. D'Annunzio of Chieti-Pescara, Italy

Objective: To describe acquired dystonia in patient with Parkinson's disease (PD) secondary to cervical spinal lesion.
Case Report: A 76-years-old female patient, affected by rigid-akinetic PD, treated with levodopa equivalent daily dose of 575 mg, had presented subacute onset of dystonic posturing of left hand, not responsive to dopaminomimetic dose adjustments, interpreted as dystonia. One month later, the patient was referred to our Movement Disorder Clinic because of weakness of controlateral lower limb. Neurological examination showed motor signs of Parkinson's disease (H&Y 2.5); dystonic posture of left upper limb with forced flexion of the last three fingers, worsened by action; but also different signs consistent with pyramidal lesion: loss of strength in right limbs (F3-4/5 Medical-Resource-Council classification), reduction of cutaneous and pain sensation, increased right biceps, triceps and patellar reflexes, right positive Hoffmann's sign and Babinski response. No pain or sphincteric disturbance was reported. Brain MRI was normal. Cervical MRI detected a lesion in the right postero-lateral cervical spine (C1–C2 level) consistent with meningioma. The spinal cord was considerably compressed and displaced to the left. Therefore, the patient underwent surgery to remove psammomatous meningioma, with complete resolution of both pyramidal and dystonic disorders.
Discussion: Our clinical case shows that dystonia [1] could be the first symptom of compressive controlateral cervical lesion. The presence of extrapyramidal disease could delay correct diagnosis

because in the clinical practice patients with PD can develop dystonic symptoms in their clinical course [2]. Meningioma might be responsible for the dystonia, affecting rubrospinal, vestibulospinal and reticulospinal tracts, the projections from supraspinal centers on the Ia inhibitory neurons and other interconnected interneurons with reciprocal inhibition [3]. Alternatively the reduced presynaptic inhibition may be due to changes in the tonic afferent input to the interneuron from cutaneous and muscle afferents [2]. The results is a disruption of the normal reciprocal inhibition of antagonists during agonist contraction.

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PP75

Extrapyramidal signs in new diagnosed amyotrophic lateral sclerosis (ALS) patients: preliminary data from the EXTRALS study

Francesca Dematteis, Mario Giorgio Rizzone, Andrea Calvo, Stefania Cammarosano, Cristina Moglia, Carlo Alberto Artusi, Alberto Romagnolo, Serena Angrisano, Andrea Bernardini, Maurizio Zibetti, Adriano Chiò, Leonardo Lopiano

Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy

Introduction: ALS is a progressive, neurodegenerative disorder due to involvement of cortical, bulbar and spinal motor neurons. Recent data suggested that different phenotypic expression in ALS patients, in particular the presence of frontotemporal, parkinsonian and psychiatric symptoms, may represent the manifestation of a spectrum of diseases.
Objectives: To determine the presence of extrapyramidal signs in a prospective series of ALS patients.
Methods: We recruited 112 consecutive patients from Torino ALS centre with a new diagnosis of ALS, according to El Escorial-Rev criteria, between July 2012 and December 2013 (67 M, 45 F; mean age 67.0 years). All patients were evaluated by neurologists expert in movement disorders and scored by the MDS-UPDRS to detect the presence of extrapyramidal signs. Patients with parkinsonian signs underwent ^{123}I-Ioflupane SPECT and genetic analysis for SNCA, parkin, PINK1, DJ-1, LRRK2 and GBA genes. This study will go on for 3 years, with follow up visits at 1 and 2 years.
Results: At baseline 26 of 112 patients (9 classic, 10 bulbar, 4 flail leg, 2 flail arm, 1 upper motor neuron) showed extrapyramidal signs (UPDRS I mean score 13.0, UPDRS II mean score 18.3, UPDRS III mean score 39.2). Bradykinesia was present in 100 %, gait disturbances in 82.0 %, postural instability in 50.0 %, rigidity in 78.5 %, rest tremor in 18.0 %, postural tremor in 35.7 % and kinetic tremor in 32.0 %. 22/26 patients underwent ^{123}I-Ioflupane SPECT (4 patients did not execute it for respiratory problems). Only 3/22 patients (13.6 %) showed a reduction of putaminal dopamine transporter binding. A mutation in LRRK2 gene was found in one patient.
Conclusion: Extrapyramidal signs in ALS patients are a frequent clinical feature. Despite a relevant percentage of new diagnosed ALS patients showed parkinsonian signs (23.2 %), nigrostriatal damage was observed only in a low percentage (13.6 %) of patients who underwent ^{123}I-Ioflupane SPECT.

PP76

Usefulness of FDG-PET in the differential diagnosis of parkinsonisms on individual basis

