

# **III Congresso Congiunto LIMPE/DISMOV-SIN**

## **Malattia di Parkinson e disturbi del movimento**

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**ABSTRACTS**

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*Comunicazioni  
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## C1

**Levodopa-carbidopa intrajejunal gel (LCIG) treatment and freezing of gait (FOG) in advanced Parkinson disease (PD)**

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*Background:* FOG and unstable gait with poor balance are common and disabling disorders in advanced PD, causing falls with further reduction of patients' mobility. The relationship between FOG and dopaminergic medication is complex and often non-linear, even when PD patients appeared optimally treated.

*Patients/Methods:* We evaluated the effect of LCIG in a group of 7 non-demented patients with advanced PD who displayed prominent episodes of gait difficulties and FOG also during "ON" phase. Clinical assessments were performed before starting LCIG, while patients were on their standard oral levodopa (O-LD) and during infusional treatment. The main outcome measures were FOG Questionnaire and UPDRS motor score. Evaluations were performed in O-LD OFF state (12 hours after last dopaminergic medication intake) in O-LD "ON" state (45-60' after intake of usual morning oral levodopa dose) and in LCIG-ON (45-60' after starting LCIG infusion). Levodopa Equivalent Daily Dose (LEDD) was calculated for oral therapy and LCIG dose was recorded for each patient.

*Results:* At basal evaluation age was  $67.6 \pm 9.7$ ; mean PD duration was  $13.3 \pm 5.7$ ; duration of LCIG treatment was  $14.1 \pm 8.1$  months. During ON state (with both oral LD and LCIG treatment) all patients showed a similar improvement of parkinsonian features, as compared with the O-LD OFF state (UPDRS motor scores O-LD OFF  $49.2 \pm 9.5$ ; O-LD ON  $26.9 \pm 7.7$ ; LCGI-ON  $20 \pm 5.9$ ) except for gait FOG which significantly improved (45.1%.) only on LCIG (FOGQ O-LD  $19 \pm 1.4$ ; LCGI:  $10.4 \pm 1.6$ ). In 5 out of 7 patients the LCIG dose was equivalent or slight higher while in 2 patients lower compared to pre-operative LEDD.

*Conclusion:* Continuous stimulation provided by LCIG is a useful therapeutic strategy in patients with FOG persisting despite optimization of oral dopaminergic therapy but the mechanism may differ. In "pseudo-on" FOG it would increase dopaminergic stimulation up to the threshold for full therapeutic effect while in paradoxical "on" FOG it would prevent suprathreshold peak dose dopamine concentrations.

## **Brain functional changes after action observation therapy in Parkinson's disease patients with freezing of gait**

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*Introduction:* The systematic observation of actions followed by their imitation (Action Observation Treatment, AOT) enhances the beneficial effects of motor training on motor memory formation, possibly through the mirror neuron system (MNS).

*Objective:* To assess brain functional changes following AOT in Parkinson's disease patients with freezing of gait (PD-FoG).

*Methods:* 23 PD-FoG patients underwent a 4-week (W4) rehabilitation training. Subjects were randomized into 2 groups: in AOT-group, therapy consisted of AO combined with practicing the observed actions; control-group performed the same training combined with landscape-videos observation. At T0 and W4, patients underwent: clinical and motor functional evaluations, and functional MRI. At T0, 15 age-matched healthy controls (HC) performed the same MRI protocol. FMRI tasks consisted of: foot simple-movement; observation of videos showing a man in circumstances precipitating FoG; motor imagery in the same circumstances as observation task. Clinical/ motor functional assessments were repeated at week 8 (W8).

*Results:* At W4, both groups showed reduced FoG severity and walking speed improvement. AOT-group showed additional UPDRS III, balance, and quality of life (QoL) improvements. At W8, functional improvements and positive effects on UPDRS III and QoL were observed in AOT-group only. FMRI showed that PD patients had a reduced recruitment of basal ganglia, motor and fronto-parietal network relative to HC. AOT was associated with increased recruitment of primary sensorimotor/premotor cortices, MNS and caudate nucleus bilaterally during simple-motor and motor imagery tasks. At W4, control-group showed reduced recruitment of the primary sensorimotor areas and parietal regions during all tasks. Only in AOT group, functional brain changes were associated with clinical improvements at W4 and predicted clinical evolution at W8.

*Conclusion:* AOT has a positive additional effect on walking ability recovery of PD-FoG patients. In PD, AOT promotes brain functional plasticity of both the primary sensorimotor and MNS.

*Funding:* Jacques and Gloria Gossweiler Foundation.

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

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*Objective:* We performed this study with the aims to estimate the proportion of patients developing Pisa Syndrome (PS) in a large cohort of patients with Parkinson's Disease (PD) and to assess relationships between PS and demographic/clinical variables.

*Materials and Methods. Study Design:* Multicentre cross-sectional observational study. Setting: 21 Italian centres participated.

*Participants:* Patients with PD were selected from consecutive sample of outpatients attending the participating centres. Patients treated with dopamine receptor blocking agents 6 months before the recruitment and patients with spinal diseases were excluded from the study. 6 months of enrolment phase.

*Outcome measures:* Sex, age, body mass index, age at onset of PD, disease duration, Hoehn & Yahr scale, UPDRS I-II-III-IV, dominant PD phenotype, distribution of PD symptoms onset, clinical asymmetry, PDQ-8, latency between PD symptoms onset and drug administration, the first and ongoing pharmacological therapy, levodopa-equivalent daily dose, comorbidities, associated medical conditions, falls, and gait disturbances.

*Results:* A total of 1631 patients with PD met the eligibility criteria and entered into the study. PS was detected in 143 patients (8.77%). The mean degree of PS was 17(SD 7.4). Out of the 143 patients with identifiable motor asymmetry at disease onset, the lateral flexion was ipsilateral to the side of PD symptoms onset in 40.5% and contralateral in 41.3% and both in 18.2%. Low back pain was observed in 101 (70.6%) patients with a mean VAS score of 6(SD 2.3).

Multiple explanatory variable logistic regression models indicated a significant association of PS with an advanced stage of disease scored at H&Y scale (adjusted OR, 1.48; 95% CI, 1.01 to 2.15;  $p=0.04$ ), a combination of levodopa and dopamine agonists agents (adjusted OR, 1.93; 95% CI, 1.10 to 3.40;  $p=0.02$ ), associated medical conditions (adjusted OR, 1.64; 95% CI, 1.09 to 2.44;  $p=0.01$ ), and gait disturbances (adjusted OR, 3.59; 95% CI, 2.29 to 5.64;  $p=0.001$ ).

*Discussion/Conclusion:* These results suggest that PS is a relatively frequent and often disabling complication in PD especially in the advanced course of disease. The association is independent of a number of potentially relevant demographic-clinical variables.

## Diagnostic accuracy of advanced brain MR biomarkers in differentiating progressive supranuclear palsy and Parkinson's disease

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*Introduction:* Few studies compared diagnostic accuracy of advanced brain MR techniques for the often challenging differential diagnosis between Progressive Supranuclear Palsy (PSP) and Idiopathic Parkinson's Disease (IPD) [1,2,3].

*Objective:* To evaluate the diagnostic accuracy of putative advanced MR biomarkers in the differential diagnosis of PSP and IPD.

*Methods:* We obtained brain scans from 23 PSP and 21 IPD patients using a 1.5 T MR scanner. All participants underwent the same MR protocol [axial T2 FLAIR, coronal FSE T2, T<sub>1</sub>-weighted volumetric FSPGR, axial Diffusion Tensor Imaging (DTI) with 25 directions and cerebellar proton-MR spectroscopy (<sup>1</sup>H-MRS)]. DTI analysis was performed by using Regions of Interest (ROIs) and histogram methods. We performed manual morphometry for the brainstem and cerebellar peduncles and, for supratentorial structures, a semi-automated volumetric analysis based on FMRIB's Integrated Registration and Segmentation Tool (FIRST). We compared MR parameters in PSP and IPD groups using the *t* Test, and for parameters showing a significant difference we calculated accuracy using a ROC curve.

*Results:* Disease duration was similar in the IPD and PSP patients studied, while the latter group had higher median Hoehn-Yahr scores. We demonstrated cerebellar metabolic changes, brainstem, cerebellum, cerebellar peduncles, basal ganglia and hemispheric white matter macro- and micro-structural alterations in PSP patients compared to IPD. Overall, morphometric biomarkers showed the highest accuracy (>90%) in discriminating PSP from IPD, in particular midbrain area, pons/midbrain areas ratio and MRPI. Other parameters showed a moderate accuracy (70-90%), in particular diffusion parameters in the posterior fossa, brain hemispheres, pre-frontal hemispheric white matter, basal ganglia and superior cerebellar peduncles, volumes of putamen, thalamus, pallidum, nucleus accumbens and lateral ventricles and cerebellar NAA/Cr ratio.

*Conclusion:* A multimodal MR approach, in particular morphometric analysis, is sensitive to brain alterations in PSP, facilitating the differential diagnosis with IPD.

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## Corpus callosum damage and motor function in Parkinson's disease

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*Introduction:* Assessing the microstructural alterations of corpus callosum (CC) may improve the understanding of the pathogenetic mechanisms associated with motor impairment in Parkinson's disease (PD).

*Objective:* To investigate CC microstructural damage and its relationship with motor impairment in patients with PD at different disease stages.

*Methods:* We enrolled 173 PD patients (98 with Hoehn and Yahr score [HY]=1-1.5, 37 with HY=2-2.5, 29 with HY=3-3.5, 9 with HY=4-5) and 39 matched healthy controls (HC). Diffusion tensor (DT) MRI tractography was performed to obtain the CC and its main three partitions: CC-genu, CC-body, and CC-splenium. Mean tract fractional anisotropy (FA) and mean diffusivity (MD) values were measured. Between group comparisons adjusting for age were assessed. Pearson's correlations were used to explore the relationship between CC DT MRI metrics and UPDRS III score.

*Results:* All PD patients relative to HC showed decreased FA and increased MD of the whole CC and its partitions. Such a microstructural damage to the CC is more marked with increasing PD severity, being only mild in PD patients with HY=1-1.5 (who showed the greatest damage in the CC-body) and severe (same degree of damage in all CC partitions) in patients at the later stages of the disease. UPDRS III score correlated significantly ( $p < 0.001$ ) with FA values of the whole CC ( $r = -0.399$ ), CC-genu ( $r = -0.199$ ), CC-body ( $r = -0.481$ ), and CC-splenium ( $r = 0.270$ ) and MD values of the whole CC ( $r = 0.367$ ), CC-body ( $r = 0.438$ ), and CC-splenium ( $r = 0.257$ ).

*Conclusion:* PD is associated with microstructural damage to the CC that becomes more significant with disease worsening. In PD patients, the best predictor of CC deterioration of motor functions is the involvement of the CC-body, which includes the transcallosal motor tracts.

*Funding:* Italian Ministry of Health (#GR-2009-1577482); Ministry of Science and Technology of the Republic of Serbia (#175095).

**Clinical phenotype, imaging and neuropsychological features in Sardinian patients affected by parkinsonism and carriers of 20-22 repeats of C9ORF72 hexanucleotide expansion**

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*Background:* Expansions of more than 30 hexanucleotide repetitions (long expansions) in the first intron of the C9ORF72 gene are considered pathogenic and currently are a recognized cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Instead expansions of less than 30 hexanucleotide repetitions are considered non pathogenic. Rarely they are been reported in literature 20-30 repeats (short expansions), and the meaning of this range remains completely to understand. In rare studies the intermediate range of 20-22 hexanucleotide repetitions have been related with Parkinson's disease (PD), atypical and atypical-atypical parkinsonism.

*Objective:* To study a population of subjects suffering from degenerative primary Parkinsonism for the search of C9ORF72 repeat expansions.

*Design:* We studied a cohort of 91 patients with primary degenerative parkinsonism for the search of C9ORF72 repeat expansions; 60 patients were in accordance with the criteria for a diagnosis of atypical Parkinsonism (MSA-P, MSA-C, LBD, CBD, PSP); 19 (all with past or present psychosis) were in accordance with the Gelb's criteria for a PD diagnosis, while 12 patients had a clinical picture quite different from classical atypical parkinsonism, which, in accordance with the literature, we have called atypical-atypical parkinsonism.

*Results:* None of the 91 probands had a long expansions of C9ORF72 repeats, while three patients presented with the short expansion between 20-30 repeats. Among the three patients, two (one with 20 and the other with 28 repeats) were within the 12 patients with atypical-atypical parkinsonism (2.2% of all parkinsonisms investigated, 17% of the atypical-atypical parkinsonism) and one surprisingly (with 22 repeats) had a clinical picture of typical PD. We present the clinical phenotype, imaging and neuropsychological features of these three patients.

*Conclusion:* Our data confirm that the clinical presentation of the C9ORF72 repeat short expansions may include forms of parkinsonism, more frequently with clinical phenotype of atypical-atypical parkinsonism and more rarely of classic form of PD. Further studies are needed to explore these data.

## Effectiveness of lidocaine injection in abdominal muscles in the management of camptocormia in Parkinson disease

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*Introduction:* Camptocormia is a very disabling symptom, frequently present in Parkinson's disease. The exact etiology of this condition has not been determined yet and treatment options are limited and often futile. A recent study assessed the primarily role of external oblique muscles (EO) in its pathogenesis [1].

*Objective:* We describe the case of a 66 year-old parkinsonian patient with no important motor disabilities but a worsening upper camptocormia, that severely limited him during his activities of daily living. The aim of this study is to confirm the role of EO muscles in upper camptocormia and evaluate the beneficial effect of lidocaine injections in the treatment of this disorder.

*Methods:* We performed 3D gait analysis with surface EMG (sEMG) of abdominal and lower arm muscles that showed an abnormal bilateral hyperactivation of EO at rest and during movements. Needle EMG confirmed this datum. Therefore we inoculated 50 mg per day of lidocaine in EO bilaterally for 5 consecutive days. In addition the patient underwent a regular daily rehabilitation program. The functional evaluation was performed before treatment (T0), at the end (T1), 7 days after (T2) and 1 month after the end of treatment (T3). Outcomes measures were: trunk Flexion angle, Camptocormia Questionnaire (CQ-32); the Ten-Meter Walk Test (10mWT); the Timed Up and Go Test (TUG) and the Six Minutes Walking Test (6MWT).

*Results:* At T1 we detected a reduction of trunk flexion angle from 50° to 30°. The 10MWT, TUG, 6MWT did not show significant changes. The CQ-score showed a reduction from 18/32 to 9/32 points. The Patient referred a subjective improvement with greater independence in the ADL. We observe a worsening of camptocormia at T2 and return to baseline condition at T3.

*Conclusion:* We confirm the primarily role of EO muscles in upper camptocormia and the positive but transient effect of lidocaine injection in these muscles. An expansion of the study is currently in progress.

### References

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## Pattern of regional cortical thickness in patients with Parkinson's disease and impulse control disorders

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*Objective:* To investigate the pattern of gray matter (GM) atrophy and cortical thickness (CTh) in patients with Parkinson's disease (PD) with and without impulse control disorders (ICD).

*Materials and Methods:* Fifteen patients with PD (mean age: 62.87±8.6; H&Y<2) with ICD (ICD+), fifteen patients with PD (mean age: 62.58±8.4; H&Y<2) without ICD (ICD-) and 24 age and sex-matched healthy controls (HCs) were enrolled in the study. PD was defined according to the UKBB criteria; patients were screened for ICDs by the Minnesota Impulsive Disorders Interview (MIDI). Whole brain structural imaging was performed on a 3T GE MR scanner. Surface-based investigation of CTh was carried out by using Freesurfer Software. We also used voxel-based morphometry (VBM-SPM8) to investigate the pattern of GM atrophy.

*Results:* No significant differences were detected between the groups in any of the demographic or clinical variables. The voxel-wise analysis of the regional differences in Cth revealed a specific abnormal pattern involving the limbic system in the comparisons between: a) ICD- and ICD+ patients and b) ICD+ patients and HCs. In particular, ICD+ patients showed a statistically significant ( $p<0.05$ ) cortical thickening when compared to both ICD- patients and HCs in the anterior cingulate (ACC) and orbitofrontal (OFC) cortices. Moreover, cortical thickening in these areas is correlated ( $p<0.05$ ) to MIDI score. No statistically significant differences were observed in the comparison between ICD- patients and HCs. VBM data did not reveal any statistically significant differences in local GM between ICD+ and ICD- patients and between patients and controls.

*Discussion and Conclusion:* Our results demonstrated that ICD+ patients have a stronger pattern of cortical thickness in limbic regions compared with ICD-. Thus, aberrant anatomical and cytoarchitectural features in OFC and ACC, involved in reward-related decision making and especially activated by positive reward, may play a role in the lack of inhibition of compulsive behaviors.

**The spectrum of movement disorders in chronic liver disease: a cross-sectional study**

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*Background:* Chronic liver failure has been associated with progressive neurological symptoms including parkinsonism, ataxia and cognitive decline, globally referred to as acquired hepatocerebral degeneration. Parkinsonism has been reported in most cases; however, the spectrum of movement disorders in chronic liver disease has not been described in detail so far, and few data are available in patients without cirrhosis.

*Objective:* To define the clinical spectrum of movement disorders (MDs) in patients with chronic liver disease of various aetiology and stage; to individuate which factors may increase the risk of developing movement disorders.

*Methods:* 126 patients (42F/84M) were evaluated by a neurologist trained in movement disorders. Motor symptoms were scored using the UPDRS part III scale. Patients' clinical and demographic features were reviewed and correlated with the presence of movement disorders.

*Results:* Patients' mean age at assessment and mean liver disease duration were 65 and 12.4 years, respectively. Aetiology of liver disease included viral cirrhosis (42%), viral hepatitis (25%), alcoholic cirrhosis, (24%), other causes (9%). MDs were present in 67% of cases (85/126) and included bradykinesia (52%), tremor (43%) and rigidity (21%). Phenotypes encompassed parkinsonism in 35% of cases, subtle motor signs (59%) and other MDs (6%). These included adult-onset paroxysmal dystonia, tremulous cervical dystonia and RLS. Child-Pugh class B or C (OR 7.11) and the presence of portosystemic shunts (OR 5.58) increased the risk of developing MDs, as well as alcoholic aetiology (OR 3.11). Child Pugh class A patients showed MDs in 56% of cases. MDs were subclinical in 41% of patients.

*Conclusion:* Progressive movement disorders are common in chronic liver disease, and are more frequent, but not limited to advanced disease stages. Subtle motor signs are the most frequent presentation, and phenotypes other than parkinsonism can be observed. Alcoholic liver disease aetiology specifically increases the risk of developing movement disorders regardless sex, age and disease duration.

## Reduced facial expressiveness in Parkinson's disease: a pure motor disorder?

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*Background and Aims:* Impaired emotional facial expressiveness is an important feature in Parkinson's disease (PD). Although there is evidence of a possible relationship between reduced facial expressiveness in PD and altered emotion recognition or imagery, it is unknown whether other aspects of the emotional processing, such as subjective emotional experience (alexithymia), might influence hypomimia in PD. We aimed to investigate the interplay between reduced facial expressiveness and altered emotion processing (facial recognition and alexithymia) in patients with PD.

*Objective:* To report different clinical phenotypes of patients with intracranial calcifications (IC) of various aetiology.

*Methods:* Forty PD patients and seventeen healthy controls (HC) were evaluated. Facial expressiveness was rated on video recordings, according to the UPDRS-III item 19 and using an ad hoc scale assessing static and dynamic facial expression and posed emotions. Six blind raters evaluated the patients' videos. Emotion facial recognition was tested using the Ekman 60 Faces Test; alexithymia was assessed using Toronto Alexithymia Scale (TAS-20).

*Results:* PD patients had a significantly reduced static and dynamic facial expressiveness and a deficit in posing happiness and surprise. They performed significantly worse than HC in recognizing surprise ( $p=0.03$ ). The Ekman total score positively correlated with the global expressiveness ( $R^2=0.39$ ,  $p=0.01$ ) and with the expressiveness of disgust ( $R^2=0.32$ ,  $p<0.01$ ). The occurrence of alexithymia was not different between PD patients and HC; however, a significant negative correlation between the expressiveness of disgust was found for a subscore of TAS ( $R^2= -0.447$ ,  $p=0.007$ ).

*Conclusion:* Reduced facial expressiveness in PD may be in part related to difficulties with emotional recognition in a context of an unimpaired subjective emotional experience.

## C11

**Motor cortex excitability during linguistic and non-linguistic tasks in spasmodic dysphonia**

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*Objective:* Adductor-type spasmodic dysphonia (ASD) is an adult-onset focal dystonia affecting laryngeal muscles during speech and other linguistic tasks. Its pathophysiology is largely unknown. In healthy subjects (HS), transcranial magnetic stimulation (TMS) applied during linguistic tasks discloses excitability changes in the dominant hemisphere primary motor cortex (M1). We investigated whether linguistic task-related M1 excitability modulation is altered in ASD.

*Methods:* We studied patients with 10 ASD (4 drug-naïve and 6 patients chronically-treated with botulinum neurotoxin-type A-BoNT-A injections) and 10 HS. All participants were right handed. Speech examination included voice cepstral analysis. Single-pulse TMS was used to investigate excitability in the dominant and non-dominant M1 hand area at baseline and during various “linguistic” and “non-linguistic” tasks: reading a single word aloud, reading a single word silently, looking at non-letter strings, producing simple oral movements, and producing simple two-syllable phonation.

*Results:* In HS, TMS over the dominant M1 elicited larger motor evoked potentials (MEPs) during “reading aloud” than during the other “linguistic” and “non-linguistic” tasks. In patients with ASD, TMS over the dominant hemisphere elicited increased-amplitude MEPs during “reading aloud” and also during the “two-syllable phonation” task. M1 excitability changes observed during “linguistic” tasks were similar in drug-naïve and chronically-treated patients under or not under BoNT-A-induced effects. BoNT-A improved speech as tested by cepstral analysis and restored the neurophysiologic abnormalities.

*Conclusion:* ASD alters excitability in the dominant M1 specifically related to “linguistic” tasks probably by interfering with functional connectivity between the cortical speech networks and M1. BoNT-A returns these excitability changes to normal.

## Role of $\alpha$ -synuclein gene variations in progression of idiopathic Parkinson's disease

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*Background:*  $\alpha$ -synuclein is a major constituent of Lewy bodies and mutations of its gene cause familial young onset PD. Genome wide studies outlined an association of SNCA loci to IPD as well. A previous study suggested that the 263bp allele of Rep1, a microsatellite in the promoter region of SNCA, is associated to faster motor progression in IPD.

*Objective:* To evaluate the influence of  $\alpha$ -synuclein (SNCA) Rep1 promoter variations on disease progression in patients with Idiopathic Parkinson's Disease (IPD).

*Methods:* 280 patients (160M, mean age at diagnosis 62±7 years; disease duration 10.5±6 years) with age at onset >40 years and IPD history longer than 4 years were recruited. We investigated presence and time of occurrence of wearing-off, dyskinesia, freezing of gait, cognitive decline and visual hallucinations and genotyped SNCA-Rep1 by PCR amplification with a fluorescent primer and sizing by capillary electrophoresis.

*Results:* 25/280 IPD patients carried 263bp allele. Demographic characteristics were similar for both 263bp and non-263bp groups. Frequency at five years from onset of any complication, wearing-off and cognitive decline were significantly higher in 263bp compared to non-263bp carriers [p=0.04, 0.04 and 0.01 respectively].

*Conclusion:* 263bp Rep1 carriers showed increased risk of early motor and non-motor complications. Our findings not only confirmed a previous observation of faster motor progression in 263bp carriers, but they also highlighted a role of this gene variation in non motor evolution, especially in predisposing to cognitive deterioration.



**C13****A time-to-effect analysis of long duration response in Parkinson's disease patients treated with 250 mg of L-dopa once a day**

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*Background:* L-dopa motor response in Parkinson's disease (PD) is characterized by an immediate motor improvement lasting hours, the Short Duration Response, and a more sustained response, the Long Duration Response (LDR). It has been shown that a therapeutic regimen of 250 mg of L-dopa once a day may be sufficient to achieve of a sustained LDR lasting more than one year compared to a regimen scheduling small, divided doses during the day.

*Objective:* To assess the median time to maintain a sustained LDR based on a therapeutic regimen of 250 mg of L-dopa at Inter-Dose Interval (IDI) of 24 hours and clinical factors associated with a possible lack of efficacy.

*Methods:* We retrospectively analyzed data of N = 44 PD patients who presented at least two complete clinical evaluations (first and last) at the same therapeutic regimen of 250 mg of L-dopa at IDI of 24 hours. Patients were tested using the UPDRS-ME and the Movement Time (MT) at baseline and peak-of-dose during the assessments. All patients presented a sustained LDR equal or greater than 50% computed using MT and a standardized protocol at the first evaluation, which was performed three months after starting treatment. A Kaplan-Meier survival analysis was performed to compute the median time to maintain a sustained LDR at the second evaluation.

*Results:* At the first evaluation, study patients age was  $61.6 \pm 9.4$  years. Age at disease onset was  $58.1 \pm 9.5$  years. Time between assessments was  $109 \pm 107$  weeks. N = 29 (65.9%) patients preserved a sustained LDR at the second assessment. Comparing patients with and without a sustained LDR at the second assessment, we found a significant difference in UPDRS-ME scores at baseline ( $p = 0.026$ ) and peak-of-dose ( $p = 0.015$ ), while no significant differences between groups were found in terms of age, age at onset, sex, hand dominance, onset signs lateralization and time between assessments. Median value for time to maintain a sustained LDR was 101 weeks (S.E.: 27.82) in our study sample.

*Conclusion:* Our data suggest that a sustained LDR to L-dopa with a therapeutic regimen of 250 mg once a day may last over 2 years in half of treated PD patients. Baseline and peak-of-dose severe motor conditions at the first chronic evaluation may be associated with the lack of a sustained LDR over time.

## C14

**Cerebellar proton MR spectroscopy in the differential diagnosis between Parkinson's disease and atypical parkinsonian syndromes**

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*Introduction:* *In vivo* differential diagnosis between idiopathic Parkinson's disease (IPD) and atypical parkinsonian syndromes (PS) [progressive supranuclear palsy (PSP) and cerebellar and parkinsonian variants of multiple system atrophy (MSA-C and MSA-P)] is often challenging. Neuroimaging is an essential part of the diagnostic work-up of PS. Proton-MR spectroscopy (<sup>1</sup>H-MRS) demonstrated cortical and subcortical biochemical alterations in PS [1,2,3].

*Objective:* To assess <sup>1</sup>H-MRS accuracy in the evaluation of cerebellar metabolism for the differential diagnosis between IPD and atypical PS.

*Methods:* We obtained <sup>1</sup>H-MRS spectra of 21 IPD, 35 atypical PS, and 13 unaffected controls by using a 1.5 Tesla scanner with PRESS single-voxel technique (TR= 4.000 ms; TE= 35 ms). We quantified N-acetyl-aspartate (NAA), neuronal marker, creatine (Cr), energetic marker, choline-containing compounds (Cho), membrane-turnover indicators, and myoinositol (mI), glial marker, within a volume of interest in the left cerebellar hemisphere.

*Results:* Disease duration and Hoehn and Yahr stages were similar in IPD and atypical PS patients. NAA/Cr and NAA/mI ratios were lower ( $p < 0.01$ ) in atypical PS (mean±SD: 0.98±0.25 and 1.36±0.42, respectively) compared to IPD (1.24±0.19 and 1.71±0.25) and controls (1.22±0.23 and 1.92±0.38). NAA/Cr and NAA/mI ratios were lower ( $p < 0.01$ ) in MSA-C (0.70±0.13 and 0.81±0.23) compared to IPD, MSA-P (1.22±0.29 and 1.64±0.29), PSP (1.01±0.17 and 1.49±0.32) and controls. MSA-C patients showed greater mI/Cr ratio (0.80±0.13) compared to controls (0.63±0.12;  $p < 0.01$ ). PSP group showed reduced NAA/Cr ratios compared to IPD ( $p < 0.01$ ) and controls ( $p < 0.05$ ). NAA/Cr ratio demonstrated 83% accuracy in discriminating IPD from atypical PS and values higher than 1.016 showed 100% sensitivity and negative predictive value, 63% specificity and 62% positive predictive value.

*Conclusion:* <sup>1</sup>H-MRS detected cerebellar biochemical alterations indicating neuronal and axonal degeneration in atypical PS. This technique could therefore represent an accurate diagnostic tool to differentiate IPD from atypical PS.

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*Video*

## Valproate-induced generalized choreo-athetosis

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*Introduction:* Valproate (VPA), a GABAergic antiepileptic drug [1], is most often associated with iatrogenic parkinsonism [2]; however it can induce chorea or choreo-athetosis in the setting of pre-existent basal ganglia injury, directly or along corticostriatal pathways [3].

*Case Report:* A 53 years-old white woman with history of mental retardation and epilepsy complicating a childhood meningitis, well controlled with chronic phenytoin, developed two breakthrough generalized tonic-clonic seizures. Neurological examination at admission was normal. EEG showed epileptiform activity and phenytoin blood level was in the therapeutic range (20 mg/l). VPA was added, titrated to 900 mg/day, with seizure remission. After few days, she developed lethargy and generalized involuntary movements with dystonic posturing of foot and trunk. Laboratory investigations including electrolytes, serum ammonia, phenytoin and VPA blood levels were within normal ranges. No EEG epileptiform activity was detected and a brain CT scan showed bilateral basal ganglia calcifications; parathyroid hormone, vitamin D levels, serum lactate and pyruvate were normal. Based on the temporal relationship between VPA administration and the onset of involuntary movements, VPA was slowly discontinued. This resulted in marked improvement within the first three days and complete recovery in a week. Our case is the first report of VPA-induced generalized choreo-athetosis in a patient with bilateral pallidal calcifications which can be detected in 0.3–1.5% of routine CTs, or can be related to inherited (i.e. mitochondrial diseases, idiopathic basal ganglia calcifications) or sporadic disorders (ischemic, neoplastic, infectious cerebral insults, metabolic alterations). In our patient, a negative family history and the absence of progressive neurological dysfunction suggest that calcifications may represent a possible sequelae of her childhood meningitis. We hypothesize that VPA-induced chorea may be due to unbalanced GABAergic activity in the presence of pre-existing brain injury.[3] It has been demonstrated that high or toxic serum VPA concentrations, inactivate GAD, which is the rate-limiting enzyme in the production of GABA and it is normally activated by VPA [1]. The resulting GABAergic tone reduction would be expected to overactivate the motor cortex leading to the subsequent development of a hyperkinetic (i.e. choreo-athetosis) rather than hypokinetic (i.e. parkinsonism) complication from VPA administration.

*Conclusion:* This case report highlights the importance of an accurate pharmacological history when approaching a patient with subacute onset of movement disorders. Moreover the VPA, singly or in combination with phenytoin or carbamazepine, should be used with caution in those with pre-existing basal ganglia injury.

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**Diagnostic accuracy of advanced brain mr biomarkers in differentiating progressive supranuclear palsy and Parkinson's disease**

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A 49-year female, in good physical conditions, no relevant clinical history or any medical treatment before, came to our ambulatory for a peculiar movement disorder.

She described as episodic involuntary movements in her trunk and right hemysoma, each one lasts from thirty second to one minute and they repeat until several times at day.

They arise only in the summer time, particular in warmer days, changing from seated to stand up, in particular when she gets out by the car by the passenger-site (never occurred by the driver-site). They occurred thirty years ago for the first time when she got out from a train but no other symptoms occurred in this long period.

A brother of her had an intentional tremor, but had never gone under a medical investigation.

She went under an MRI of the brain and an EEG-holter in the previous years but the results were unremarkable.

She had a video of one episode, filmed by her husband.

Dyagnosis was Familiar Parossistic Dyskinesyas (corea kinesigenic).



### **Movement disorder: a manifestation of HIV**

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Viral infections of the central nervous system often result in a spectrum of movement disorders. The basal ganglia are especially susceptible to some viruses because of their intrinsic neurotrophism. Both akinetic and hyperkinetic movement disorders may rarely be the presenting feature of human immunodeficiency virus (HIV) infection and have been reported in 2-3% of patients with HIV. Movement disorders include hemichorea, ballismus, myoclonus, tics, dystonia, tremors and parkinsonism. Mirror movements (MM) are involuntary movements of homologous muscles during voluntary movements of contralateral body region. MM may be common in many movement disorders. We describe a MM in case of AIDS.

A 50 years-old male presented progressive involuntary movement involving lower limb, distal more than proximal. Two years before he presented a nucleo-capsular bilateral ischemia reported pyramidal signs. The patient also had memory impairment and slurring of speech and slowness of activities. The patient was a chronic alcoholic and stopped drinking alcohol six months before.

Physical examination revealed ataxia with hyperreflexia and MM of both lower limb. All the laboratory tests were normal. Serology for HIV type 1 was positive (CD4 count was 371 cell), toxoplasma antibody IgG was 300IU/l. He was positive for HBsAg while serum VDRL and TPHA were negative.

Magnetic resonance imaging (MRI) of brain, T2 weighted and FLAIR images revealed cerebral atrophy with hyperintense lesion involving both hemispheres.

Patient was started on pregabalin with improvement of involuntary movements.

The pathogenesis of movement disorders in HIV infection remains unclear. Opportunistic infections are the common case. Infection related pathology involving basal ganglia and brainstem may result in movement disorder. Ischemic infarction is common in patients with HIV and is related to hypercoagulable state associated with HIV infections. MM may be common in many movement disorders, mostly neurodegenerative (PD, CBD, ET, CJD, HD).

We describe MM in AIDS and improvement after pregabalin therapy.



*Poster*

**P1****Dopamine transporter availability in motor subtypes of de novo drug-naïve Parkinson's disease**

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*Introduction:* Tremor dominant (TD) and akinetic-rigid type (ART) are two motor subtypes of Parkinson's disease associated with different disease progression and neurochemical/neuropathological features. The role of presynaptic nigrostriatal dopaminergic damage is still controversial, poorly explored and only assessed in medicated patients.

*Objective:* In this study we investigated with FP-CIT SPECT the striatal dopamine transporter (DAT) availability in drug-naïve PD patients with ART and TD phenotypes.

*Methods:* Fifty-one de novo, drug-naïve patients with PD underwent FP-CIT SPECT studies. Patients were evaluated with Unified Parkinson's Disease Rating Scale (UPDRS) part III and Hoehn and Yahr scale (H&Y) and divided into ART (24/51) and TD (27/51) according to UPDRS part III.

*Results:* ART and TD patients were not different with regard to age, gender and disease duration. However, compared to TD, ART patients presented higher UPDRS part III ( $p=0.01$ ) and H&Y ( $p=0.02$ ) and lower DAT availability in affected and unaffected putamen ( $p=0.008$  and  $p=0.007$ , respectively), whereas no differences were found in caudate. Moreover, in the whole group of patients, rigidity and bradykinesia, but not tremor scores of UPDRS part III were significantly related to FP-CIT binding in the putamen.

*Conclusion:* These results suggest that in newly diagnosed drug-naïve PD patients DAT availability might be different between ART and TD in relation to different disease severity.



## Effects of pallidal stimulation on the neuropsychiatric profile in primary and secondary dystonia: a long-term follow-up

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*Introduction:* Neuropsychiatric symptoms are common in patients with dystonia [1]. They are an important determinant of disability and quality of life [2]. Deep brain stimulation (DBS) of the globus pallidus internus (GPI) has been showed to benefit motor function and disability in dystonia [3,4], but the long-term effects of GPI DBS on the neuropsychiatric profile have not been well investigated.

*Objective:* Long-term changes in the diagnosis of Axis I disorders after GPI DBS compared to baseline in patients with primary generalized/segmental dystonia (PGSD), primary cervical dystonia (PCD) and secondary dystonia (SD).

*Methods:* Psychiatric assessments for Axis I disorders according with the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV were performed before and after surgery in 57 patients. The mean ( $\pm$  SD) psychiatric follow-up was  $21.8 \pm 15.4$  (range, 3-67) months in PGSD,  $28.3 \pm 15.4$  (range, 11-60) months in PCD and  $23.7 \pm 9.8$  (range, 3-120) months in SD.