Daniela Frosini[1], Alice Accorroni[2], Asso Giorgetti[3], Duccio Volterrani[4], Giulia Puccini[4], Elena Filidei[3], Ubaldo Bonuccelli[1], Roberto Ceravolo[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Scuola Superiore Sant'Anna, Pisa, Italy; [3]Fondazione Toscana Gabriele Monasterio, Pisa, Italy; [4]Nuclear Medicine Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Introduction: The distinction between atypical parkinsonisms (AP) and Parkinson's disease (PD) in early stage might be very difficult. Positron emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) can identify characteristic patterns of regional glucose metabolism in PD and AP, however most previous studies were based on a group-comparison approach. Aim of this study is to evaluate the diagnostic accuracy of FDG-PET in parkinsonisms on an individual basis.
Materials and methods: One-hundred and twenty patients with undetermined parkinsonisms underwent FDG-PET at baseline (mean disease duration at scan time 2 years) and were then followed-up for at least 5 years. The final diagnosis was performed according to current diagnostic criteria for PD and degenerative AP. The FDG-PET scans were then retrospectively processed by a dedicated software Pneuro, and maps obtained were evaluated by two blinded examiners that had to distinguish PD from AP and subsequently the specific AP subtype. Parameters of diagnostic accuracy were calculated.
Results: Nineteen patients were excluded because the final diagnosis was vascular parkinsonism or anyway inconsistent with current diagnostic criteria. The clinical diagnosis at the follow up were: 17 PD (mean age 65), 23 Multiple System Atrophy (MSA) (mean age 72), 30 Progressive Supranuclear Palsy (PSP) (mean age 74), 16 Cortico-Basal Degeneration (CBD) (mean age 72), 15 Lewy Body Dementia (LBD) (mean age 75). The sensitivity and specificity for the diagnosis of AP were 94 % and 88 % respectively. Specificity for individual AP ranged between 92 and 97 %, sensitivity between 70 and 87 % with worst performance for PSP and better for DLB diagnosis. The inter-rater agreement was between good and excellent (Kappa Cohen 0.60–0.86).
Discussion: Our data demonstrate the usefulness of a computer-supported FDG-PET analysis to help the clinicians in early distinction between PD, PSP, MSA, CBD and LBD from each other on an individual basis.

PP77

DaTSCAN in the differential diagnosis between dementia with Lewy bodies (DLB) and non-DLB dementia: a systematic review with meta-analysis

Giulia Turri, Francesco Brigo, Michele Tinazzi

Department of Neurological and Movement Sciences, University of Verona, Policlinico G.B. Rossi, Verona, Italy

Introduction: Differentiating dementia with Lewy bodies (DLB) from other dementia syndromes may represent a diagnostic challenge, especially during the first stages of disease. Hence, a reliable test to differentiate DLB from non-DLB dementia would be of utmost importance for an accurate prognosis and management. The functional integrity of dopaminergic nigrostriatal pathway can be studied with single photon emission computed tomography (SPECT) imaging. A reduction of SPECT ligand binding to pre-synaptic dopamine transporter (DAT) correlates with the loss of presynaptic dopamine. The rationale beyond the use of [^{123}I]FP-CIT SPECT (DaTSCAN) as a supportive tool in the diagnosis of DLB is the nigrostriatal degeneration and loss of pre-synaptic dopamine transporters in the striatum occurring in DLB. For these reasons, low dopamine transporter uptake in basal ganglia on DaTSCAN has been listed as a feature suggestive of DLB in the international consensus criteria for the diagnosis of DLB.
Objectives: Aim of this study is to systematically review the utility of DaTSCAN in the differential diagnosis between DLB and non-DLB.
Methods: We systematically searched MEDLINE (accessed by Pubmed), the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library) and ClinicalTrials.gov to identify prospective and retrospective studies reporting data on DaTSCAN performed in patients with DLB or non-DLB. Two review authors independently extracted data from the published reports. Accuracy measures (sensitivity and specificity) for each study, pooled accuracy measures and diagnostic odds ratio were synthetized in a random-effect model meta-analysis using Meta-DiSc software 1.4. Results Unlike other non-DLB dementias, DLB is characterized by low dopamine transporter uptake in basal ganglia on DaTSCAN. Accuracy measures of this technique for the diagnosis of DLB will be presented in detail at the Congress.
Discussion: This updated and systematic overview of the literature support the use of DaTSCAN in the differential diagnosis between DLB and non-DLB.

PP78
Neurophysiological evaluation of pain processing in Progressive Supranuclear Palsy

Micol Avenali[1,2], Cristina Tassorelli[1,2], Roberto De Icco[1,2], Mariangela Berlangieri[1,2], Irene De Paoli[1,2], Eliana Berra[2], Giorgio Sandrini[1,2]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy; [2]Neurological Rehabilitation Unit, IRCCS National Neurological Institute "C. Mondino", Pavia, Italy

Pain is a common non-motor symptom in Progressive Supranuclear Palsy (PSP), which has received very little attention in terms of clinical characterization and nature. In this study we investigated central nociceptive processing in a group of 12 PSP patients by means of the neurophysiological evaluation of the threshold of the nociceptive flexion reflex (TR-NWR) and the temporal summation threshold (TST-NWR). The investigation was conducted comparatively in a group of 15 patients with Multiple System Atrophy (MSA), in 15 patients with Parkinson's disease (PD) and in 24 healthy controls (HC). In the patients' group, the neurophysiological investigation was performed without levodopa therapy and 30 min after levodopa administration, in 2 separate sessions. The data obtained show a significant reduction of the TR-NWR and the TST-NWR in PSP, MSA and PD patients when compared with HC, without any statistical differences among the 3 patients' groups. After L-dopa administration, we found a statistically significant increase of the TR-NWR only in the PSP group, while no significant effect of levodopa was detected in the other 2 groups of patients. Our findings suggest an increased facilitation of pain processing in PSP, MSA and PD. This is likely a consequence of the degenerative phenomena involving central projections implicated in the modulation of pain, which make patients more predisposed to develop pain condition. The modulatory effect of levodopa, on pain, observed in this study exclusively in the PSP group, seems apparently in contrast with the lower motor response to levodopa typical of PSP patients. This unexpected finding may be related to the different distribution and severity of the neurodegenerative process in PSP as compared to PD or MSA.