*Results:* The pre-operative and post-operative % of psychiatric disorders was, respectively, in PSGD: Mood, 19.2% and 7.7%; Anxiety, 26.9% and 23.1%; Obsessive Compulsive Disorder, 3.8% and 0%; one (3.8%) new postoperative diagnosis of Addiction (alcohol); in PCD: Mood, 25% and 20%; Anxiety, 30% and 25%; Addiction (alcohol), 15% and 20%; in SD: Mood, 27.3% and 36.4%; Anxiety, 45.5% and 27.3%; Addiction (cannabis), 8.3% and Psychosis 8.3% were unchanged. We reported two suicides (rate 3.5%) after surgery. Overall, there was a marked positive psychiatric outcome (70.3% of the patients did not worse and 23% improved, 10.8% had a new diagnosis).

*Conclusion:* GPI DBS is a relative safe treatment in dystonic patients with previous history of major psychiatric symptoms. Nevertheless, considering the frequent psychiatric morbidity and the high risk of suicide in dystonia population, psychiatric assessment before and after surgery is strongly recommended.

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## P3

**Impulsive-compulsive behavior in Parkinson's disease: the interplay of increased reward sensitivity, anxiety and depression**

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*Introduction:* Impulsive Compulsive Behaviour (ICB) in Parkinson's disease (PD) might not be a pure drug-induced phenomenon, but rather the expression of a maladaptive response to dopaminergic drugs in a sub-type of patients with selective impairment of the mesolimbic system.

*Objective:* We evaluated whether sensitivity to reward characterizes PD patients with ICB. We also tested whether markers of mesolimbic involvement, such as depression and anxiety, are correlated to development of ICB and ultimately to reward and punishment sensitivity in PD patients with ICB.

*Methods:* We enrolled 16 PD-ICB patients as revealed by QUIP-RS (7 males; mean age: 57.6±13.5 years) and 22 PD-no-ICB (11 males; mean age: 60.3±10.8 years); 29 healthy subjects (HS) (8 males, mean age 53.1±10.5) were included. The 3 groups were matched for exposure to environmental (i.e. hours spent going shopping) and social factors. PD patients were matched for levodopa and dopamine-agonists equivalent daily dose. All subjects underwent the following assessments: Beck's depression inventory (BDI-II); Hamilton anxiety Rating Scale (HARS); Apathy Evaluation Scale (AES), Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ), Brief Self-Control Scale, BIS/BAS scale.

*Results:* SPSRQ total score and SPSRQ-reward sub-score were significantly increased in PD-ICB compared to HC and PD-no-ICB. When comparing the two groups of PD patients, sensitivity to "punishment" was found to be significantly increased in PD-ICB compared to PD-no-ICB ( $p = 0.002$ ), as well as sensitivity to "reward" ( $p = 0.0003$ ). SPSRQ-reward subscore positively correlated with HARS, BDI-II and with the PDQ-8 score. Moreover QUIP-RS was directly correlated to SPSRQ punishment and reward sub-scores.

*Conclusion:* Our data demonstrate the interplay among sensitivity to reward and punishment, depression and anxiety in PD patients with ICB, supporting the presence of a selective impairment of the mesolimbic system in these sub-group of patients.

**Prevalence of psychiatric symptoms in a cohort of Sardinian PD patients carriers of GBA mutation**

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*Introduction:* Homozygous mutations in the  $\beta$ -glucocerebrosidase gene (GBA) have traditionally been implicated in Gaucher disease. However an association between heterozygous mutations of GBA gene and Parkinsonism has been demonstrated. Mutations of GBA gene are now considered one of the most common genetic risk factor for sporadic Parkinson disease (PD).

Different reports tried to define the phenotypic picture of GBA-associated PD [1]; some of them found that GBA-PD patients are more likely to have symmetrical onset of motor manifestations and an earlier onset of PD symptoms. The relationship between mutations in glucocerebrosidase and Lewy body disease postulates an increased risk of dementia during the clinical course of PD in GBA carriers [2]. Finally, some few reports suggested that depression and other neuropsychiatric symptoms could be more frequent in GBA-associated PD, with a higher risk to develop visual hallucinations.

The aim of this study was to evaluate the possible existence of different clinical characteristics between GBA-PD and idiopathic PD patients.

*Methods:* 16 PD patients carriers of GBA mutation (out of 300 Sardinian patients screened) and 76 consecutive PD patients without the GBA mutation were included. For each patient we assessed the presence of symmetric motor manifestations at disease onset, the presence of cognitive impairment and psychiatric symptoms.

*Results:* Our sample GBA carriers accounted for 5% of Sardinian PD patients. No significant difference was found between the two groups on gender, age, symmetry of motor symptoms and age at onset, PD family history and presence of hallucinations. Prevalence of psychiatric disorders was significantly higher in the GBA-PD group compared to controls ( $p=0.0003$ ).

*Conclusion:* Our Sardinian GBA-PD cohort show a clinical picture indistinguishable from that of idiopathic PD. However our results could suggest the existence of a peculiar phenotypic trait of the GBA mutation, based on the higher prevalence of psychiatric symptoms. To our knowledge GBA mutations are most common identified genetic factor of PD in Sardinian patients.

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**Identification of circulating microRNAs for the differential diagnosis of Parkinson's disease and Multiple System Atrophy**

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*Background:* Parkinson's disease (PD) is a progressive neurodegenerative disorder which may be misdiagnosed with atypical conditions such as Multiple System Atrophy (MSA), due to overlapping clinical features. There is emerging evidence that alterations in RNA metabolism may be critical in the pathogenesis of PD. MicroRNAs (miRNAs) are small noncoding RNAs with a key role in post-transcriptional gene regulation. Recent studies have also reported deregulated miRNAs levels in PD patients plasma compared to normal subjects.

*Objective:* We tested the hypothesis that specific panels of cmiRNAs could differentiate PD from MSA patients and represent a potential biomarker to be applied in clinical setting.

*Methods:* In the discovery set, we enrolled six patients affected by PD, nine patients affected by MSA and five healthy subjects with no history of neurological or psychiatric diseases. Using TaqMan Low Density Array (TLDA) technology we analysed 754 miRNAs and we found several cmiRNAs differentially expressed in PD and MSA patients if compared to healthy controls. However, we tested the expression of DE cmiRNAs in a separate and independent cohort of patients (25 PD and 25 MSA) and 25 healthy controls by using single TaqMan assays.

*Results:* We found 9 cmiRNAs differentially expressed in PD and MSA patients compared to healthy controls. We also validated a set of 4 differentially expressed cmiRNAs in PD and MSA patients vs. controls. More specifically, miR-339-5p was downregulated, whereas miR-223\*, miR-324-3p, and mir-24 were upregulated in both diseases. We found cmiRNAs specifically deregulated in PD (downregulation of miR-30c and miR-148b) and in MSA (upregulation of miR- 48b). Finally, comparing MSA and PD, we identified 3 upregulated cmiRNAs in MSA serum (miR-24, miR-34b, miR-148b).

*Conclusion:* Our results suggest that cmiRNA signatures discriminate PD from MSA patients and healthy controls and may be considered specific, non-invasive biomarkers for differential diagnosis.

## Secondary upper limb dystonia associated with structural lesions of the brain

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*Introduction:* Upper limb dystonia (ULD) is a form of focal dystonia. The pathogenesis of ULD and the neuroanatomic substrates involved are not fully understood. Dysfunction of the basal ganglia traditionally is presumed to be the main cause of most forms of dystonia.

*Objective and Methods:* To identify potentially contributing of brain lesions, we examined the medical records of patients with ULD seen at our centre in the last 5 years. In addition, we conducted a systematic review of the published literature.

*Results:* Among patients with ULD at our centre 7 had focal lesions on imaging studies available for review. The literature review revealed 23 articles describing 58 additional cases of ULD associated with focal lesions. Among all cases, lesions were found in multiple regions including thalamus (n=38), lower brainstem (n=3), basal ganglia (n=19), midbrain (n=1), and cortex (n=4). Stratifying patients by task specific ULD (n=6) and non task specific ULD (n=59) yielded a significant association between focal lesions in the thalamus and non task specific ULD (chi square test: 13.9; p=0.003).

*Conclusion:* These data support a model of dystonia in which a network of different regions plays a role in pathogenesis. Damage to the thalamic stations seems to more likely produce non task- specific ULD.

P7

**Three year follow-up of botulinum toxin A intradetrusorial injections in patients with Parkinson's disease and refractory neurogenic detrusor overactivity: clinical and urodynamic results***Marilena Gubbiotti<sup>1</sup>, J.A. de Vermandois<sup>1</sup>, A. Conte<sup>2</sup>, A. Berardelli<sup>2</sup>, A. Giannantoni<sup>1</sup>*<sup>1</sup>Università di Perugia, Dip. di Urologia e Andrologia, Ospedale S. Maria della Misericordia, Perugia, Italy<sup>2</sup>Università di Roma "La Sapienza", Dip. di Neurologia e Psichiatria, Rome, Italy

We previously assessed the efficacy and safety of a single intradetrusorial injection of botulinum A toxin (BoNT/A) in Parkinson's disease (PD) patients with refractory overactive bladder syndrome (OAB) and detrusor overactivity (DO). Because most patients may require retreatment the efficacy and safety of multiple injections must be addressed clearly. We investigated the effectiveness and safety of BoNT/A intradetrusorial multiple injections in a group of PD patients with refractory DO. 11 female and 3 male PD patients were enrolled. Hoehn and Yahr stage of the disease was  $3 \pm 0$ . Baseline evaluation: clinical, neurological and urological assessment, a standardized quality-of-life questionnaire (I-QoL) and urodynamics.

After the first injection (100 U), clinical evaluation and urodynamics were repeated every 4 mo during the first year. When patients had a worsening of symptoms, they underwent urodynamics and a further treatment with BoNT/A was performed. Outcome measures: reduction in daytime and night-time urinary frequency and episodes of urge urinary incontinence and increase in first volume and maximum pressure of uninhibited detrusor contractions and maximum cystometric capacity on urodynamics. At 3-yr follow up, 4 patients had dropped-out due to large post-void residual volume requiring intermittent catheterizations in 3 cases, and discovery of bladder cancer in one. A total of 54 injections were performed in 10 patients; the mean number of injections was  $3.42 \pm 2.49$  for each patient and the mean interval between two consecutive injections was  $5.85 \pm 1.64$  mo. In these 10 patients we detected a reduction in daytime (before:  $9.8 \pm 2.7$ ; after:  $4.9 \pm 2.5$ ) and night-time urinary frequency (before:  $4.2 \pm 3.5$ ; after:  $2.5 \pm 1.6$ ) and the QoL scores improved (before:  $25 \pm 21$ ; after:  $82 \pm 14$ ). Urodynamics showed that all the parameters testing urinary function improved.

Intradetrusor injection of BoNT/A induced clinical, urodynamic and QoL improvement in OAB symptoms that lasted at least 3 yr in PD patients. The novel finding of the study is that BoNT/A injections is an effective treatment for PD patients with moderate neurological disability, affected by refractory OAB and DO.

**Sensorimotor modulation in segmental dystonia induced by sensory repetitive stimulation**

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*Background:* The possibility to study plasticity in dystonia by the means of a new paradigm of stimulation prompted our study.

*Methods:* We applied a new model of high frequency electrical sensory stimulation in seven patients with isolated idiopathic segmental dystonia (cervical dystonia plus right shoulder/arm involvement) and seven age-matched healthy voluntaries (all right handed). We tested sensorimotor modulation by means of behavioral tests (namely somatosensory temporal discrimination time, STDT) and neurophysiological investigations (namely Somatosensory Evoked Potentials, SEPs, - P14 and N20 components- by stimulating right I and II fingers, paired SEPs, and SEPs by simultaneous stimulation of right I and II fingers and motor cortex excitability by means of Transcranial Magnetic Stimulation, TMS, applied on M1 and recorded from APB, ADM and FDI). Measurements have been performed at baseline (T0) and soon after the stimulation (T1).

*Results:* Baseline STDT values were slightly higher in patients when compared to the controls. At T1, they significantly increased on right I and II fingers in patients and decreased only on the stimulated finger in controls. At baseline, SEPs recovery function at ISI 5 was significantly reduced in patients when compared to controls. At T1, SEPs recovery function improved in controls and worsened in patients. At baseline, patients showed larger amplitudes of the resultant SEPs recorder from stimulating simultaneously right I and II fingers, when compared to controls. After the stimulation, the gap further increased. Finally, TMS study at baseline revealed a reduced SICI in the patient group when recorded from all the examined muscles. At T1, SICI significantly decreased in patients and increased in controls, but only when measured from the APB.

*Conclusion:* Our study confirms the impairment of inhibitory mechanisms in patients with segmental dystonia. RSS further hampers the sensorimotor abnormalities in dystonic patients, while it improves the behavioral and neurophysiological parameters in healthy voluntaries.

**Relationship between freezing of gait and falls in Parkinson's disease and dopaminergic dysfunction: evidences from a five years follow-up clinical study**

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*Introduction:* Freezing of gait (FOG) is characterized by difficulty in initiating or maintaining locomotion, frequently associated with falls in advanced disease, often related to the OFF state and may be responsive or unresponsive to dopaminergic therapy. The role of dopamine depletion in the pathogenesis of FOG and falls is still debated.

*Objective:* We aimed to evaluate the role of <sup>123</sup>I-FP-CIT-SPECT imaging in predicting FOG and falls in a cohort of PD de-novo patients followed up for five years.

*Methods:* Ninety-four PD de-novo patients underwent <sup>123</sup>I-FP-CIT SPECT at baseline. Basal ganglia matching tool was used to obtain semiquantitative measures of caudate and putamen uptake. Each patient was assessed with Unified Parkinson's Disease Rating Scale (UPDRS) part II and III and Mini Mental State Examination (MMSE) at baseline and each year in the follow up. FOG and falls were assessed through UPDRS II. We compared baseline clinical, demographic, and SPECT indices between patients who developed FOG and falls and subjects who did not.

*Results:* During follow-up, 47% patients developed FOG, 17% falls. No significant statistical differences in UPDRS III and MMSE at baseline were found between patients with FOG and falls and those without these features. Patients with FOG had a decreased uptake at baseline in caudate (Right: 2,77vs.3,32; p<0,005; Left: 3,38vs.3,02; p<0,05) and in putamen (Right: 1,42vs.1,86; p <0,002, Left: 1,67vs.1,97; p<0,05). No significant differences in baseline striatal uptake were observed in relationship with risk of falls.

*Conclusion:* A baseline lower uptake value of striatum seems to be predictor of FOG and this evidence might support a link between FOG and dopamine depletion both in caudate and putamen, at least in the early stage of disease. Risk of falls, although often associated with FOG in PD, doesn't relate to dopaminergic dysfunction, supporting the hypothesis of its complex multifactorial genesis.



**P10****Bilateral Prefrontal or Parietal transcranial Direct Current Stimulation (tDCS) for treating freezing of gait in Parkinson's disease. A placebo controlled trial**

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*Introduction:* Progression of PD is characterized by motor and cognitive deficits which interact each other to generate drug-resistant symptoms, as freezing of gait (FOG).

*Objective:* To investigate the effects of transcranial Direct Current Stimulation (tDCS) in not-demented patients with Parkinson's Disease (PD) complicated by drug-resistant FOG.


*Methods:* Ten patients (3 men; age: 67.6(SD8.3); disease duration: 14.5(SD5.2); LEDD: 971(SD529)mg; UPDRS II: 16.6(SD6.1); FOGQ: 15.6(SD5.1); FAB: 12.7(SD3.1)) underwent two sessions of 2.0 mA anodal tDCS, respectively delivered to the prefrontal cortex (DLPFC) and the parietal cortex (PC) and one sham-stimulation session. Each session lasted 40 minutes, with the right and left hemispheres being separately stimulated, for 20 minutes.

Sessions were scheduled at 30-day intervals, in a random order. Outcome was measured by: UPDRS-motor part (UPDRSm), Timed Up and Go (TUG), TUG with motor dual task (TUGm), TUG with cognitive dual task (TUGc), digit span (forwards and backwards), Corsi's spatial span (forwards and backwards), phonetic verbal fluency, semantic verbal fluency and STROOP test. Each measure was taken before and at the end of each session.

*Results:* DLPFC tDCS induced a significant improvement in the UPDRSm score ( $Z=-2.1$ ,  $p=.03$ ), STROOP time ( $Z=-2.6$ ,  $p=.007$ ) and errors ( $Z=-2.0$ ,  $p=.04$ ). PC tDCS induced an improvement in the TUGm time ( $Z=-2.5$ ,  $p=.01$ ) and the FOG total duration ( $Z=-2.1$ ,  $p=.03$ ). No changes were observed on cognitive tests after PC stimulation. The sham stimulation was not associated with any appreciable variation of the motor or cognitive outcome measures.

*Conclusion:* tDCS, bilaterally delivered on the DLPFC, can exert a beneficial effect on both motor and cognitive symptoms, where bilateral PC tDCS has a positive impact on freezing.

The findings are consistent with the scientific evidence regarding the involvement of the PC in the genesis of FOG.



## The role of alexithymia in the development of functional motor symptoms (conversion disorder)

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*Background:* The mechanisms leading to the development of functional motor symptoms (FMS) are of pathophysiological and clinical relevance, yet are poorly understood.

*Aim:* The aim of the present study was to evaluate whether impaired emotional processing at the cognitive level (alexithymia) is present in patients affected by FMS. We conducted a cross-sectional study in a population of patients with FMS and in two control groups [patients with organic movement disorders (OMD) and healthy volunteers].

*Methods:* Fifty-five patients with FMS, 33 patients affected by OMD and 34 healthy volunteers were recruited. The assessment included: the 20-item Toronto Alexithymia Scale (TAS-20), the Montgomery-Asberg Depression Rating Scale (MADRS), the Reading the Mind in the Eyes' Test and the Structured Clinical Interview for Personality Disorders (SCID II).

*Results:* Alexithymia was present in 34.5% of patients with FMS, 9.1% with OMD and 5.9% of the healthy volunteers, which was significantly higher in the FMS group (X square (2)=14.129,  $p<0.001$ ), even after controlling for the severity of symptoms of depression. Group differences in mean scores were observed on both the difficulty identifying feelings (DIF) and difficulty describing feelings (DDF) dimensions of the TAS-20, whereas the externally-orientated thinking (EOT) subscale score was similar across the three groups. Regarding personality disorder, X square analysis showed a significantly higher prominence of obsessive-compulsive personality disorder in the FMS group (X square (2)=16.217,  $p<0.001$ ) and 71.4% of those with OCPD also reached threshold criteria for alexithymia.

*Conclusion:* Because alexithymia is a mental state denoting the inability to identify emotions at a cognitive level, one hypothesis is that some patients misattribute autonomic symptoms of anxiety, e.g. tremor, paraesthesiae, paralysis, to that of a physical illness. Further work is required to understand the contribution of OCPD to the development of FMS.

**P12****Freezing of gait in Parkinson's disease. Possible contribution of increased executive load during turning**

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*Background:* Gait deficits, including freezing of gait (FOG), are common in Parkinson's disease (PD). PD-patients likely increase their attention and executive load during walking to compensate for their automatic gait deficits. The interplay between executive functions and gait can be investigated by evaluating a secondary task during gait.

*Objective:* We hypothesized that the ability to perform a secondary task decreases during challenging walking tasks in PD.

*Methods:* Twenty-nine PD-patients and 14 age-matched controls performed a simple reaction task that involved squeezing a ball as fast as possible in response to an auditory tone.

Participants performed this reaction task while: 1) walking at preferred speed; 2) walking with short steps at preferred speed; 3) walking with short steps as rapidly as possible; 4) making full rapid turns. We used surface electromyography to determine onset latencies, and we used a pressure sensor located within the ball to determine movement onset.

*Results:* Reaction times were on average 42 ms slower in PD-patients compared to controls. In both groups, reaction times were significantly slower in the turning condition compared to the other conditions. FOG-episodes were most often seen during the turning condition. In PD-patients, reaction times were significantly slower during FOG-episodes compared to trials without FOG.

*Conclusion:* Our results suggest that turning requires more attention and executive resources compared to other walking tasks, both in PD-patients and controls. This observation, in combination with the notion that turning requires complex bilateral coordination that is hampered in PD, suggests that executive compensation might become overloaded during turning, leading to FOG-episodes.

**P13****Study of the somatosensory temporal discrimination threshold in patients with newly diagnosed Parkinson's disease**

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*Introduction:* Sensory abnormalities can be present in patients with Parkinson disease (PD). Somatosensory temporal discrimination threshold (STDT) is defined as the threshold at which two tactile stimuli applied to the skin are perceived as clearly distinct and it has been shown to be increased in patients with moderate and advanced Parkinson's disease (PD). [1] [2]

*Objective:* To verify whether the STDT is altered in patients with very early stage PD.

*Methods:* STDT was investigated in 17 drug-naïve PD with onset of motor symptoms within two years (de novo), and 31 age-matched healthy subjects. STDT was investigated by delivering paired electrical stimuli starting with an inter-stimulus interval (ISI) of 0 ms, and progressively increasing the ISIs in 10-ms steps. The clinical evaluation included scales for motor and cognitive assessment of the patients. All subjects underwent Posner test to rule out any confounding factors related to attentional deficits.

*Results:* Between-group ANOVA showed no significant differences in STDT values between PD de novo patients and healthy subjects. ANOVA for the reaction-times latency differences between "invalid cue" and "valid cue" trials, revealed no significant differences between patients with de novo PD and normal subjects.

*Conclusion:* We now show that de novo PD patients have normal STDT values. Differently from dystonia in which STDT abnormalities represent an endophenotypic feature, STDT abnormalities in PD develop during the course of the disease.

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**P14**

**A quantitative stress study of people caring for Parkinson's disease patients**

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Caregivers play a crucial role in the long term care of patients affected by Parkinson's disease. They suffer an enormous physical, emotional, financial and psychological burden as a consequence of the demands of caring. The smaller the social health services contribution to Parkinson's disease pts, the greater the caregiver's stress and financial burden which in turn will affect the caregiver's satisfaction and quality of life. In order to assess and improve our diagnostic and treatment role we carried out 175 carers of pts with Parkinson's disease. The purpose was to measure their satisfaction and quality of life, appraising their expectation for help from relatives and social services. We did the SAT-P (satisfaction profile) test, the Hamilton Rating Scale for depression and the Caregiver Strain Index. The results revealed a caregivers profile consisting of the following characteristics: female (83%), average age 68 (range 28-85), married, living in an urban area, elementary school education and a housewife. These caregivers seek help from the family, starting with the husband/wife if health.

The main causes of dissatisfaction were lack of freetime, lack of good sleep quality and emotional turmoil. Family Doctor and Neurologist were indicated as essential support figures, while relatives, neighbours, the church and social services were less significant. The Hamilton Rating scale for depression was less than 17 in the 50% and between 17 and 24 in the other 50% of the cases. Caregivers asked for more information about the disease, home nursing help, psychological support, self-help group support and specialized voluntary aid in the areas where they would like to improvements.



**Presence and progression of non-motor symptoms in relation to uric acid in de novo Parkinson's disease**

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*Introduction:* Uric acid (UA) has been studied extensively as a valuable biomarker of Parkinson's disease (PD), but its relationship with non-motor symptoms (NMS) in de novo PD has poorly been investigated.

*Objective:* We aim to evaluate the usefulness of baseline serum UA as a marker of NMS progression in newly diagnosed PD.

*Methods:* We enrolled sixty-nine newly diagnosed PD patients. At baseline, all patients completed the NMS Questionnaire (NMSQuest), and serum UA levels were measured. After 2 years, NMSQuest was completed, and patient were categorized into four groups: NMS improvement (domain involvement at baseline, but not at two-year follow-up visit), NMS absence (domain not involved at baseline or two-year follow-up visits), NMS presence (domain involvement both at baseline and two-year follow-up visits), and NMS worsening (domain not involved at baseline, but involved at two-year follow-up).

*Results:* ANOVA analysis with post-hoc Bonferroni correction showed that patients with NMS absence presented significantly higher UA values than patients with NMS presence with regard to Attention/Memory ( $p=0.023$ ), Depression/Anxiety ( $p=0.028$ ) and Cardiovascular domains ( $p=0.002$ ), while no differences were found with regard to both NMS improvement and worsening groups. In addition, multinomial regression analysis, showed that the lowest tertile of NMS progression presented higher UA levels ( $p=0.023$ ; OR=0.488), as compared to patients with greater NMS progression.

*Conclusion:* This is the first report of a relationship between serum UA and presence/progression of multiple NMS in de novo PD, providing additional evidence of the reliability of UA as a biomarker of PD, and opening new insights on PD neuroprotection.

**P16**

**Patological gambling in Parkinson's disease patients: dopaminergic medication or individual traits?**

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*Introduction:* Impulse control disorders (ICDs) are common and clinically relevant in Parkinson disease (PD) patients, with a well established association with PD medication. However, previous studies demonstrated that ICDs are equally common in newly diagnosed, untreated PD patients and in normal population (approximately 20%). This finding suggests a strong drug effect. However not all PD patients develop ICD, but only a subset of patients.

*Objective:* Aim of our study was to detect whether the increase frequency of ICDs reported in PD patients compared to normal controls is exclusively related to dopaminergic medications, to personality traits or to an interaction of both these two aspects.

*Subjects and Methods:* 40 Patients affected by PD according with Brain Bank Criteria were included in our study. None of them was affected by cognitive decline. Twenty patients of the studied group have had an history of pathological gambling (PG) developed after PD onset, during dopaminergic medication. The remaining 20 PD patients on the contrary had never experienced PG nor any other ICD. The two groups (PG-PD and Non PG-PD) were matched for sex, age and disease duration and severity). All subjects were tested with the Minnesota Multiphasic Inventory Personality scales (MMPI-2) that have expected high sensitivity to apparent addictive behaviors.

*Results:* Our data analyzed by comparing the two groups across the numerous variables of the MMPI (Mann whitney test) demonstrated a significant difference in PG-PD vs non PG-PD concerning depression, anxiety, social introversion and difficulty, limited compliance to rules, with a higher lying frequency ( $p > 0.001$ ).

*Conclusion:* Accordingly with our results PG as part of ICDs seem to be secondary not only to dopaminergic medications but also to precise personality traits. MMPI-2 may be a useful test in PD patients to assess their ICD susceptibility before adding dopaminergic treatment.

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**P17**

**Possible advantages from the use of a dedicated software for Parkinson's outpatients**

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We suggest that a custom made software solution made with a database builder, such as FileMaker pro advanced version 13, would allow an easier, and more accurate and precise introduction and retrieval of information. The authors concentrated their efforts on making it easy to introduce data to the system. The 2nd, 3rd and 4th part of one of the more common rating scales was used to monitor progression or regression, e.g. under therapy, of signs and symptoms, i.e. the Unified Parkinson Disease Rating Scale (UPDRS). Not only can you use the software to write down answers for every item, but you can also have useful reminders of possible answers, methods of testing and results of previous exams. This is all done upon the Movement Disorder Society items. At the end of each examination everything is automatically archived and it is easily retrievable.





## Validation of the Italian version of the FOG-Q

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*Background:* Freezing of gait (FOG) is a common and disabling symptom in Parkinson's disease (PD) [1] whose assessment is complex because of its episodic and subjective characteristics. Patient-reported assessments are essential to study this phenomenon. The Freezing of Gait Questionnaire (FOG-Q) is a valid and reliable tool for the assessment of FOG severity [2].

*Aim:* To translate and validate the Italian version of the FOG-Q and to explore relationships between FOG-Q scores and other clinical aspects of PD patients.

*Methods:* The Italian version of the questionnaire of the FOG-Q was developed according to a standardized protocol. Then, fifty-one people with PD were assessed with the FOG-Q, Unified PD Rating Scale (UPDRS), Hoehn and Yahr (H&Y), Falls-Efficacy Scale [FES(S)] [3] and timed gait tests [4].

*Results:* Mean (SD) FOG-Q item scores ranged between 1.5 and 2.7 (1.0–1.4); corrected item–total correlations ranged between 0.63 and 0.86. Reliability was 0.91. Mean (SD) and median (q1–q3) FOG-Q scores were 12.0 (9.0–17.0) and 13.0 (10.5–18.5). FOG-Q correlated with H&Y (0.36,  $p=0.0091$ ), UPDRS part III ( $r_s=0.27$ ,  $p=0.054$ ). FOG-Q correlated with FES(S) ( $r_s=0.58$ ,  $p<0.001$ ) and the Timed Up and Go test ( $r_s=0.51$ ,  $p=0.001$ ). The FOG-Q scores correlated significantly with PD duration, TUG, FES(S). Positive correlations were observed (although not significant) with dyskinesia and motor fluctuations.

*Conclusion:* Our study provided the validation of the Italian version of the Freezing of Gait-Questionnaire originally proposed by Giladi et al. Thus, FOG-Q Italian version can be easily utilized to evaluate the Italian PD patients.

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**Pisa Syndrome in Parkinson's disease: an electrophysiological, imaging and biomechanical study**

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*Objective:* To clarify the role of dystonia and muscle weakness in the pathophysiology of Pisa Syndrome (PS) by means of a quantitative EMG analysis, magnetic resonance imaging (MRI) and postural assessment in patients with Parkinson's disease (PD).

*Materials and Methods:* We enrolled 8 PD patients with PS, 2 without PS and an aged-matched normal subject. Each patient underwent EMG with fine-wire electrodes inserted within the Iliocostalis Lumbar (L2-L4) and Thoracic (T8-T10) muscles, Gluteus Medius and abdominal External Oblique Muscles. A quantitative EMG motor unit action potential analysis (QEMG) and the root mean square (RMS) during voluntary isometric muscle contraction was obtained and compared when patients standing and during voluntary right and left lateral trunk flexion while standing. All patients underwent MRI, posturography assessment and gait analysis.

*Results:* Demographic and clinical findings of PD patients with PS (7 men and 1 woman, mean age:  $66.1 \pm 13$ , mean disease duration:  $8.5 \pm 3.7$  years), without PS (2 men, mean age  $75 \pm 2.8$ ) and a normal subject (1 man, 73 years old). All the patients were in chronic therapy with dopaminergic drugs achieving a good motor compensation on the appendicular function. No patient had psychiatric disturbances and never took neuroleptics. Mean laboratory blood, serum and urine tests were normal. At the time of the assessment, PS duration was  $5.8 \pm 3.5$  years on average (range 1–10) and it consisted in a lateral flexion of the trunk towards the right ( $34.4^\circ \pm 19.6^\circ$  on average) and the left side ( $14.6^\circ \pm 4.1^\circ$  on average) in five and three patients, respectively. Anterior trunk flexion of different severity was present in four out of 8 patients ( $14.3^\circ \pm 16.3^\circ$ , range 0–50). The leaning side was contralateral to the side of PD onset in three of the eight cases with identifiable motor asymmetry at onset. QEMG showed different data for number of MUAPs (n), amplitude ( $\mu\text{V}$ ), area ( $\mu\text{V} \times \text{ms}$ ), duration (ms), Firing rate (Hz), turns (n) and polyphasic potentials (%). The RMS suggests a reduction of muscle power when compared with patients with PD only and normal subjects. MRI ruled out major structural muscles and bony changes in all patients.

*Discussion:* Whether patients with PD would develop a localized myopathy of paraspinal muscle is unclear. Dystonia of paraspinal muscles appear to have a causative role for developing PS.

*Conclusion:* Future studies should address the several unsolved issues related to the pathophysiology of PS.

**P20****Action tremor relates to rest tremor and rigidity in early Parkinson's disease**

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*Background:* Action tremor (AT) of the upper limbs may occur in Parkinson's disease (PD) and its presence may confound PD diagnosis especially at the earlier stages.

*Objective:* To investigate the frequency of AT and its relationship to other motor and non motor features in PD patients staging 1 to 2 on Hoehn-Yahr (H&Y) scale.

*Methods:* All patients underwent a neurological evaluation using the Unified Parkinson's Disease Rating Scale motor section (UPDRS-III) stratified for axial and segmental symptoms scores and H&Y scale. Demographic and clinical features were ascertained in 237 PD patients (mean age of PD onset, 61.9±10 years; mean duration of PD, 5.2±3.8 years; mean UPDRS-III total score, 23.9±10; levodopa equivalent dose, 476±356 mgs). Neuropsychological tests and non motor symptoms (NMS) scale were also administered.

*Results:* On clinical examination 108/237 patients had AT, either alone (n.18) or associated with rest tremor (n.90). Patients who had AT and those who had not were similar for sex, age at disease onset, disease duration, LED and UPDRS-III axial symptom severity score, whereas UPDRS-III segmental symptom severity score was greater in patients with AT. Multivariable logistic regression analysis (adjusted for sex, age at disease onset, disease duration and LED) yielded significant independent associations between presence of AT and severity of rest tremor and rigidity. On multivariable linear regression analysis there were significant correlations between AT and rest tremor scores (adjusted RC 0.28;  $p<0.001$ ) and between AT and rigidity scores (adjusted RC 0.05;  $p=0.01$ ); no correlation emerged between AT and other motor signs. Patients with and without AT showed similar distribution of NMS domains and similar neuropsychological test performances.

*Conclusion:* AT was present in 45% of cases and was associated with both presence and severity of rest tremor and severity of rigidity. No association was evident between AT and any other motor or non motor sign.

**Psychosocial problems in Parkinson's disease. Translation and validation of Italian version of BELA-P-k questionnaire**

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*Introduction:* Parkinson disease (MP) is characterized by motor symptoms, but also by cognitive deficits and emotional and motivational symptoms. The quality of life (QoL) of patients with Parkinson's disease is the result of the interaction between motor and neuropsychological symptoms. The Belastungsfragebogen Parkinson kurzversion (BELA-P-k) evaluate the psychosocial issues resulting from three components: the presence of the problem, perceived discomfort and the need for help. In this regard, to evaluate the psychosocial impact of Parkinson's disease, we decided to translate and to test the internal consistency and the validity of this disease-specific instrument.

*Subjects and Methods:* The BELA-P-k consist of 19 items grouped into 4 subscales: physical symptoms, emotional symptoms, social functioning, partner-bonding/family.

For each item, three aspects are investigate: the presence of the problem, the perceived discomfort and the "need for help" from the caregiver. Each question is scored on a 5-point Likert scale. The total score is obtained by summing the 19 responses in the three areas of investigation.

The BELA-P-k was administered to 80 Parkinson's disease patients and compared with PDQ-39, UPDRS, and MOCA.

*Results:* All data were analyzed using SPSS 17.0. Reliability of the BELA-P-k was tested by investigating the internal consistency of results using Cronbach's  $\alpha$  coefficient (Cronbach's  $\alpha$  : 0.95). The correlation between the BELA-P-k score and the PDQ-39 ( $p < .000$ ) is high. BELA-P-k also correlate with UPDRS ( $p < .000$ ). There is no correlation between BELA-P-k and Moca score.

*Conclusion:* The BELA-P-k is a questionnaire for the assessment of QoL in MP. A strength of this tool for clinical neuropsychological practice is to investigate for each item the presence of the problem, the perceived discomfort and the need for help. So, from this study, we can conclude that the Italian version of the BELA-P-k is a relevant, reliable and valid measure for assessing psychosocial problems of MP.

## Neuropsychological evaluation in parkinsonian syndromes at onset

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*Introduction:* Cognitive impairment (CI) has been reported both in idiopathic Parkinson disease (PD) and in the other parkinsonian syndromes (PS) at onset [1].

*Objective:* To evaluate if neuropsychological assessment can be a useful tool to discriminate PD from PS at onset.

*Methods:* We consecutively selected patient with a progressive disease starting with parkinsonian features and disease duration up to 3 years to take part in the Bologna-motor and non motor Prospective study on Parkinsonisms at onset. Each patient underwent neurological examination, neuroimaging studies, quantification of motor response to standard oral levodopa test, evaluation of autonomic control of the cardiovascular system, assessment of sleep disturbances by means of a whole night video-polysomnographic study, autonomic symptoms and sleep questionnaires, cognitive and behavioural assessment by means of Brief Mental Deterioration Battery (BMDB) [2], Stroop Test, Simple Copy Design Test, Phonemic and Semantic Fluency Task. Each patient was tested twice, at baseline and sixteen months later.