PP79
Progressive Supranuclear Palsy patients show abnormal response to Transcranial Magnetic Stimulation compared to Parkinson's disease and healthy subjects

Mario Fichera, Elise Houdayer, Federica Avantaggiato, Raffaella Chieffo, Giancarlo Comi, Maria Antonietta Volonté, Letizia Leocani

Scientific Institute University Hospital San Raffaele, Institute of Experimental Neurology, Milan, Italy

Introduction: Progressive Supranuclear Palsy-PSP is the second most common parkinsonian syndrome after Parkinson's disease-PD, with some overlapping clinical features in the early phases. Non-invasive neurophysiological techniques, such as transcranial magnetic stimulation (TMS), could prove useful to gain insight into these pathologies and as widely available methods for differential diagnosis.
Methods: Seventeen PD, 13 PSP and 11 healthy controls (HC) subjects were included in this study. TMS evaluation included resting motor threshold (RMT), motor evoked potentials (MEP) amplitude and latency, response to inhibitory (SICI) and facilitating (ICF) conditioned stimuli, cortical silent period (CSP) and ipsilateral silent period (iSP). Statistical analysis was performed using either parametric or non-parametric ANOVA and post hoc tests according to data distribution. For paired-pulse a repeated measures ANOVA was adopted, using interstimulus interval (ISI) and group as factors.
Results: PSP and PD groups did not significantly differ in UPDRS. TMS assessment showed different distribution of RMT across groups (p.008), with PSP patients showing highest values and PD lowest (PSP vs PD p.002). Group also affected iSP duration (p.016), being longest in PSP and lowest in HC (PSP vs HC p.005). On paired-pulse inhibition and facilitation, a significant effect of ISI ($p < 0.001$) and GROUP (p.035) but not interaction was found, with lower SICI and higher ICF in PSP vs both PD (p.017) and HC (p.032) and no significant difference between the latter two groups.
Conclusion: This study suggests that TMS can help differentiate PD and PSP. PSP patients displayed different response to the perturbation induced by conditioning stimuli and iSP elongation, probably due to impairment of GABA-mediated neurotransmission.

PP80
A case of monolateral freezing of gate

Alberto Lerario[1,2], Andrea Ciammola[1], Floriano Girotti[1], Vincenzo Silani[1,2]

[1]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milan, Italy; [2]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, 'Dino Ferrari' Center, Università degli Studi di Milano, Italy

Introduction and objectives: Freezing of gait (FoG) may be defined as a sudden, episodic inability to generate effective stepping in the absence of any known cause other than parkinsonism or high level gait disorders. FoG is typically common in advanced Parkinson's disease (PD) and other parkinsonian syndromes. Even in vascular parkinsonism, FoG is characterized by an irregular gait pattern that involves both lower limbs. We present an unusual case of unilateral FoG.
Methods: We present a case of a 88 years old woman affected by epilepsy secondary to cerebrovascular disease. She has come to our attention for an acute episode of transient nonfluent aphasia associated with clumsiness of the right leg when walking.
Results: On neurological examination patient showed a unilateral FoG: marked reduction of forward progression only of the right feet despite the intention to walk, without loss of strength or lower limb apraxia. Brain MRI revealed an ischemic stroke involving the territory of lenticulo-striates arteries. Part the corona radiata and the left posterior portion of the putamen were damaged.
Conclusion: Monolateral FoG cases are reported very rarely in literature. Changes in imaging studies, suggests a major role of cortico striatal connections in the pathology of FoG.

PP81
Altered connectivity within the cerebello-thalamo-cortical network in essential tremor: evidence from a resting state fMRI study

Valentina Nicoletti[1], Ilaria Pesaresi[3], Serena Fabbri[3], Ubaldo Bonuccelli[1], Mirco Cosottini[2], Roberto Ceravolo[1]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Neuroradiology Unit, Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa, Italy; [3] Neuroradiology Unit, S. Chiara Hospital, Pisa, Italy

Introduction: The pathophysiology of essential tremor (ET) is still poorly understood, although neuroimaging and neurophysiological evidences suggested the involvement of cerebello-thalamo-cortical network.
Objective: to evaluate the tremor network in ET patients in rest conditions with respect to healthy controls (HC).
Methods: 23 patients with diagnosis of possible or probable ET and 23 matched HC underwent a 3T-MRI with acquisition of a resting state sequence maintaining their eyes closed. Connectivity was investigated using a seed-based regression analyses approach. Regions of interest were identified from a between-group activation map (HC > ET) obtained in a previous task-related functional MRI study on the same cohort. They were located in primary motor, premotor cortex, somatosensory cortex, thalamus and cerebellum hemispheres. Statistical correlation maps obtained for each seed and for each subject were registered to MNI before group analyses. Between group differences were evaluated by using FSL Fixed Effect with correction for multiple comparisons.
Results: In ET patients compared to HC reduced connectivity between primary motor cortex and premotor and supplementary motor areas, and between thalamus and basal ganglia was detected. ET patients exhibited also increased connectivity between cerebellar hemispheres each other and between inferior cerebellar hemisphere and thalamus. Finally increased connectivity was found in patients compared to HC between somatosensory cortex and primary motor, premotor cortex, supplementary motor area.
Conclusion: The increased connectivity within the cerebellum as well as the altered connectivity between cerebellum and thalamus and between BG and thalamus in ET patients compared to HC are consistent with the putative crucial role of cerebellum and thalamus. Finally the dysregulation of cortical sensory-motor network in ET patients could be due to a dynamic entrainment of several mutually linked cortico-subcortical drivers.