Diagnosis was made at the second evaluation, according to international diagnostic criteria.

We defined impairment in each test according to cut-off of scores corrected for sex, age and education of Italian population. Dementia was defined according to PD and Dementia with lewy bodies' criteria.

*Results:* We recruited 55 patients. At first examination 24 out of 55 patients demonstrated cognitive performances within the normal range. 31/55 patients were impaired in one or two cognitive domains. This evaluation was substantially confirmed at the second evaluation. 20 out of 24 (83%) cognitively normal patients were diagnosed as PD and 4/24 (16%) as PS. 23 out of 31 (74%) patients with one or two impaired cognitive domains were diagnosed as PD and 8/31 (26%) as PS.

*Conclusion:* Dementia has not been observed at onset in parkinsonian syndromes. CI can be observed in patients with parkinsonism at disease onset, independently from the clinical diagnosis.

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## Parkinson's disease and cognitive reserve

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*Introduction:* Dementia is a frequent feature of Parkinson's disease (PD). The main risk factors for PD dementia have been extensively explored but recent studies suggest that cognitive reserve (CR) needs to be considered when monitoring the evolution of cognition in PD. CR refers to the modality of cognitive system elaboration of information and it has been used to explain the individual differences in the ability to cope with neurological damage: individuals with more efficient neural networks could be more resilient to neurological damage.

*Objective:* The aim of this study is to evaluate the role of CR in PD, specifically, if the presence of a high CR may be related to a better cognitive and/or motor performance.

*Methods:* Eighteen consecutive PD patients (16 males, mean age:  $69 \pm 7,3$  years; mean disease duration:  $8 \pm 4,8$  years; mean education:  $12 \pm 4,6$  years) were enrolled in the study and underwent clinical and neuropsychological evaluations, during ON state, with: Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr scale, a standard neuropsychological test battery and the Cognitive Reserve Index questionnaire (CRIq).

*Results:* The Mini Mental State Examination (MMSE) raw score showed a greater correlation with CRIq score than with age and with years of education. The regression analysis showed that higher CRIq scores were significantly associated with higher raw scores on MMSE and semantic fluency test. The analysis of the other clinical and neuropsychological test scores confirmed that disease duration is a good predictor of cognitive function. No correlation emerged between CR and the UPDRS score.

*Conclusion:* CR may be considered a good predictor of the clinical manifestation of cognitive impairment in PD. Long term prospective detailed studies on larger populations are useful to study effects of CR on cognition, cognitive decline and the time of onset of dementia in PD.

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**P24****Divergent thinking and de novo Parkinson's disease patients: preliminary study after follow-up**

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*Introduction:* Creativity is commonly thought of as a positive advance for society that transcends the status quo knowledge. Indeed, it is hard to imagine any human progress without this capacity. A broadly accepted definition of creativity is the ability to generate ideas that are both novel and useful in a particular setting.

*Objective:* The introduction of dopaminergic therapy (DRT) has consequently reported the emergence of de novo artistic ability in Parkinson's Disease (PD). Until now the relationship between artistic productivity, behavioral disorder (ICD) and creativity is controversial.

The aim of our study is to evaluate the DT in drug-naïve PD patients at the onset of disease (T0) and after 24 months (T1) from the introduction of dopaminergic therapy.

*Patients and Methods:* We enrolled consecutively 10 drug naïve PD patients matched to healthy controls (HC) by sex and age. All the subjects underwent at T0 and T1 neurological (UPDRS, HY), neuropsychological (MMSE; FAB) and mood assessment (GDS; HAM-A; mMIDI). Divergent thinking (DT) was evaluated by means Abbreviated Torrance Test for Adults (ATTA) which includes various aspects, like fluency, flexibility, originality and elaboration.

*Results:* Ten patients were included (all data are means(SD)): age at T0 was 60,6(9,3), age at onset of disease was 59,7(9,5), education (yrs) was 11,3 (3,4). All patients at T1 were in DRT for at least 12 months. Two patients at T1 were positive at mMIDI scales, none showed punding.

ATTA total score was 59,5(6,7) and 68,9(24,1) at T0 and T1 respectively. ATTA total score in HC was 62,0(22,0).

*Conclusion:* Our preliminary data suggest that the DT measured by means of ATTA does not change after the introduction of dopaminergic treatment (DRT). From the data collected divergent thinking and creative output seem to respond differently to dopaminergic exposure.

**Inclusion of REM behavioural disorders (RBD) improves the diagnostic classification of parkinsonism**

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*Introduction:* REM Sleep Behavior Disorders (RBD) are often present in the alpha-synucleinopathies Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB) and Multisystem Atrophy (MSA) and more rarely reported in Progressive Supranuclear palsy (PSP) or Corticobasal degeneration (CBD). Clinical criteria for PD and atypical parkinsonism do not include RBD and other non-motor features to support the diagnostic process.

*Objective:* To assess RBD prevalence in a wide parkinsonism spectrum and to determine whether adding RBD to current clinical criteria may improve alpha-synucleinopathies clinical classification accuracy.

*Materials and Methods:* The study included 103 PD, 29 DLB, 13 MSA, 32 PSP and 29 possible CBD patients, who underwent an extensive motor, cognitive and behavioral assessment, including the Italian version of RBD screening questionnaire (RBDSQ).

The prevalence of RBD was established in blind according to the clinical diagnosis. Discrimination between alpha-synucleinopathies and other parkinsonism was tested with current criteria and after adding RBD with a crossvalidated classification and logistic regression analyses.

*Results:* The prevalence of RBD was higher ( $p < 0.001$ ) in alpha-synucleinopathies (49% in PD, 55% in DLB, 39% in MSA) compared with 25% of PSP and 10% of CBD. RBD evaluation besides classical criteria brought clinical classification accuracy from 78 up to 82% in all cohort and from 65 to 71% in PSP and CBD. High RBDSQ total score, no supranuclear gaze palsy, no apraxia were the strongest clinical predictors of alpha-synucleinopathies by logistic regression analyses.

*Conclusions:* Our results confirmed that RBD is a strong alpha-synucleinopathies predictor, improving the clinical classification beyond current criteria. Thus, RBD and non-motor symptoms evaluation may help in the differential diagnosis among parkinsonism. The identification of clinical markers for distinguishing the different forms of parkinsonism could drive the discovery of potential disease-modifying therapy.



**Non-motor symptoms profile of PD patients: clinical and genetic aspects**

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*Background:* Non motor symptoms weightily account for Parkinson's disease (PD) severity and progression and impact on quality of life and life expectancy. Neuropathology of non motor-symptoms (NMS) is thought to be related to neurodegeneration on populations of neurons driven by the accumulation of Lewy Bodies and Lewy neurites, with a mechanisms similar to that observed in neurons of Substantia Nigra for the motor symptoms. No biological or genetic marker is currently available for the analysis of risk stratification and progression of NMS in PD. *MAPT* (Microtubule-associated Protein Tau) gene is a well-established risk factor for PD and for cognitive impairment during its course. Recently we have shown that *MAPT* gene is a contributor for the phenotypic expression of PD.

*Objective:* The aim of our study was to evaluate the non motor profile of PD patients according to their clinical characteristics and *MAPT* haplotype.

*Methods:* Sixty-one patient with idiopathic PD were enrolled in the study. Patients were consecutively recruited from a group of 181 patients that were previously genotyped for the presence of H1 homozygosity or the presence of H2 haplotype. Exclusion criteria were: 1. Dementia, according to the Movement Disorders task force criteria for PD-D; 2. Cardiologic or other medical condition that could account for dysautonomia; 3. History of stroke or severe cerebrovascular burden. 4. Age > 80 years. Patient were assessed with NMSS, SCOPA-AUT, NPI, MOCA, EPSS, MOCA and BDI.

*Results:* Disease duration was similar in the IPD and PSP patients studied, while the latter group had higher median Hoehn-Yahr scores. We demonstrated cerebellar metabolic changes, brainstem, cerebellum, cerebellar peduncles, basal ganglia and hemispheric white matter macro- and microstructural alterations in PSP patients compared to IPD. Overall, morphometric biomarkers showed the highest accuracy (>90%) in discriminating PSP from IPD, in particular midbrain area, pons/midbrain areas ratio and MRPI. Other parameters showed a moderate accuracy (70-90%), in particular diffusion parameters in the posterior fossa, brain hemispheres, pre-frontal hemispheric white matter, basal ganglia and superior cerebellar peduncles, volumes of putamen, thalamus, pallidum, nucleus accumbens and lateral ventricles and cerebellar NAA/Cr ratio.

### Parkinson's prevalence in Provincia Autonoma di Trento (2012)

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*Introduction:* Knowing the prevalence of Parkinson Disease (PD) cases is essential for planning health-care, ensuring an adequate service for people with this condition and looking for possible correlation with genetic or environmental factors. A small number of prevalence studies have previously been carried out in various Italian regions over the last two decades.

The aim of this study is to calculate the prevalence and demographic features of patients with PD in the Provincia Autonoma di Trento (PAT) and to compare these data with those of other epidemiological studies on PD already in literature.

*Methods:* We used data from 2012, identifying PD patients from different sources:

- Neurology Unit database
- ICD-IX hospitalization code for Trentino Residents
- Exemption code according to the diagnosis
- Medical drug prescriptions
- Invalidation codes
- Patients living in private or public residential and nursing homes

We collected about 6.000 patients who were compared to remove those present more than once. All cases were individually examined using the provincial informatics system, going back to their clinical history and diagnostic tests. We identified patients with a definite diagnosis of PD according to Gelb's diagnostic criteria. The prevalence of the condition was calculated as the proportion of those who had PD, then stratified by gender, age and geographical district.

*Results:* Based on the record linkage among the different sources we have established 1.244 individual cases of PD for a total number of residents equal to 533.594.

PD prevalence rate in 2012 was calculated for males and females as 233/100.000.

PD prevalence rate is slightly higher among females (246/100.000) than among males (213/100.000).

The highest PD prevalence rate is among those aged 80+years (1803/100.000).

Our study identifies with a high reliability level cases with definite diagnosis of PD, excluding those with atypical or secondary parkinsonism.

**Case report: unusual worsen of gait under high dose continuous Levodopa infusion**

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*Background:* Motor fluctuation and freezing of gait (FOG) are a common complaint in advanced Parkinson disease (PD). Continuous delivery of Levodopa/carbidopa intestinal gel (Duodopa®) through percutaneous jejunal gastrostomy (J-PEG) significantly improves symptoms control, motor fluctuations and Quality of life (QoL) in advanced PD.

We report an unusual motor response during LICG therapy.

*Case report:* A 79 y.o man, diagnosed with PD at age 51. He complained severe motor fluctuation and peak-dose dyskinesia, severe dysphagia (PEG). Still partially autonomous in daily life, able to walk with minimal assistance during the ON state, in OFF gait was severely affected by FOG, start hesitation and postural instability. Cognitively intact. LEDD 1060 mg.

A jejunal tube extension was added to the pre-existing PEG and he was started on Duodopa® with a daily dose equivalent at his previous oral therapy (continuous infusion 2.9 ml/h). Enteral feeding was continued at night.

During next days c.i. was increased up to 4.1 ml/h, with improvement of motor fluctuation and disappearance of the troublesome dyskinesia.

After few days he referred worsening of gait with subcontinuous FOG and inability to walk unassisted, with short benefit from 3 ml extra dose. He refers no symptoms' fluctuation during the day and he described his status as "a very good ON, except for walking".

Continuous infusion was progressively improved up to 6 ml/h. This provided no sensible modification of walking but increased dyskinesia. Infusion speed was then reduced back to 4 ml/h, this leading to reduction of dyskinesia, FOG and postural instability, slight increase of bradykinesia.

*Discussion:* Duodopa improved fluctuation and QoL in our patient, but high dose LCIG, thought improving bradykinesia and rigidity, caused worsen of FOG. Finally the best benefit on motor function and QoL was obtained by intermediate dosage that provided the best balance between bradykinetic/rigid symptoms and gait disturbance.

**Clinical and imaging determinants of Mild Cognitive Impairment in a large cohort of de novo Parkinson's disease patients**

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*Introduction:* Although the cardinal features of Parkinson's disease (PD) are motor symptoms, many PD patients present cognitive impairment and the relationship between dopaminergic denervation and cognitive deficits are not well understood.

*Objective:* To compare the degree of nigro-striatal denervation and motor phenotype in drug-naïve PD patients with and without Mild Cognitive Impairment (MCI).

*Methods:* One hundred and nine consecutive de novo drug naïve PD patients performed baseline SPECT with FP-CIT to assess presynaptic striatal dopaminergic system integrity. Automatic extraction of uptake of the basal ganglia nucleus level was conducted through the BasGan software. Motor symptoms were evaluated by UPDRS part II/III and cognitive state was examined using a large neuropsychological battery. Of the whole population, 21 patients scored 1,5 DS or more below the standard reference, in one or more cognitive domains and were diagnosed as MCI. Mann-Whitney U for statistical analysis was performed.

*Results:* Disease duration was similar in the IPD and PSP patients studied, while the latter group had higher median Hoehn-Yahr scores. We demonstrated cerebellar metabolic changes, brainstem, cerebellum, cerebellar peduncles, basal ganglia and hemispheric white matter macro- and microstructural alterations in PSP patients compared to IPD. Overall, morphometric biomarkers showed the highest accuracy (>90%) in discriminating PSP from IPD, in particular midbrain area, pons/midbrain areas ratio and MRPI. Other parameters showed a moderate accuracy (70-90%), in particular diffusion parameters in the posterior fossa, brain hemispheres, pre-frontal hemispheric white matter, basal ganglia and superior cerebellar peduncles, volumes of putamen, thalamus, pallidum, nucleus accumbens and lateral ventricles and cerebellar NAA/Cr ratio.

*Conclusion:* The study showed that the presence of cognitive impairment in de novo PD patients is associated with lower education and higher axial involvement and rigidity score. Caudate dopaminergic denervation, although greater in patients with MCI, seems to play a minor role with respect to cognitive reserve (as measured by education). Moreover the association of MCI with higher axial motor signs might support the predominant role of non dopaminergic dysfunction in cognitive impairment.

**P30**

**A case-control study on environmental and occupational risk factors in Parkinson's disease**

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*Introduction:* Parkinson's disease (PD) is a progressive neurodegenerative disease. PD tends to recur in the same family more frequently than it would occur by chance. Many epidemiological studies have shown that environmental and occupational exposures tend to recur in the same family and may have a role in determining the familial aggregation of the disease.

*Aims:* The aim of our study was to investigate the role of environmental and occupational risk factor in determining PD by comparing their prevalence among PD patients and healthy controls.

*Methods:* In our study we included 250 consecutive PD outpatients of IRCCS San Raffaele Pisana and 250 controls, similar to the PD group for age ( $\pm 5$  years) and sex. After signing an informed consent, all subjects were administered, by trained investigators, a newly developed questionnaire for investigating risk factors and environmental exposures.

*Results:* The analysis of data showed that the area of residence is not associated with PD, with over 90% of subjects living in an urban area. Regarding the profession, it was found that a higher number of cases had been a farmer, handy worker or craftsman (16% vs 8%, respectively for cases and controls). In our sample smoking habits do not appear to be associated with the disease, with approximately 50% of subjects who have never smoked in both groups. Yet there is a higher proportion of cases that have used substances of abuse (14% vs 3%) compared to controls. An analysis on the dietary habits showed that cases tend to eat vegetables less frequently than controls (65% vs. 78% of daily intake) and deli meats more frequently (14% vs. 6% of daily consumption). A higher number of cases is wine drinker compared to controls (47% vs. 32%).

*Conclusion:* These preliminary results support a role for environmental factors in the etiology of PD.



**P31****Association between nocturnal/supine hypertension and depressive symptoms in elderly patients with Parkinson's disease**

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*Introduction:* Depression is a relatively common condition in persons with Parkinson's disease (PD). Furthermore, non-motor symptoms, including autonomic disturbances, are sources of considerable burden in people with PD, compromising their mood and quality of life.

*Objective:* This study was designed to explore the association between circadian regulation of blood pressure (BP) and depressive symptoms in elderly with PD.

*Methods:* A total of 75 persons with PD were enrolled in the study. The presence of depressive symptoms was assessed via the Geriatric Depression Scale (GDS). Twenty-four hour BP were recorded with ambulatory BP monitoring. In particular, the dipping patterns of nocturnal blood pressure were evaluated.

*Results:* Among 75 patients (mean age  $72 \pm 8$  years, 31% women) the average GDS score was  $4.6 \pm 3.4$ . Average BP dipping was 0.1% for systolic and 2.3% for diastolic pressure, respectively. GDS was negatively correlated with both dipping systolic ( $R = -0.255$ ,  $p = 0.026$ ) and diastolic pressure ( $R = -0.380$ ,  $p = 0.001$ ). The negative association was confirmed by linear regression models adjusted for age, sex and other potential confounders (systolic dipping:  $\beta = -0.275$ , IC 95%:  $-0.136 - -0.012$ ; diastolic dipping:  $\beta = -0.320$ , 95%:  $-0.146 - -0.026$ ).

*Conclusion:* The alterations in dipping patterns of nocturnal BP are negatively associated with depressive symptoms in older persons with PD. The dissection of the pathophysiological determinants (e.g. nigrostriatal system degeneration) underlying this association will be crucial for the development of new therapeutics aimed at improving both the affective disorders and the cardiovascular alterations affecting elderly with PD.

**Apathy in untreated, de novo patients with Parkinson's disease: validation study of Apathy Evaluation Scale**

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*Introduction:* Apathy is a behavioural disturbance occurring alone or in concomitance with depression in Parkinson's Disease (PD).

*Objective:* We present a validation study for the self-report version of the Apathy Evaluation Scale (AES-S) in untreated, drug-naïve PD patients.

*Methods:* A sample of 60 non-demented, non-depressed untreated, drug-naïve, de novo PD patients completed the AES-S and a neurological and cognitive assessment; 20 patients of the sample (33.3%) were classified as apathetic according to current clinical criteria.

*Results:* Mean AES-S score was 34.43. AES-S did not show floor or ceiling effect. Cronbach's alpha was 0.872. Principal component analysis revealed three factors: the first (34.4% of the variance) represented constitutive aspects of the construct of apathy; the second (8.5% of the variance) represented a social dimension; the third factor (7.9% of the variance) represented a dimension related to insight. With respect to clinical criteria for apathy considered as the gold standard, receiver operating characteristics curve analysis showed that a cut-off of 36/37 has the maximum discrimination power. High sensitivity and negative predictive values were obtained with cut-off scores of 33/34 or lower; high specificity and positive predictive values were obtained with cut-off scores of 38/39 or higher. AES-S score correlated with scores on frontal tasks, but not on Beck Depression Inventory, Unified Parkinson's Disease Rating Scale, Hoehn & Yahr scale.

*Conclusion:* The AES-S is a reliable and valid questionnaire for detecting apathy in PD. For screening purposes a 33/34 cut-off score is indicated, but a 38/39 cut-off score is necessary when a high specificity is desired.

**The Study Centre "Lorenzon" and the multidisciplinary approach to Parkinson's disease: a patient-caregiver meeting methodology**

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*Introduction:* Parkinson's disease is a common cause of disability, especially in the elderly. It has been found that the main factors influencing quality of life are depression, disability, postural instability, and cognitive decline. There is a role for non-pharmacological interventions. We offer a multidisciplinary group rehabilitation program for Parkinsonian patients and their care-givers, named "Lorenzon Methodology".

*Objective:* To evaluate the effects on mood, anxiety, empathy and care-giver burden of "Lorenzon Methodology" addressed to patients and their caregivers (hereafter: *caremates*).

*Methods:* Patients and caremates, hosted by the Centro Studi "Achille e Linda Lorenzon", along with the Parkinson Association of Treviso, attend educational lectures about the aspects of this disease and partake a psychological support group and group rehabilitation activities, organized by a multidisciplinary team chaired by a neurologist, a psychiatrist, a physiotherapist and an occupational therapist at the Department of Geriatrics, Neuroscience and Orthopaedics at the Rome "Agostino Gemelli" Hospital. Additional guest specialists are geriatricians, physiatrists and logopedists. This free course consists in 12 two-day monthly meetings. 100 people attended. Patient-caremates couples (N=33) were assessed, at baseline and after six monthly meetings, by Hamilton Depression (HDRS) and Anxiety Rating Scales (HARS), Empathy Quotient (EQ) and Alexithymia Scale (AS). Patients were then assessed by Unified Parkinson's Disease Rating Scale (UPDRS) and Parkinson's Disease Quality of Life Scale [PDQL39]. Caremates were checked by Care-giver Burden Inventory (CBI).

*Results:* Although disease severity as measured by both UPDRS III was unchanged, after six months both depression and empathy improved for almost all the subjects ( $p=0.015$  and  $p<0.001$ ;  $p=0.021$  and  $p<0.001$ , respectively for patients and caremates). Finally, caremates also improved significantly HARS ( $p=0.005$ ) and CBI functional evaluation ( $p<0.001$ ).

*Conclusion:* A multidisciplinary rehabilitation course, answering patients' and caremates' unmet needs, may particularly improve non-motor aspects of the disease comprehension, applying strategies for better mobility, awareness and mutual understanding, prevention of burn-out.



**Non-motor predictors for Levodopa requirement in de novo patients with Parkinson's disease**

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*Background:* The variability in the clinical phenotype of Parkinson's disease suggests the existence of several subtypes of the disease. Motor heterogeneity of Parkinson's disease is well established, but we still miss markers able to identify those patients who are prone to develop a faster disease progression.

*Objective:* We aimed to examine the heterogeneity of PD by attempting to identify baseline non-motor factors highly associated with the rate of motor progression and functional decline, as measured by the time to reach the need of levodopa therapy during the first 4 years from diagnosis in a large cohort of early untreated PD patients.

*Methods:* At baseline, all patients completed the Non-Motor Symptoms Questionnaire (NMSQuest), a validated and recommended tool for detection of NMS in PD. A complete motor evaluation was also performed. For the aim of the current study, patients were declared to have reached the end point when the supervising investigator, on personal evaluation of patients at a scheduled or unscheduled follow-up visit, argued that they had experienced a functional disability that was severe enough to warrant levodopa treatment.

*Results:* The median time to introduction of levodopa for patients with urinary symptoms was significantly shorter than that for those without (20 months vs 37 months;  $p=0.001$ ). Cox regression model showed no influence of such confounders as sex, age, and baseline UPDRS-III, bradykinesia sub-score, and axial sub-score, being Urinary domain independently associated with a higher probability of starting levodopa (HR: 2.1,  $p=0.002$ ). Patients with urinary symptoms had higher baseline and follow-up motor and non-motor disturbances than those without.

*Conclusion:* Our study suggests the existence of a sub-group of patients, who show urinary symptoms along with overall higher motor and non-motor burden. Such patients are prone to manifest a rapid functional decline and shorter time span to require levodopa treatment over the first 4 years of the disease. Urinary symptoms might be a clinical marker of a severe subtype of PD.

## Quantitative gait analysis in Parkin disease

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*Introduction:* Parkin disease is an autosomal recessive early-onset parkinsonism closely resembling idiopathic Parkinson disease (PD); it usually has early onset, slow clinical course and sustained response to levodopa. A peculiar feature of parkin disease is the early occurrence of dystonia that particularly affects the lower limbs [1].

*Objective:* To describe a parkin gait in OFF phase and to compare gait parameters in parkin disease during the OFF and the ON state with those of healthy age-matched control subjects (HS).

*Methods:* A group comparison study was performed in a gait analysis laboratory with integrated optoelectronic system (SMART-D, BTS bioengineering, Italy) of a neurological research institute. Fifteen patients with parkin disease and fifteen healthy aged matched controls were studied. Spatiotemporal, kinematic, and kinetic gait parameters at a self selected speed were recorded during two sessions, in the OFF and ON conditions.

*Results:* The parkin group gait spatial-temporal data showed, compared with controls, both in OFF and ON conditions significant reduction of walking velocity and stride length, increased step width and decreased percentage of double support. In the kinematics, the main features of the parkin group both in OFF and ON conditions were: at the ankle significant increase of dorsiflexion at Initial Contact (IC); at the knee an increased flexion and a greater range of motion during the stance phase; at hip increased flexion and reduced max extension in stance; at pelvis increased mean tilt in antiversión. Kinetics data showed both in OFF and ON conditions increased knee power generation in stance.

*Conclusion:* Parkin patients have a typical gait pattern which is different from HS and PD patients [2,3]. These features are likely related to the dystonic movement component at lower limbs which influences the kinematic more than the dynamic parameters of gait.

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### Chronotype and Parkinson's disease, which link?

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Nighttime sleep disturbances affect up to 90% of Parkinson disease (PD) patients.

The most common sleep disorders in PD include insomnia, REM sleep behavior disorder, sleep apnea, and restless legs syndrome/periodic limb movement disorder. Changes in circadian rhythmicity have been associated with reduced nighttime sleep quality, daytime alertness and cognitive performance. Aim of this study is to define the chronotype of PD patients and the relationship between chronotype, sleep disturbances and clinical features of PD.

274 subjects with PD completed successfully the Morningness Eveningness Questionnaire-short version (MEQ). Each patient, with the help of the caregiver, was also subjected to a brief semi-structured interview in order to investigate the nocturnal sleep quality, the presence of hallucinations and confusional arousals. Moreover, all the patients filled in the Epworth Sleepiness Scale (ESS) and were evaluated with Mini Mental State Examination (MMSE) and UPDRS.

From the MEQ analysis 129 subject resulted "Morning" and 145 "Intermediate" oriented and only 3 subject "Evening" oriented.

Morning oriented subject (age 70.5 ±8.6 years) presented a ESS score 5.45 ±4.24 and MMSE 25.01±4.60.

Intermediated oriented subject (age 71.07 ±10.67 years) presented a ESS score 4.92 ±3.75 and MMSE 24.54±4.16.

The two groups did not differ significantly respect to age, duration of illness, motor impairment (UPDRS) and cognitive function (MMSE).

Within the group of intermediate, 42% of the subjects had visual hallucinations (21.1% compared to the subject of the morning oriented,  $p = 0.007$ ); while 28% had confusional arousals (vs. 8.2% of subjects morning oriented,  $p = 0.005$ ).

The two groups did not show significant differences concerning sleep quality: duration, continuity and quality of nocturnal sleep, daytime sleepiness, presence of respiratory disorders and parasomnias. These preliminary results suggest a possible association between chronotype and presence of visual hallucinations and confusional arousals in subjects with PD.

**P37****Evaluation of motor response in CAPSIT PD: Foot Mechanical Stimulation versus Levodopa**

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Motor fluctuations play a key role in the natural course of Parkinson's Disease (PD), influencing the patients' motor performances and severely worsening their quality of life. In previous studies and in reports by clinicians and patients, foot mechanical stimulation, provided by a mechanical device (GONDOLA®), induced improvements of gait and OFF symptoms.

Aim of this double-blind, randomized study is to evaluate the magnitude of motor response to Foot Mechanical Stimulation, compared to the effect of levodopa treatment, in patients with PD complicated by motor fluctuations.

We enrolled 25 CAPSIT PD patients (age  $62.4 \pm 9.0$  years, Hoehn–Yahr scale 2–4, years from onset  $9.4 \pm 3.3$ ) with ON-OFF response to the treatment with levodopa. The patients were randomly divided into 2 groups, one group (n=15) undergoing a real stimulation (2 minutes long, with a mechanical pressure (0.8 kg/mm<sup>2</sup>) at the big toe tip and at the big toe metatarsal joint on both feet) and the other group (n=10) undergoing sham stimulation, which was indistinguishable from the real stimulation. On day one a clinical evaluation with UPDRS III and a video-taped Sit-Walk-Sit (SWS) were performed at basal condition (OFF therapy, T<sub>0</sub>) and 60 (t<sub>1</sub>), 90 (t<sub>2</sub>), 120 (t<sub>3</sub>), 180 (t<sub>4</sub>) and 360 minutes (t<sub>5</sub>) after the administration of Levodopa. On day two the same evaluations were performed at basal condition (OFF therapy, t<sub>0</sub>) and after real or sham Foot Mechanical Stimulation (t<sub>1</sub>-t<sub>2</sub>-t<sub>3</sub>-t<sub>4</sub>-t<sub>5</sub>).

The UPDRSIII-score improved by an average of 21.76% ( $\pm 11.62$ ) in the patients who underwent real Stimulation, versus 11,2% ( $\pm 2.1$ ) of placebo group. UPDRS III-score improved by an average of 42.35% ( $\pm 14.34$ ) after levodopa challenge. 6 patients with real Stimulation improved UPDRS III by 25% or more in both axial and appendicular symptoms, along with significant improvements in SWS-time.

Foot mechanical stimulation induced a significant improvement of UPDRSIII-score and SWS-time in 6 out of 15 patients, with a recovery time curve similar to the pharmacodynamics response to levodopa. Gondola® seems an encouraging device to treat PD patients showing short term efficacy in this model study. Further studies are needed in order to understand the supposed long term efficacy of the treatment and its physiological basis.

**Apathy and striatal dopamine transporter levels in de-novo, untreated Parkinson's disease patients**

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*Objective:* Apathy is a neuropsychiatric symptom in Parkinson's Disease (PD) which has a negative impact on quality of life and might be related in part to damage of presynaptic dopaminergic system. Little is known about relationship between striatal dopamine levels and apathy in PD patients without dementia and/or depression. The aim of the present study was to investigate the relationship between "pure apathy" and striatal dopamine uptake in untreated, drug-naïve PD patients without clinically significant dementia and/or depression.

*Methods:* Fourteen PD patients with pure apathy and 14 PD patients without apathy, matched for age, side of motor symptoms at onset, motor disability and disease duration, underwent both neuropsychological and behavioural examination including self-rated version of the Apathy Evaluation Scale (AES-S). All patients underwent <sup>123</sup>I-FP-CIT (DaT-SCAN) SPECT to assess dopamine transporter (DAT) striatal uptake.

*Results:* PD patients with apathy showed more reduced DAT levels in the striatum than non-apathetic patients. After Bonferroni correction the difference between groups was significant in the right caudate. In the whole PD sample, correlation analysis revealed a significant negative correlation between AES-S and DAT levels in right caudate and putamen.

*Conclusion:* Apathy is associated with reduced striatal dopamine transporter levels, independent of motor disability and depression in non-demented PD patients. These findings suggest that dysfunction of dopaminergic innervation in the striatum and particularly in the right caudate may contribute to development of apathy in early PD.

**Discipline: a new concept in the global management of Parkinson's disease**

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Parkinson's disease (PD) is a progressive neurodegenerative disorder with predominantly extrapyramidal motor signs such as rest tremor, rigidity, postural imbalance and bradykinesia, but frequent are also non motor signs including anxiety, depression and pain. In some parkinsonian syndromes and in the later stages of PD psychiatric phenomenon especially obsessive-compulsive behaviour are common. Furthermore, clinical aspects of PD are complicated by dopaminergic drugs in terms of motor and non motor complications such as end-dose and peak-dose effects, on-off fluctuations, accentuation of anxiety, depression, pain and insomnia, sometimes driven by dopaminergic drugs used to treat PD. All these factors have to be considered for the treatment of PD which is generally an overall difficult tool and requires a global management including pharmacological, rehabilitative and social-psychological approaches. For these proposals a multidisciplinary team of physicians, neurologists, psychologists, physiotherapists and others has been postulated, but evidently the most burden lies on the caregivers who assist the patient in the daily and nocturnal life.

But what is about the patient? Does he or she has to suffer passively the many inconveniences due to PD and its treatment? Often PD patients do assume a rather passive attitude against all the social and health assistance. What is about his or her rule as family member, job colleague, human being? PD patients have to be assisted in all circumstances?

Obviously, the aforementioned questions might fulfill global management criteria for many other chronic diseases, but neurodegenerative movement disorders have the particular characteristic that responsible participation in daily life activities and also the sensation of usefulness can really represent a form of treatment and may contribute to ameliorate symptoms and perhaps modulate the course of disease. In our opinion applying the right discipline in the global management of PD has to do with improving quality of life.

We will discuss our experiences with patients and caregivers and we will propose a different behaviour codex able to give instructions of how to conduct PD management on both sides.



**Predicting the Freezing of Gait in Parkinson's disease with a smartphone: comparison between two algorithms for detecting FOG**

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*Introduction:* The freezing of gait (FOG) is a common and highly distressing motor symptom of patients with Parkinson's Disease (PD). Effective management of FOG is difficult given its episodic nature, heterogeneous manifestation and limited responsiveness to drug treatment.

We have built a smartphone-based architecture which is able to detect FOG and provide acoustic feedback to the patient.

*Objective:* The aims of this work is to compare the reliability of a real-time FOG detection using two different algorithms.

*Methods:* Two kinds of algorithm are tested:

- Algorithm 1: the first is the same algorithm described by Bächlin (2010);
- Algorithm 2: the second algorithm adds to the Bächlin's (2010) algorithm the computation of the cadence by taking the second component of the power spectrum.

Eighteen patients suffering from PD complicated by FOG (mean age 69.0[SD9.7], years of disease 14.1 [SD4.6], UPDRS Section III 15.5[SD7.7], LEDD 799.7[SD 220]mg, MMSE 26.5[SD 3.2], FAB 12.1[SD 2.9]) were assessed while performing three types of video-recorded Timed Up and Go (TUG) test: the standard one (TUG), TUG with motor dual task (TUGm), TUG with cognitive dual task (TUGc). They always wore the smartphone, during the tests. Video and accelerometer recordings were synchronized.

*Results:* Fourteen (77.78%), out of the 18 enrolled patients, showed at least one freezing episode during the assessment. A total 75 FOG events were recognized by clinicians based on video recordings, while only 1 FOG event was missed by the application. Sensibility and specificity were 74.02% and 85.46%, respectively, for the algorithm 1, rising to 88.31% and 94.72%, respectively, for algorithm 2.

*Conclusion:* Results confirm previous data on the reliability of algorithm 1 [Bachlin '10], while indicating that the evolution of this architecture may identify FOG episodes with higher sensitivity and specificity values.

**P41****Group psychological support for the caregivers of Parkinson's disease patients: our 3-years experience**

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*Introduction:* Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by a variety of motor and non-motor symptoms, producing progressive disability.

Many PD patients are cared for by family members; the burden of caregiving can affect caregiver's health and quality of life, so that PD may become a real family problem. Although caregiver support represents a priority, structured interventions are not enough diffused.

*Objective:* On the basis of these premises we have defined and realized a protocol addressed to the psychological support of PD patients' caregivers, realizing a psychosocial and educational intervention.