PARKINSON - MOVEMENTS DISORDERS 2

PP82
Interoceptive awareness in patients with functional neurological symptoms

Benedetta Demartini[1,2], Lucia Ricciardi[1], Laura Crucianelli[3], Charlotte Krahè, Mark J. Edwards[1], Aikaterini Fotopoulou[4]

[1]Sobell Department, UCL Institute of Neurology, London, UK; [2]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Cattedra di Psichiatria, Milano, Italy; [3]Department of Psychology, University of Hertfordshire, London, UK; [4]Division of Psychology and Language Sciences, CEHP Research Department, University College London, London, UK

Historically, emotional factors, such as trauma or psychological conflict, have been suggested as causal factors of functional motor disorders (FMD). More recent approaches have instead stressed potential neural and cognitive abnormalities in the allocation and maintenance of attention. Yet these studies have mostly focused on how attention is allocated to exteroceptive signals about the state of the body. Given the proposed important role of interoception for emotion, the study of FMD patients' ability to monitor their interoceptive signals may serve as a useful, mechanistic link between studies that aim to identify key emotional factors in FMD, and those that examine specific sensorimotor or cognitive abnormalities. In the current study, we compared the interoceptive awareness of a group of individuals with FMD ($n = 16$) with a group of healthy controls ($n = 17$). We employed a commonly used heartbeat detection task which tracks the level of concordance between one's heart rate and its subjective perception, as a proxy for interoceptive awareness more generally. We found that FMD patients have lower interoceptive accuracy than healthy subjects, and such reduced interoceptive accuracy was predictive of their depressive symptoms, as well as their tendency to focus on the external features of their body (self-objectification). Contrary to our predictions, interoceptive accuracy was not predictive of alexithymia. These results suggest a potental trade-off between the allocation of attention to internal versus external aspects of the body in FMD. More generally, they warrant further investigation of interoceptive awareness in this population, as a means to understand their emotional abnormalities at a more mechanistic level than studies concentrating on traumatic life events and related risk factors.

PP83
Assessment of somatic complaints in patients with functional movement disorders by the Dissociative Disorders Schedule Interview

Paola Vincenza Mancino[1], Roberta Pellicciari[1,2], Angelo Fabio Gigante[1], Daniele Liuzzi[1], Giovanni Defazio[1]

[1]Department of Basic Medical Sciences, Neuroscience and Sense Organs, "Aldo Moro" University of Bari, Bari, Italy; [2]Department of Neurology and Psychiatry, "Sapienza" University of Rome, Rome, Italy

Introduction: Functional movement disorders (FMDs) result from non-voluntary conditions and are unexplained by neurological disturbance or organic disease. Fahn and Williams proposed some diagnostic criteria suggesting a psychogenic origin of the disease and showed high frequence of multiple somatizations in FMDs patients. To our knowledge however there are not previous studies that investigated the frequency of somatic complaints in FMDs patients.
Objective: To evaluate the presence of multiple somatizations in 33 patients with FMDs diagnosis according to Fahn and Williams criteria and 33 sex- and age-matched patients with organic movement disorders.
Methods: The Dissociative Disorders Interview Schedule (DDIS) was administered to case and control subjects. This is a highly structured interview which makes DSM-5 diagnoses of several psychiatric disorders. It includes four sections one of which focused on somatization disorders, with particular reference to gastrointestinal complaints, pain, sexual complaints and similneurological complaints (headache, dizziness, blurred or double vision, paralysis or muscle weakness, amnesia, seizure or convulsion, difficulty swallowing, trouble walking, fanting or loss of consciousness, urinary retention). Comparisons were performed by multivariable logistic regression analysis adjusted for age, sex and age of dystonia onset.
Result: In our sample similneurological complaints (Adjusted Odds Ratio, 1.9; Confidence Interval 95 %, 1.1–3.4, $p < 0.02$) were more frequently observed in FMDs patients, whereas gastrointestinal complaints (Adjusted Odds Ratio, 0.5; Confidence Interval 95 %: 0.15–1.5, $p < 0.2$), pain (Adjusted Odds Ratio, 1.3; Confidence Interval 95 %: 0.6–2.7, $p < 0.5$) and sexual complaints (Adjusted Odds Ratio, 1.5; Confidence Interval 95 %: 0.6–3.5, $p < 0.4$) were similarly reported in the two groups.
Conclusions: These data confirm the presence of multiple somatizations in FMDs patients. Moreover this is the first study that strongly suggest the relevance of similneurological complaints in these patients as a factor contributing to the phenomenology of functional movement disorders.

PP84
Heterogeneous spectrum of autoimmune movement disorders

Simone Gallerini, Luca Marsili, Manuele Bartalucci, Laura Giovanditti, Francesca Rossi, Chiara Scarpini, Sergio Pieri, Katrin Plewnia, Roberto Marconi

U.O. Neurologia, Ospedale della Misericordia, Grosseto, Italy

Introduction: Autoimmune syndromes of CNS are a heterogenous group of diseases (postinfectious, paraneoplastic or idiopatic process). Movement disorders have been known to be associated with a variety of autoimmune diseases, including chorea, pediatric neuropsychiatric disorders, gluten sensitivity, systemic lupus erythematosus, antiphospholipid syndrome, et al. The onset can be acute ore subacute with rapid progressive disease evolution. Clinical features are extremely variable ranging from cognitive symptoms and seizures to movement disorders.
Objectives: Although antibodies directed against CNS have been implicated, the pathogenesis of these autoimmune movement disorders have not yet been fully understood. So, if the clinical features are typical of a well defined paraneoplastic syndrome, after exclusion of other potential causes, the priority is to search for a tumor and onconeural antibodies. But in other neurological syndromes the major difficulty is to think early to a possible immune mediated nervous system disease.
Methods: We describe nine patients admitted in the Neurological Unit of Grosseto from Emergency Department with complex movement disorders or neuropsychiatric syndromes and an acute or subacute onset. Diagnostic exams included extensive blood exams, brain and spinal MRI, EEG, neurophysiological studies, CSF examination, whole body CT and PET to reveal associated tumors, detection of antineuronal antibodies. Patients were treated with corticosteroids or intravenous immunoglobulin with improvement in six of them.
Results: The neurologist should consider that CNS pathologies with acute or subacute onset of movement disorders and other symptoms associated can also have an autoimmune basis. We consider that while tumor screening is the most important target in classical paraneoplastic neurological syndrome, the early diagnosis and immunotherapy are the most important target in the other syndromes.
Conclusion: In this view, a systematic approach can help in the diagnosis, so that treatments can start as soon as possible in the hope of restoring health, limiting hospitalization and optimising outcomes.