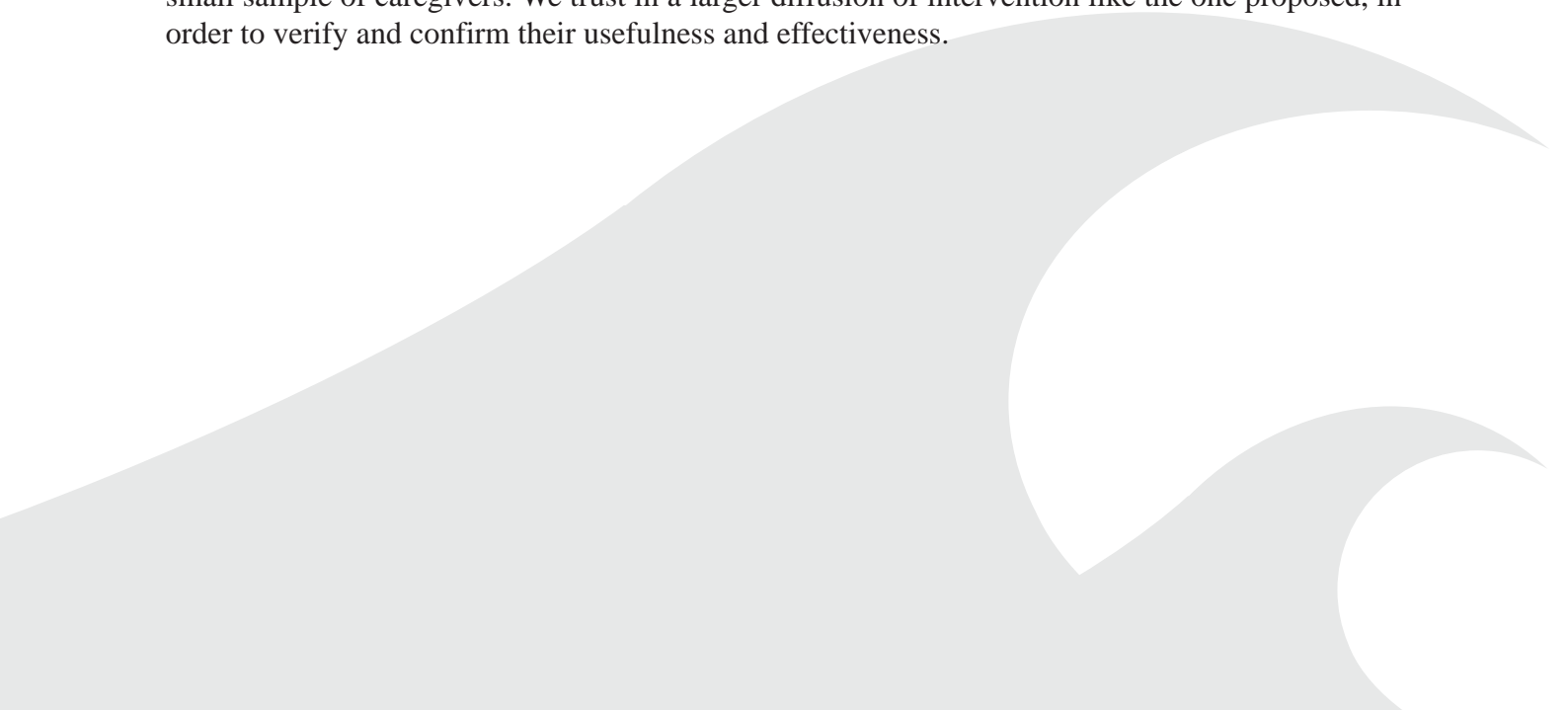
*Methods:* Twelve caregivers have been enrolled to take part in group meetings aimed to educational and psychological support, proposed every 15 days for 3 consecutive years. The meetings were leaded by two Psychologists. The effect and relevance of our intervention has been evaluated using a questionnaire created *ad hoc* and analysing the scores of the Caregiver Burden Inventory (CBI) administered before and after the proposed treatment.

*Results:* Although no statistical significant differences were found analysing the total score of CBI, the statistical analysis of CBI subdomains revealed a significant reduction of the emotional burden ( $p = .031$ ) and a trend toward significance for the social burden ( $p = .076$ ).

The analysis of our *ad hoc* questionnaire highlighted the importance of educational interventions, as psychological aspects of PD and BPSD are not widely recognized.

*Conclusion:* On the basis of our 3-years experience we can state that structured group psycho-educational support for caregivers can be useful in reducing caregiver burden.

Psychological support should follow a comprehensive intervention aimed to describe and explain all the clinical features of PD, so often underestimated. Our data are only preliminar, as based on a small sample of caregivers. We trust in a larger diffusion of intervention like the one proposed, in order to verify and confirm their usefulness and effectiveness.





## Impulse control disorders may herald dementia in Parkinson's disease

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*Introduction:* The most established risk factors for early dementia in Parkinson's Disease (PD) are old age, severity of motor symptoms, mild cognitive impairment and visual hallucinations. Until now, no longitudinal study explored Impulse Control Disorders (ICDs) as possible contributor to development dementia in PD (PDD).

*Objective:* Therefore, the aim of the present 5 year-follow-up study was to investigate the cognitive evolution in PD patients with and without ICDs after five years from baseline assessment.

*Material and Methods:* Forty-five PD non-demented patients with ICDs (ICD+) and 19 non-demented PD patients without ICDs (ICD-) underwent behavioural rating scales and a comprehensive neuropsychological battery to assess memory, frontal/executive functions, visuospatial functions, and attention. After five years (T1), all patients were recalled to be re-evaluated according to the same neuropsychological protocol.

*Results:* At follow up, 16 of 19 PD patients without ICDs and 21 of 45 patients with ICDs at baseline were reevaluated after five years. At T1, dementia was developed by 1 patient belonging to ICD- group and by 9 patients belonging to ICD+ group ( $\chi^2=4.051$ ;  $p=0.044$ ). The binary logistic regression revealed that presence of ICDs and longer disease duration at baseline were independent predictors of PDD over time.

*Conclusion:* While disease duration is recognized as consistent predictive factor, ICDs as contributor to development of dementia have never been investigated. The present findings suggested that ICD and longer PD duration are independent predictive factors of dementia in patients with PD. Thus, early identification of ICDs and evaluation and monitoring of cognitive functions in patients affected by ICDs is relevant in clinical routine practise.

**Heart rate variability shows different profile of cardiovascular dysautonomia in Parkinson's disease patients with tremor dominant compared to akinetic rigid dominant subtype**

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*Background:* Parkinson's disease (PD) can present with different subtypes of motor impairment according to the predominant symptoms (tremor or rigidity/bradykinesia). Tremor-dominant patients show a slower progression of the disease and less cognitive decline, confirmed by neuroimaging and pathologic findings which describe a more favorable outcome in tremor-dominant patients than in akinetic-rigid subjects. Autonomic cardiovascular disorders have been associated with variable manifestations in patients affected by PD, although the definite correlations with different subtypes of PD is not clear. In this context, Heart Rate Variability (HRV) analysis represents a not invasive and established tool in assessing cardiovascular autonomic dysfunction.

*Objective:* To investigate cardiovascular autonomic function in PD patients with tremor dominant subtype in comparison to akinetic rigid dominant subtype, and compared with normal subjects using HRV analysis.

*Methods:* Twenty-eight consecutive PD patients (17 with tremor dominant subtype and 11 with akinetic rigid dominant subtype) were enrolled and compared to seventeen age and sex-matched healthy controls. The following parameters were assessed: standard deviation of RR intervals (SDNN), root mean square of the successive differences of RR intervals (RMSSD), total power (TP), low frequency power (LF), high frequency power (HF).

*Results:* We found that LF values were significantly lower in the akinetic rigid dominant subtype than in the control tremor dominant group [LF  $41.4 \pm 13.6$  versus  $55.5 \pm 11.6$  ( $p < 0.007$ )], indicating that the disease led to a more evident impairment of the baroreflex modulation of the autonomic outflow mediated by both sympathetic and parasympathetic systems in the first class of patients.

*Conclusion:* These findings support the biological relevance of clinical subtypes supporting the idea of a possible different stage of pathophysiological process between these subtypes. These differences suggest that different subtypes may also result in different responses to therapy or in the possible development of cardiovascular side effects of dopaminergic drugs in these different population.

**Neuropathy in Parkinson Disease: what we are dealing with?**

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*Background:* Peripheral neuropathies are thought to be prevalent among patients with Parkinson disease (PD), and potentially related to motor disability in this population. However, some important questions remain open, mainly due to some methodological limitations.

*Objective:* Assess the prevalence distal symmetric polyneuropathy (DSP) in PD patients on chronic levodopa exposure on basis of neurophysiological criteria.

*Methods:* We consecutively enrolled 41 patients with diagnosis of PD according to UKBB criteria. Patients with history of other illnesses that potentially present an involvement of peripheral nervous system (PNS) were excluded. All participants underwent a detailed clinical evaluation (including the assess of non-motor symptoms with NMSS). Moreover, laboratory screening tests for neuropathy were performed. We determined serum vitamin B12, folate and homocysteine levels for all patients involved in the study. An extensive nerve conduction studies were performed in all patients using standard laboratory techniques. As control group for neurophysiological findings we evaluated 43 age and gender matched healthy subject.

*Results:* Although we observed a relative depression of sensorial potential amplitude (without statically significant differences), applying stringent neurophysiological criteria for chronic axonal neuropathy only two PD patients fulfilled the diagnosis of DSP. Moreover, NMSS was the only variable that showed a statistically significant correlation with sensory nerve action potentials (Sural Nerve Amplitude,  $R = -0.64$ ;  $p < 0.05$ ) in the whole cohort.

*Discussion:* In our study emerges a much lower prevalence of DSP in PD patients than previously reported. These findings rise the question of reliability of clinical criteria for neuropathy in PD. Indeed, the malady is characterized per se by an altered codifying of sensorial stimuli, that could lead to an overestimation of symptoms mistakenly attributed to a PNS dysfunction. Therefore, it should be defined the significance of PNS clinical signs and subtle depression of nerve action potentials, and discerned from that observed in a frank neuropathy.

**Mild Cognitive Impairment in Parkinson Disease: evaluation of cerebrovascular reactivity by Transcranial Doppler**

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*Background:* Cerebrovascular reserve has emerged as a potential biomarker for monitoring pressure–perfusion–cognition relationships. Cerebrovascular reactivity (CVR) is the change in cerebral blood flow in response to a vasodilatory or vasoconstrictive stimulus. Substantial evidence exists that supports a link between CVR and cognition, a relationship that may be mediated by impairment of vascular reserve and microvascular disease.

*Aim of study:* Explore cerebral vasoreactivity by transcranial Doppler in Parkinson Disease (PD) with Mild Cognitive Impairment.

*Methods:* Twelve PD patients classified as Mild Cognitive Impairment (PD-MCI) were matched with 12 PD patients control (PD-Ctrl). All participants underwent a detailed clinical, neuropsychological and ultrasonographic evaluation. Vasomotor reactivity was assessed with the Breath Holding Index (BHI) by transcranial Doppler Ultrasonography. Moreover, cerebral white matter hyperintensities (WMH) were quantified in all patients with the use of a semiquantitative visual rating method derived from T2-Flair weighted MRI.

*Results:* As expected from the matching procedure the patient groups did not significantly differ for age, disease severity and duration and Levodopa Equivalent Dose. While did not emerge significant difference in the extent of structural changes in cerebral microcirculation explored with WMHs burden (CHS: PD-MCI vs PD-Ctrl  $2,58 \pm 0.9$  vs  $2,33 \pm 1,0$ ) or in ultrasound parameters, a statistically significant lower response to hypercapnia was observed in the PD-MCI as compared with PD-Ctrl both in middle cerebral artery (BHI-MCA: PD-MCI vs PD-Ctrl  $1,07 \pm 0.28$  vs  $1,60 \pm 0.54$ ,  $p < 0.01$ ) and in posterior cerebral artery (BHI-PCA: PD-MCI vs PD-Ctrl  $0.60 \pm 0.34$  vs  $1,08 \pm 0.61$ ,  $p < 0.05$ ).

*Discussion:* These data suggest an impaired cerebrovascular reactivity without evidence of significant difference in microcirculation damage in patients with PD-MCI. Although the causes of a reduced CVR remain a subject for debate, these findings may support the hypothesis that a reduced metabolic activity primarily related to neurodegeneration can lead to a negative modulator effect on neurovascular homeostasis.

### **Cognitive Decline in Parkinson Disease: simply a non-linear process**

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*Background:* In the past few years the field of Parkinson discognition has enriched with the definition of clinical and "diagnostic" criteria for PDD and PD-MCI; thereafter, a number of studies assessed the rate of evolution of cognitive impairment in selected cohorts of patients and proposed models of progression, psychometric tools and prognostic features. Despite the construct that PD patients, following a phase of predementia state, ineluctably develop a frank dementia, recently some authors have objected this linear model (Burn DJ, Korkzyn AD).

*Objective:* Evaluate the prognostic significance of clinical and psychometric criteria of PD-MCI and their correlation with clinical and demographic characteristics in a cohort of PD patients.

*Methods:* Seventy-six consecutively recruited patients with idiopathic PD according to UKBB criteria were assessed with a comprehensive battery of neuropsychological tests from 2008 to 2009 and re-evaluated after 5 years. No other inclusion or exclusion criteria was initially applied in order to resemble a real-life setting. UPDRS III, axial score, total levodopa equivalent intake, use of antipsychotics and cognition enhancer drugs were recorded.

*Results:* Fifty-three subject of 76 initially enrolled (6 patients died before the second phase of the study, 8 are now bedridden or institutionalized, 9 patients refused the study) completed the follow-up phase. Our results indicate that, when extensive neuropsychological battery is administered to an unselected cohort of patients, the evolution of discognitive pattern was non-linear and that baseline demographic and clinical variables (age at onset, motor disease severity, axial score, cognitive deficits at baseline) impact the progression of cognitive impairment. Therefore, the "stratification" for assessing the dementia risk in PD represent a necessary approach to enhance the accuracy and prognostic significance of current psychometric tools.



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**Presence and severity of apathy in Parkinson's disease patients and correlation with motor and other non-motor symptoms**

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*Objective:* Although traditionally considered as a motor disorder characterized by the triad of resting tremor, rigidity, and bradykinesia, Parkinson's disease (PD) is often characterized by non-motor symptoms (NMS). The aim of this study was to examine the presence and severity of apathy in a population of PD patients and to assess whether apathy may be correlated with motor and other NMS.

*Methods:* Ninety-six PD outpatients from the Movement Disorders Center of the University of Cagliari were included in the study. The 96 PD patients included 56 men and 40 women. The Apathy Scale was used to assess apathy. NMS were assessed with the NMS Scale (NMSS). Stage of the disease and motor disability were assessed using the Modified Hoehn & Yahr (HY) staging and the UPDRS part-III and IV.

*Results:* According to the cut-off value of 14 for apathy score, apathy was present in 45 patients (46.9%). HY score was significantly higher in PD patients with apathy ( $p < 0.041$ ). Apathy score was significantly higher in female patients ( $p < 0.041$ ). Among NMS, excluding the NMSS item 8, apathy score was strongest correlated with lost interest in surroundings ( $p < .001$ ), flat mood ( $p < .001$ ), sadness ( $p < .001$ ), anhedonia ( $p < .001$ ), and fatigue ( $p < .001$ ).

*Discussion:* Apathy represents one of the most common behavioural and psychiatric disorder associated with PD. We identified a relationship between higher disability severity and apathy in PD subjects suggesting that apathy may represent a sign of disease progression. A significant relationship between depressive symptoms/fatigue and apathy was identified, although in previous studies the association between apathy and depression in PD has been described as variable.

*Conclusion:* In conclusion, our study confirmed as apathy represents a common symptom in PD patients, correlating the evaluation of apathy with NMS assessed by the NMSS. A significant higher severity of apathy related to severity of affective non-motor symptoms was observed. The assessment of these symptoms with the administration of holistic evaluation scales such as the NMSS might improve the individuation of these disabling disorders.

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**Metabolic changes in de novo Parkinson's disease after dopaminergic therapy: a proton magnetic resonance spectroscopy study***Silvia Marino*<sup>1,2</sup>, *R. Ciurleo*<sup>1</sup>, *L. Bonanno*<sup>1</sup>, *P. Bramanti*<sup>1</sup>, *G. Di Lorenzo*<sup>1</sup><sup>1</sup>IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy<sup>2</sup>Department of Biomedical Sciences and Morphological and Functional Imaging, University of Messina, Messina, Italy

*Introduction:* Neuroimaging techniques are beginning to play a greater role in monitoring treatment effects in PD. Currently, the main role of Proton Magnetic Resonance Spectroscopy (<sup>1</sup>H-MRS) in PD is the differentiation of PD from other parkinsonisms. Moreover, in recent years, the ability of <sup>1</sup>H-MRS to detect treatment effects in PD and to perform an objective outcome measure is being investigated.

*Objective:* To assess metabolic changes in the motor cortex in de novo PD patients before and after therapy with ropinirole.

*Materials and Methods:* Twenty de novo drug-naïve PD patients (mean Unified Parkinson Disease Rating Scale (UPDRS) motor sub-score =  $22 \pm 3.7$ ) and 15 age and sex-matched healthy controls underwent conventional Magnetic Resonance Imaging and <sup>1</sup>H-MRSI. The resonance intensities of N-acetylaspartate (NAA) and Choline (Cho) were normalized for the resonance intensities of Creatine (Cr). Ten months after ropinirole treatment, the patients repeated clinical and <sup>1</sup>H-MRSI evaluation.

*Results:* At baseline, lower NAA/Cr and NAA/Cho ratios and higher Cho/Cr ratios were found in the motor cortex of PD patients compared with controls ( $p < 0.001$ ). Ten months after ropinirole treatment, PD patients showed a significant clinical improvement in the UPDRS motor sub-scores ( $p < 0.001$ ) and an increase of NAA/Cr and NAA/Cho ratios ( $p < 0.006$  and  $p < 0.01$ , respectively). A highly significant correlation between NAA/Cr and NAA/Cho ratios and UPDRS motor sub-scores was observed ( $r = -0.946$  and  $r = -0.951$ , respectively).

*Conclusion:* The low NAA and high Cho levels in motor cortex of de novo drug-naïve PD patients could indicate not only the presence of cortical dysfunctions but also an early neuroinflammatory condition. We could argue that the ropinirole efficacy to improve the motor performances is the result of partial restoration of neuronal functions, which in turn may increase the NAA levels in the motor cortex.

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**Striatal  $^{123}\text{I}$ FP-CIT SPECT in current- and never-smoking patients with Parkinson's disease**

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*Background:* Epidemiological evidence suggests that cigarette smoking may reduce the risk of Parkinson's disease (PD). Preliminary in vitro and in vivo studies on non-parkinsonian subjects showed that smoking affects dopamine transporter functioning and availability in the striatum.

*Methods:* We performed striatal  $^{123}\text{I}$ FP-CIT single photon emission computed tomography in 58 PD patients and 15 healthy individuals of similar age ( $60.4 \pm 10.2$  vs.  $61.2 \pm 10.4$ ,  $p=0.4$ ) and sex (30 women and 28 men vs. 6 women and 9 men,  $p=0.3$ ).  $^{123}\text{I}$ FP-CIT uptake was averaged over both hemispheres.