PP85
Actinic Parkinsonism: a case report

Carlo Alberto Artusi, Maurizio Zibetti, Aristide Merola, Francesca Dematteis, Rosa Palmiero, Roberta Rudà, Riccardo Soffietti, Leonardo Lopiano

Department of Neuroscience "Rita Levi Montalcini", Città della Salute e della Scienza di Torino, Torino, Italy

Introduction: Secondary parkinsonism is usually associated with lesions, cerebrovascular damage and/or metabolic causes. Brain radiotherapy-related parkinsonism does not represent a well-established entity.
Objective: To describe a patient developing partially L-dopa-responsive parkinsonism 6 months after brain radiotherapy.
Case report: A 61 year-old man underwent 2 neurosurgical operation for right fronto-mesial oligodendroglioma (WHO grade-II and -III). After the first operation in 2009 chemotherapy with temozolomide and procarbazine-lomustine was administered. In 2013 a 2nd neurosurgery followed by conformational radiotherapy was performed due to tumor recurrence, with administration of 59.4 Gy between December 2013 and January 2014. Neurological examination showed moderate hemiparesis in the left limbs with autonomy in gait and in most of the daily living activities. About 6 months after radiotherapy the patient developed depression, apathy and retropulsion tendency with several falls. Successively, a sub-acute development of left limbs rigidity appeared, leading to a relevant worsening of gait and impairment in the use of the left arm, with severe loss of autonomy. Neurological examination of April 2015 showed camptocormia, hypomimia, wheelcharing for retropulsion and freezing of gait;

incoercible plastic-spastic rigidity of the left limbs, with assumption of plastic postures and severe bradykinesia. Right limbs were normal. Brain MRI showed a widespread alteration of white-matter around the surgical-lesion site, involving the fronto-parietal-temporal white-matter of the hemisphere, as result of actinic damage. No signs of lesions in the basal ganglia were revealed. DaT-Scan scintigraphy was normal. Low levodopa doses lead to moderate improvement in the rigidity of the left limbs, mild improvment in bradykinesia and no effectiveness on gait.

Conclusions: Parkinsonism is related to functional abnormalities in the motor cortico-striato-pallido-thalamo-cortical loop and related neural pathways. This case demonstrates that white-matter diffuse damage related to brain radiotherapy may be cause of parkinsonism with partial response to levodopa, also without evidence of basal ganglia involvement.

PP86
ADCY5 mutations can cause Benign Hereditary Chorea

Roberto Erro[1,2], Niccolò E. Mencacci[3,4], Henry Houlden[3], Kailash P. Bhatia[1]

[1]Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, London, UK; [2]Dipartimento di Scienze Neurologiche e del Movimento, Università di Verona, Verona, Italy; [3]Department of Molecular Neuroscience, UCL Institute of Neurology, London, UK; [4]IRCCS Istituto Auxologico Italiano, Department of Neurology and Laboratory of Neuroscience, Department of Pathophysiology and Transplantation, "Dino Ferrari" Centre, Università degli Studi di Milano, Milan, Italy

Introduction: Benign Hereditary Chorea (BHC) represents a poorly delineated syndrome, featuring chorea with onset in childhood, little progression and no other major disturbances, particularly cognitive impairment. There is often an autosomal dominant inheritance and mutations in the NKX2.1 (also called TTF-1) gene are detected in a number of BHC families, but often a genetic cause is not found, suggesting genetic heterogeneity. Familial Dyskinesia with Facial Myokymia (FDFM) is a newly identified movement disorder, characterized by early-onset of choreiform and dystonic dyskinesias together with perioral and periorbital myokymia in some cases. Recently mutations in ADCY5 have been associated with FDFM, but the phenotype spectrum is still expanding and would suggest a phenotypic overlap between FDFM and BHC.

Objective: To determine if ADCY5 mutations can cause BHC.

Methods: We screened the ADCY5 gene in 19 unrelated cases (7 familial and 12 sporadic) with a clinical diagnosis of BHC and negative for NKX2.1 mutations. Complete mutational analysis of ADCY5 was performed by whole-exome sequencing or by direct Sanger sequencing.

Results: A previously described pathogenic mutation (c.1252C>T; p.R418 W) in the ADCY5 gene was detected in two cases (1 familial and 1 sporadic). The mutation was inherited by the affected father in the familial case and was de novo in the sporadic one. The phenotype of ADCY5 positive cases mainly featured early-onset generalized chorea with further development of dystonia. There was significant intra-familial and inter-familial phenotypic variability. None of our patients had facial myokymia.

Conclusions: We identified pathogenic ADCY5 mutations as the cause of familial and sporadic cases with a BHC phenotype. Genetic analysis of ADCY5 should be therefore considered in cases with an early-onset choreic movement disorder, even in the absence of facial myokymia.

PP87
Adult onset ataxia with movement disorders and cognitive decline: an atypical presentation of Huntington's disease

Claudia Dell'Aquila[1], Pasquale Colamartino[2], Marilena Tota[1], Michele de Mari[1]

[1]U.O. Neurologia, Ospedale Civile "Bonomo", Andria (BT), Italy; [2]Neuroriabilitazione Villa San Giuseppe Casa Divina Provvidenza Bisceglie (BT), Italy

Introduction: Association of adult onset ataxia, cognitive impairment and movement disorders is described in different inherited neurodegenerative disease such as dominant spinocerebellar ataxias (SCA). Atypical Huntington's disease (HD) patients with predominant or presenting cerebellar features masquerading SCAs, were occasionally reported [1].

Case report: We report the case of a 70-years-old woman sent to our attention for a 4-years history of unbalanced gait with falls and speech disorders with no reported cognitive impairment. "Obsessive" personality and motor "tics", never brought to medical attention, have been noticed by caregiver since 12 years. Very mild facial "tics" were also reported in one patient's sister. Neurological examination revealed ataxic cerebellar gait with postural instability, cerebellar-spastic dysarthria, gaze motor apraxia and mild chorea and dystonia at face and limbs. Cognitive decline was found at neuropsychological assessment. MRI showed diffuse cortical and subcortical atrophy with cerebellar involvement mainly at vermis. Genetic causes of adult onset ataxia with movement disorders were investigated and the diagnosis of HD was made based on the molecular evidence of abnormal 41 Cytosine-Adenine-Guanine (CAG) repeats in exon 1 of Huntingtin gene.

Conclusion: HD should be taken in consideration as differential diagnosis in adult onset ataxic syndrome associated with different movement disorders and cognitive decline [2,3]. Careful family history, accurate evaluation of movement disorders and cognitive profile may support the suspicion.

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PP88
Atypical Parkinsonism and concurrent myasthenia gravis: casual or pathogenetic association?

Francesco Cavallieri[1], Laura Vandelli[1], Alessandra Ariatti[1], Giuliana Galassi[1], Franco Valzania[1], Annalisa Chiari[1]

[1]Department of Neuroscience, S. Agostino-Estense Hospital and University of Modena and Reggio Emilia, Modena, Italy

Background: Rarely movement disorders result from autoimmune mechanisms, eventually associated with underlying malignancy; in

most cases they manifest as hyperkinetic movement disorders. Paraneoplastic supra nuclear palsy (PSP)-like syndromes represent a rare clinical entity with only few cases described. Simultaneous occurrence of Parkinsonism and myasthenia gravis has so far reported only once. We describe a case of Acetylcholine receptor (AChR) antibodies positive ocular myasthenia (OMG) associated with the simultaneous observation of a PSP-like syndrome.
Case report: A 67 year-old man was admitted after 2 year history of mental slowing, gait imbalance, fluctuating diplopia, generalized fatigability and dysphagia. Neurological examination revealed hypomimia, diplopia on lateral gaze, bilateral ptosis, rare blinking, vertical upward gaze palsy, reduced horizontal saccades speed, positive applause sign, moderate bradikinesia, axial and upper limb rigidity, postural instability and anterocollis. Neuropsychological assessment revealed features consistent with frontal lobe dysfunction; DaT SCAN (123I-Ioflupane) SPECT was suggestive for left nigro striatal degeneration. Brain MRI was unrevealing, notably no mesencephalic atrophy nor vascular changes were detected. Serum AChR antibodies were positive and SFEMG was consistent with postsynaptic neuromuscular junction defect. CSF showed high protein content without cells. Total body CT, PET scans and screenings for onconeural and neuronal surface antibodies were normal. IVIg (0.4 mg/kg/d for 5 days) were administered with significant improvement of cognitive functions and gait, with almost complete resolution of ptosis and diplopia. Dopaminergic therapy was delayed because of improvement of parkinsonian symptoms.
Discussion: Our patient presented simultaneous occurrence of PSP-like syndrome and OMG in absence of detectable malignancy. Extrapiramidal and neuromuscular signs improved with immunomodulating therapy, suggesting that an immune-mediated mechanism may underlie both syndromes. Presence of antibodies to AchR receptors confirmed OMG. Neurological involvement in our patient might be due to simultaneous central and peripheral immunologically mediated cholinergic dysfunctions.

PP89
Structural MRI correlates of the MMSE in Multiple System Atrophy

Roberta Biundo[1], Eleonora Fiorenzato[1,2], Klaus Seppi[3], Marco Onofrj[4], Pietro Cortelli[5], Horacio Kaufmann[6], Florian Krismer[3], Gregor Wenning[3], Angelo Antonini[1] on behalf of the MODIMSA Neuropsychology and Imaging Working Groups

[1]Fondazione Ospedale San Camillo-I.R.C.C.S., Parkinson and Movement Disorders Unit, Venice, Italy; [2]Department of General Psychology, University of Padua, Padua, Italy; [3]Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; [4]Department of Neuroscience and Imaging, University "G. d'Annunzio", Chieti-Pescara, Italy; [5]DIBINEM, Alma Mater Studiorum, Università di Bologna, Bologna Italy and IRCCS Istituto di Scienze Neurologiche di Bologna, Bologna, Italy; [6]Dysautonomia Center, Department of Neurology, New York University Medical Center, New York, USA

Background: Cognitive deficits in MSA have been observed, although dementia is still considered as non-supporting diagnostic feature by current consensus diagnostic criteria. MMSE is commonly used in clinical practice with atypical parkinsonism, but its neuroanatomical correlates have never been investigated.
Objective: The aim of this study is to investigate the MRI structural correlates of the Mini-Mental State Examination (MMSE) in Multiple System Atrophy (MSA) patients compared with a Parkinson's disease (PD) sample.
Methods: Multicenter cohort of 69 MSA patients [mean age 63.8 (7.3) and education of 11.1 (4.7)], collected from four international centers and 70 PD [mean age 63.9 (7.3) and education of 10.5(4.4)] subjects matched for age and MMSE score. Freesurfer software was used to evaluate intergroup differences in cortical thickness (CTh) and subcortical areas, in relationship with MMSE scores.
Results: In MSA group MMSE scores did not correlate with cortical or subcortical areas. In PD, significant positive correlations were observed between MMSE scores and cortical thickness of the left medial and lateral orbitofrontal areas, caudal middle frontal area, superior frontal area, supramarginal region and superior temporal area. More focal right hemisphere significant correlations were found in the temporal pole and pars orbitalis. Subcortical analysis showed significant positive correlation in the right hippocampus and in the middle anterior side of corpus callosum. All these areas survived after Montecarlo correction.
Conclusions: Our findings in PD corroborate previous studies showing correlations between cortical areas and MMSE scores. The predominance of the left hemisphere is likely due to the presence of several verbal items included in the cognitive scale. Lack of cortical correlates of cognitive deficits in MSA suggests a different nature of cognitive decline in MSA patients.

PP90
Cognitive assessment in multiple system atrophy cerebellar type

Maria Lieto, Francesco Saccà, Teresa Costabile, Antonella Antenora, Filomena Abate, Agnese Liguori, Giuseppe de Michele, Alessandro Filla

Department of Neurosciences and Reproductive and Odontostomatologic Sciences, Federico II University, Naples, Italy

Background: Multiple system atrophy (MSA) type C is a rare, sporadic, progressive, neurodegenerative disease. Oligodendrocyte cytoplasmic inclusions of fibrillized alpha-synuclein represent the hallmark of the disease. Dementia is considered an exclusion criteria, but MMSE is abnormal in 26 % of the patients. Executive dysfunction is the most common presentation, but memory or visual spatial functions may also be impaired.
Objective: To assess multiple, domain-specific cognitive functions in patients with the cerebellar type of MSA (MSA-C) and to compare them with normal controls and Parkinson's disease (PD) patients.
Patients and methods: We included patients with probable MSA-C, PD and normal controls, matched by age, sex and scholarity. We performed the following tests: The Montreal Cognitive assessment (global assessment); Naming Nouns and Pointing (language); Raven Colored Progressive Matrices (fluid intelligence); Symbol Digit Modalities Test, Trail Making Test, Phonetic and Semantic Fluencies (executive functions); Digit Span, Modified 10/36 Special Recall Test, Rey Auditory Verbal Learning Test (memory); Segment Length Discrimination, Mental Rotation (Visuospatial functions).
Results: We enrolled 20 MSA-C, 20 PD patients, and 20 normal controls (age, sex and scholarity matched). The most frequent finding in MSA-C patients was an impairment of the executive functions, followed by attention and memory and visuospatial impairment. The impairment of the executive functions was more severe in MSA-C than in PD patients.

Conclusions: Global cognitive impairment is uncommon in MSA-C but executive functions are frequently impaired.

PP91

A mitochondrial membrane protein-associated neurodegeneration (MPAN) case from Piedmont: the age-related extension of brain iron accumulation

Umberto Manera[1], Andrea Calvo[1,2], Cristina Moglia[1], Davide Bertuzzo[1], Antonio Ilardi[1], Stefania Cammarosano[1], Antonio Canosa[1], Elisa Montanaro[1], Leonardo Lopiano[1,2], Adriano Chiò[1,2,3]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy; [2]Azienda Ospedaliero Universitaria Città della Salute e della Scienza, Turin, Italy; [3]Neuroscience Institute of Torino (NIT), Turin, Italy

Background: Mitochondrial membrane protein-associated neurodegeneration (MPAN) is one of the most recently described neurodegeneration with brain iron accumulation (NBIA) [1]: it is due to a mutation in C19orf12 gene and usually manifests with extrapyramidal signs, psychiatric findings, optic atrophy and motor axonal neuropathy.
Case report: we describe the case of a 55 years old man who presented behavioural disturbances since the infancy with difficulties to attend school. Since he was 30 years old he developed progressive hyposthenia to the right hand, with subsequent extension to the contralateral side and to distal lower limbs, gait instability and dysarthria. Cognitive function progressively worsened with memory, speech, attention and executive function impairment. His parents were not referred as consanguineous; he has not familiarity for neurodegenerative disorders, except for his 20-year-old brother's daughter diagnosed with autism. Neurological examination revealed moderate dysarthria with poor verbal fluency, mild dysphagia, mild camptocormia and sensory ataxic gait with postural instability, diffuse distal muscular atrophy and hypoactive deep tendon reflexes in all four limbs. He presented psycomotor agitation and performed stereotyped aimless head and limbs movements. Sporadic myoclonic jerks were noted. Nerve conduction studies showed motor axonal neuropathy in all four limbs. Fundus oculi examination shows a pale optic disc. 3T MRI T2-weighted and SW images revealed hypointensity of caudate, putamen, globus pallidus and substantia nigra associated with mild cerebral atrophy. Haematological assessment showed iperCKemia. A sequencing of C9orf12 gene was performed by CeGat GmbH and a mutation c.32C>T; p.T11 M in exon2 in a homozygous state was found.
Conclusion: this is the first Italian patient carrying this mutation [2] and the oldest one described in literature. The extension of iron accumulation seems to be an age-related process often following clinical onset [3,4] and unrelated with clinical phenotype and outcome.
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PP92

Relationship between cognitive impairment and parkinsonism in iNPH patients: a retrospective study

Marta Picascia[1,2], Brigida Minafra[1], Roberta Zangaglia[1], Nicolò Gabriele Pozzi[1,3], Elena Sinforiani[2], Claudio Pacchetti[1]

[1]Parkinson's Disease and Movement Disorders Unit, National Neurological Institute Foundation "C. Mondino", IRCCS, Pavia, Italy; [2]Laboratory of Neuropsychology/Alzheimer Assessment Unit, National Neurological Institute Foundation "C. Mondino", IRCCS, Pavia, Italy; [3]Department of Neurology, University Hospital Wurzburg, Wurzburg, Germany

Background/aims: Idiopathic normal pressure hydrocephalus (iNPH) is characterized by a progressive disorder of the gait and balance, whereas cognitive decline and urgency/incontinence appear as disease progresses. The interest for this condition is due the fact that it can be considered a potentially reversible dementia; cerebrospinal fluid shunt surgery indeed has been reported to improve the symptoms. The cognitive and behavioural disturbances accompanying iNPH have been commonly described as "fronto-subcortical dementia". This clinical term is used to refer to a pattern of mental decline characterized by executive dysfunction, psychomotor slowing and mood symptoms. This definition may be reductive because patients with iNPH may be impaired in broader cognitive domains: the cognitive deficits extend beyond executive function, attention, memory to visuoperceptual and visuospatial functions. The objective of this study was to delineate a comprehensive profile of cognitive impairment in iNPH and then to evaluate a relation with clinical data, particularly gait and posture.
Methods: Fifty-three iNPH patients (28 M, 25 F, age 73.7 ± 7.5) referred to Parkinson's Disease and Movement Disorders Unit, National Neurological Institute Foundation "C. Mondino", IRCCS Pavia, from 2009 to 2014. They underwent neuropsychological assessment (memory, attention, language, executive functions and visuospatial abilities). MMSE mean score (± DS) was 21.8 ± 4.9. Average age of disease was 20 months. Twenty-two patients (42 %) showed a global cognitive impairment. Twelve patients (23 %) showed typical deficit in attention and executive abilities, ten patients (18 %) showed a mild cognitive impairment, single domain, and nine patients (17 %) had no cognitive impairment.
Results/conclusions: The analysis shows a positive correlation between motor impairment, evaluated with Unified Parkinson's Disease Rating Scale, part III: Motor Exam (UPDRS III), and cognitive impairment. In particular, a positive correlation was observed with items inherent axial symptoms (28, 29, 30: posture, gait, postural stability). Moreover, the degree of cognitive impairment was significantly related to disease duration.

PP93
Parkinsonism in frontotemporal dementia: data from a Sardinian cohort

Francesca Di Stefano[1]*, Antonino Cannas[2], Giuseppe Borghero[2], Maria Rita Murru[3], Maria Giovanna Marrosu[3], Francesco Marrosu[1,2], Gianluca Floris[2]

[1]Department of Neurology, University of Cagliari, Cagliari, Italy; [2]Department of Neurology, University Hospital of Cagliari, Cagliari, Italy; [3] Multiple Sclerosis Centre, University of Cagliari, Cagliari, Italy *corresponding author Dr Francesca Di Stefano Department of Neurology, University of Cagliari, Monserrato (CA)

Background: In clinical practice, parkinsonism appears to be quite frequently associated with frontotemporal dementia (FTD) but few studies focused on its prevalence and characteristics [1–3].
Objective: We aim to describe data on parkinsonism in a cohort of Sardinian patients affected by FTD.
Methods: We investigated our cohort of FTD patients diagnosed using Rascovsky criteria. Parkinsonism was identified by the presence at least of two clinical features between bradykinesia, rigidity, resting tremor and postural instability.
Results: In our Sardinian cohort of 69 FTD patients 48 were affected by BvFTD, 8 by semantic dementia, 8 by the non-fluent primary progressive aphasia (PPA) and 5 by unspecified PPA. Among patients with BvFTD 13 patients were carriers of C9ORF72 mutation and 5 of the p.A382T missense mutation of the TARDBP gene. 1 other patient with unspecified-PPA was TARDBP mutated. 26 patients (37 %) in the whole cohort showed parkinsonism of whom 23 had BvFTD, 1 unspecified PPA, 0 SD and 2 PNFA. There were no differences in term of familiarity between patients with parkinsonism or not (13/26vs12/43, $p = 0.06$) and the prevalence of parkinsonism in familial and sporadic patients was similar (13/25vs14/44, $p = 0.09$). Parkinsonism was in most cases an early onset feature during the disease course and was mainly of the rigid-akinetic type, symmetric or slightly asymmetric. Tremor PD like was present only in two patients with BvFTD. 5 patients had a CBS-like parkinsonism and 2 PSP-like. The comparison between C9ORF72 + BvFTD and the C9ORF72- BvFTD group showed a significant prevalence of parkinsonism in the former group (10/13vs13/35, $p = 0.03$) [4]. None of the patients with TARDBP mutation had parkinsonism.
Conclusion: In our population we found a little higher prevalence of parkinsonism (37 %) than previously reported in literature (16–30 %) [2,3]. Parkinsonism is largely more frequent in BvFTD than others FTD variants and particularly in C9ORF72 + BvFTD.

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