*Results:*  $^{123}\text{I}$ FP-CIT caudate and putamen uptake in PD patients were significantly lower than in controls. PD patients included 46 never-smokers and 12 current-smokers, staging  $1.8 \pm 0.5$  on the Hoehn and Yahr (HY) scale. The two groups did not differ for age, disease duration, HY staging, and levodopa equivalent dose, whereas men predominated in current-smokers group. UPDRS total motor score was lower in current-smokers than in never-smokers ( $16.9 \pm 9.2$  vs.  $21.8 \pm 9.5$ ,  $p=0.06$ ). As compared to never-smokers, current smokers showed slightly lower  $^{123}\text{I}$ FP-CIT uptake in both caudate ( $3.3 \pm 0.5$  vs.  $3.7 \pm 0.7$ ,  $p=0.06$ ) and putamen ( $2.4 \pm 0.4$  vs.  $2.6 \pm 0.4$ ,  $p=0.02$ ). Logistic regression analysis adjusted for relevant demographical/clinical variables confirmed a significant lower  $^{123}\text{I}$ FP-CIT uptake in both putamen (OR, 0.1; 95% CI, 0.01 to 0.71,  $p=0.02$ ) and caudate (OR, 0.2, 95% CI, 0.05 to 0.86,  $p=0.03$ ) of current-smokers.

*Conclusion:* Our findings does not support a protective effect of smoking on dopamine neurons in PD. Rather, the lower  $^{123}\text{I}$ FP-CIT uptake and the lower UPDRS total motor score observed in our PD smokers would support a symptomatic effect of smoking on PD motor signs.



## White matter microstructural damage and cognitive impairment in Parkinson's disease

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*Introduction:* Cognitive deficits are common in Parkinson's disease (PD) and can occur even in the early stages. Cognitive deficits in PD usually involve executive functions causing a "frontal-type dysfunction" and can result in a mild cognitive impairment (MCI) or dementia.

*Objective:* The aim of this study was to investigate white matter microstructural damage and its relationship with cognitive impairment in a large population of patients with PD at different disease stages.

*Methods:* We enrolled 168 PD patients (105 without cognitive impairment [PD-ncog]; 48 MCI [PD-MCI] and 15 with dementia [PD-DEM]), and 41 matched healthy controls (HC). PD patients and controls underwent a complete clinical and neuropsychological evaluation. Tract-based spatial statistics (TBSS) was used to perform a brain voxel-wise analysis of fractional anisotropy (FA) and mean diffusivity (MD), adjusted for subject's age. Patient groups were compared with controls and between each other.

*Results:* All PD patients relative to HC showed decreased FA and increased MD in the splenium of corpus callosum, right frontal white matter and right internal capsule. In PD-MCI relative to HC, microstructural white matter damage spreads to more anterior regions of the corpus callosum, bilateral frontal white matter, anterior temporal white matter and parietal white matter. White matter microstructural damage further increased in severity in PD-DEM, involving the majority of frontal and parietal white matter tracts. When patients groups were compared between each other, PD-DEM showed significant alterations in the body of corpus callosum compared to PD-ncog. There were no significant differences in DT MRI metrics when PD-DEM were compared to PD-MCI cases.

*Conclusion:* Assessing white microstructural alterations in PD patients with cognitive impairment brings important highlights to the understanding of the relationship between PD pathology and changes in cognition.

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**Brain structural and functional abnormalities in Parkinson's disease patients with freezing of gait**

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*Introduction:* Freezing of gait (FoG) is a disorder often associated with Parkinson's disease (PD). Few studies so far have investigated the neural correlates of FoG in PD, suggesting an altered fronto-parietal connectivity in these patients.

*Objective:* The aim of this study is to assess brain functional and structural alterations in PD patients with FoG (PD-FoG).

*Methods:* T1-weighted, diffusion tensor (DT) MRI and resting state (RS) fMRI were obtained from 22 PD-FoG patients and 36 healthy controls. Patients underwent clinical (FoG Questionnaire and UPDRS-III), motor functional (Time-Up-and-GO and Berg Balance Scale), and neuropsychological evaluations. Gray matter (GM) volumes were assessed using Voxel Based Morphometry. White matter (WM) damage was assessed using Tract-Based Spatial Statistics. RS fMRI data were analyzed using a model free (MELODIC) approach investigating the main sensorimotor and cognitive brain networks. The relationships between MRI findings and clinical/cognitive variables were assessed.

*Results:* Compared to controls, patients performed lower in tests assessing executive, visuospatial and verbal learning functions. No GM atrophy was found in PD-FoG patients relative to controls. Compared with controls, they showed WM damage in the entire corpus callosum and cingulum, WM underneath the frontal, parietal and occipital cortices and corticospinal tracts, bilaterally. RS fMRI analysis showed that PD-FoG is associated with a decreased functional connectivity of the following regions: superior frontal gyrus and precuneus bilaterally within the default mode network; bilateral insula, right middle cingulum, left thalamus and putamen within the ventral attentional network; left cerebellum within the right fronto-parietal network; left inferior occipital gyrus within the visual-associative network. More severe motor disability and lower cognitive scores were associated with greater WM damage and reduced functional connectivity.

*Conclusion:* This study supports the theory of FoG as the result of a poor integration between motor programming, visuo-spatial and attentional abilities.

*Funding:* Jacques and Gloria Gossweiler Foundation.

## MRI Diagnosis of Parkinson's disease: comparison of 3T and 7T SWAN Imaging of the Substantia Nigra

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*Introduction:* Seven Tesla MR target imaging of the Substantia Nigra (SN) with susceptibility weighted imaging has been demonstrated to be useful in diagnosing Parkinson's Disease (PD) [1]. Since the neuroimaging-based diagnosis of PD could be a support to the clinical diagnosis, the role of susceptibility weighted imaging should be evaluated in clinical MR scanner at 3T [2,3].

*Objective:* To evaluate if Susceptibility Weighted ANgiography (SWAN) images allows a PD diagnosis with a 3T scanner.

*Methods:* We performed a comparative study with a case-control design that prospectively evaluates the diagnostic accuracy of SWAN at 3T and 7T. Fourteen PD patients and 13 healthy subjects underwent MR examination at both 3T and 7T by using Susceptibility Weighted Angiography sequence.

Two expert blinded observers evaluated the 3T and 7T images of the sample to identify SN abnormality indicative of PD. Diagnostic accuracy, intra and inter-observer agreement were calculated separately for 3T and 7T acquisitions.

*Results:* SWAN 7T-MRI allows a Parkinson's Disease diagnosis with a mean sensitivity of 93%, specificity of 100% and diagnostic accuracy of 96%. Three Tesla MRI supported a diagnosis of Parkinson's Disease with a mean sensitivity of 79%, specificity of 94% and diagnostic accuracy of 86%. Intra-observer agreement and inter-observer agreement were excellent at 7T. At 3T intra-observer agreement was excellent for experts and inter-observer agreement ranged between good and excellent.

*Conclusion:* SWAN images obtained both at 3T and 7T are able to differentiate healthy subjects from PD patients, with a higher diagnostic accuracy at 7T. The use of 3T-MR clinical scanner in parkinsonian patients is useful and the diagnostic accuracy is competitive with that reported by the clinical and nuclear medicine observations.

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## Telemedicine and Parkinson's disease

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Telemedicine is a widely accepted tool, utilized in many branches of medical care. Thanks to information technology progress and diffusion, important cardiological data for example, have been transferred since many years through Telecommunication devices.

Based on the peculiar features of neurological consultation in parkinsonian patients, we sought to verify the feasibility of follow-up outpatient consultations through a video-connection. The first contact between patient and physician on the contrary should remain a direct one.

The aim of this study is to realize a web-based platform to interconnect a group of neurologists trained in Movement Disorders Clinic with their patients. In order to realize the tele-consultation, patients should check on the platform calendar the doctors' availabilities and choose the one suitable for them. In so doing they fix a meeting time at which both Neurologist and Patient will connect to Internet establishing a web-based medical contact.

In this first step the protocol will be limited to those patients who are resident in the Puglia Region. This should allow a more frequent follow up, eventually saving time and money for patients' and caregivers' transportation, a tight control on compliance to therapy, etc. Moreover we forecast a reduction of hospitalizations for PD patients.

Our model includes the video-recording facility, allowing the collection of a library of UPDRS III videoclips. Patients' information will be stored in the respect of the Italian laws on Privacy and the whole program is designed to fit with the Neurological Regional Network which is currently being built.



**Diagnostic use of transcranial B-mode sonography in Parkinson's disease and parkinsonism: an experience on over 260 cases**

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*Background:* Transcranial B-mode sonography (TCS) to assess brainstem has become an important tool for the diagnosis of movement disorders. Although substantia nigra (SN) hyperechogenicity can be found in more than 90% of idiopathic Parkinson's disease (IPD) patients, it is very rarely found in patients with atypical parkinsonism.

*Purpose:* The aim was to evaluate the effectiveness of TCS in diagnosis of IPD and parkinsonism. TCS was performed in 265 patients. Sixty patients were without insonation area. 205 patients was considered: seventy-eight patients (38%) had a clinical diagnosis of IPD; 33 patients (16%) had parkinsonism, of which 8 multiple system atrophy (MSA), 11 progressive supranuclear palsy (PSP), 1 corticobasal degeneration, 13 are in diagnostic phase. Thirty-six had an essential tremor (17.5%). Eighteen patients had a secondary parkinsonism, of which 5 vascular parkinsonism.

*Results:* In 64 patients with IPD (82%), in 6 patients with atypical parkinsonism (18%) TCS showed an increased SN hyperechogenicity. Sensitivity of TCS was of 82% in both cases.

*Conclusion:* Although the limitation due to the bone window, TCS represents a non invasive and available approach and it provides informations about the morphology of the brain for refinement of the diagnosis of several movement disorders.

**Interaction between Cerebello-thalamo-cortical circuits and basal ganglia in Parkinson's disease patients with bilaterally implanted deep brain stimulating electrodes into Subthalamic Nuclei**

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*Introduction:* In Parkinson's disease (PD), Deep brain stimulation (DBS) of the Subthalamic Nucleus (STN) represents an effective therapy, through mechanisms still largely unexplored. It is of interest to understand whether STN-DBS exerts peculiar effects (different from levodopa) on cortico-mediated plasticity. Using a combined Transcranial Magnetic Stimulation (TMS)/EEG approach we explored the effects of cerebellar cTBS over cortical activity in PD patients manifesting a beneficial response to STN-DBS.

*Methods:* Eight PD patients under STN-DBS (surgical procedure ended at least 1 year before) were tested in 3 conditions, on distinct days: 1. Ther-On/Stim-On (2 h after the first daily dose of standard medication); 2. Ther-Off/Stim-On (after overnight therapy withdrawal); 3. Ther-Off /Stim-Off (as in condition 2 but the stimulus was switched Off 90' in advance). Motor performances were evaluated by UPDRS part III. In each condition, before and after cerebellar cTBS, 80 single pulse TMS were delivered over M1, contralateral to the clinically more affected side while acquiring EEG. Event-related desynchronization/synchronization was than calculated for theta (4-7Hz), alpha (8-12Hz) and beta (13-30Hz) band.

*Results:* During On-On condition, TMS induced a higher beta synchronization when compared to all other conditions ( $p=0.006$ ) and Off-OFF condition was associated with lower level of beta. cTBS promoted an increased beta synchronization regardless the condition ( $p<0.05$ ), boosting the beta level of Off-On and Off-OFF conditions to the On-ON induced level. All effects were restricted to the closest electrode to M1.

*Conclusion:* The increase of beta level after cTBS suggests a plausible interaction between CTC and basal ganglia circuits. On-going analysis aims at clarifying specific effects of each therapeutic option.

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**Writer's cramp primary dystonia shows brain gray and white matter alterations: a multimodal imaging study**

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*Introduction:* The traditional view commonly holds that dystonia is a disorder of basal ganglia-controlled motor circuits. However, several recent neuroimaging studies showed cortical thickening as well as white matter (WM) damage in sensorimotor as well as extra-sensorimotor regions, suggesting a complex network dysfunction playing a role in the development of dystonia.

*Objective:* This study is aimed at investigating the cortical gray matter (GM) and WM patterns of alterations characterizing Writer's Cramp (WC) primary dystonia in comparison with healthy controls.

*Methods:* 1.5 Tesla T1-weighted and diffusion tensor (DT) MRI scans were obtained from 19 right hand-affected patients with WC, and 30 matched healthy controls. Cortical thickness, surface area and volume measures were analyzed using both a 'vertex wise' and a 'region-wise' comparison with Freesurfer. Tract-based spatial statistics (TBSS) was used to perform a brain voxel-wise analysis of fractional anisotropy and mean (MD), axial (axD) and radial (radD) diffusivity metrics. The effects of disease severity were examined by correlating cortical metrics and DT MRI with disease duration and WC severity scales (p value <0.05).

*Results:* Increases in cortical thickness, area and volume metrics were found bilaterally in paracentral gyrus, postcentral gyrus, as well as supramarginal gyrus and temporooccipital gyrus in WC patients compared with controls. Compared to controls, WC showed increased MD, axD and radD in the corpus callosum and thalamic radiations bilaterally, and in the right corticospinal tracts and right major associative tracts. Cortical measures did not correlated with clinical data. WCRS score correlated with increased radD in the corpus callosum and left cingulum bundle.

*Conclusion:* These findings corroborate the hypothesis that WC dystonia is a complex disturbance which results from the involvement of several neural circuits. Advanced MRI techniques may give insight in the pathophysiology of this multifaceted disease.

## Does STN stimulation influence Theory of Mind?

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*Introduction:* Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective surgical treatment of motor symptoms in Parkinson's disease. Theory of Mind (ToM) refers to ability to infer other people's thoughts, intentions or emotions in social situation. The effect of the stimulation on social cognition is controversial.

*Objective:* The aim of the present study is to analyze the effect of STN-DBS on ToM.

*Methods:* Participants included 11 PD patients with STN DBS tested in two condition: with stimulator turned on in on medication (ON condition) and after 1 hours of stimulator turned off in on medication (OFF condition); 9 healthy controls (HC), matched for age and education. All participants were administered tests to assess cognitive and affective ToM abilities; in particular we use 5 different ToM tasks: Perception of faces expression (KDEF) and Verbal Emotion test ("affective" tasks) and Faux Pas, Bush test and Strange Stories ("cognitive" tasks).

*Results:* We observed that patients in "ON" condition have significant worse performances in Bush test ( $p=0.03$ ) and in Faux pas ( $p=0.047$ ) compared to HC, whereas no differences were found in these tasks between "OFF" condition and HC; we also found significant impairment ( $p=0.04$ ) in "ON" condition compared to "OFF" condition in Stranges Stories. We failed to find significant differences in Verbal Emotion test and in KDEF between both "ON" and "OFF" conditions and HC.

*Conclusion:* Our study reported a worse performance on ToM specific tasks in PD patient in "ON" condition with respect to "OFF" condition and/or HC, thus supporting the hypothesis of a possible role of STN stimulation in ToM. Therefore the evidence of a predominant cognitive task impairment in "ON" condition suggests a possible different effect on cortical connections subserving the ToM substrates.



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**Cerebrospinal fluid Tau levels correlate with motor progression, but not cognitive status, in PD patients***Enrica Olivola*<sup>1</sup>, *M. Stampanoni Bassi*<sup>1</sup>, *P. Imbriani*<sup>1</sup>, *M. Pierantozzi*<sup>1</sup>, *A. Stefani*<sup>1,2</sup><sup>1</sup>Department of Systems Medicine c/o Movement Disorder Centre, University of Tor Vergata, Rome, Italy<sup>2</sup>IRCCS Fondazione S. Lucia, Rome, Italy

*Introduction:* Increasing interest is focused on cerebrospinal fluid (CSF) biomarkers that can be associated with motor and non-motor progression in Parkinson's Disease (PD) [1,2].

*Objective:* To assess CSF  $\beta$ -amyloid 42 (AB42), total-tau (t-tau), phosphorylated-tau (p-tau) levels and blood-brain barrier index (BBB) in PD. Methods: CSF was obtained from 76 PD patients and 24 age-matched control subjects. All patients underwent clinical examination, blood analysis, cognitive assessment by MMSE and lumbar puncture. Severity of motor symptoms in PD was assessed with UPDRS part III and H&Y scale.

*Results:* AB42 CSF levels were significantly decreased in PD patients compared to controls ( $p=0.0007$ ). Although without a statistical significance, t-tau levels were lower in PD compared to control subjects. P-tau did not differ between groups. CSF t-tau positively correlated with p-tau levels in all study groups (in PD  $r=0,76$ ; in controls  $r=0.66$ ). CSF t-tau and p-tau levels correlated with age, achieving statistical significance in PD patients (t-tau  $r=0,34$ ; p-tau  $r=0.40$ ). None of the CSF protein levels correlated with cognitive status. A weak correlation links t-tau to UPDRS part III ( $r=0,25$ ,  $p=0,02$ ) and BBB index ( $r=0.28$   $p=0.01$ ). No correlation linked AB42 to UPDRS part III. By stratification data by H&Y scale, we observed significant difference between stage 1 and stage 3, concerning BBB index ( $p=0.05$ ), t-tau ( $p=0.01$ ) and, as expected, UPDRS part III ( $p=0.0000$ ).

*Conclusion:* Our data support the contention that tau participate to PD motor advancing, not amyloid, as expectable. We failed to detect any correlation between cognitive functions and CSF biomarkers. CSF tau, thought to be a marker of neuronal death, is increased in advanced PD and in combination of altered BBB, suggesting increased neuronal degeneration with motor progression. Our results highlight that biomarker changes precede cognitive decline and that CSF tau levels, according to previous studies, is a marker of neuro-degeneration in PD [3].

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P59

## Serotonin impairment in CSF of PD patients without an apparent clinical counterpart

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*Introduction:* In Parkinson's disease (PD), several studies have detected an impaired serotonin (5-HT) pathway, likely affecting both motor and non-motor domains. However, the influence exerted by 5-HT impairment in PD remains unclear.

*Objective:* To determine cerebrospinal fluid (CSF) concentration of 5-HT and its main metabolite 5-HIAA in a cohort of PD patients.

*Materials and Methods:* We used a HPLC chromatographic method to assess the concentration of 5-HT and 5-HIAA in CSF obtained from lumbar puncture (LP) in a homogenous cohort (n=35) of PD patients. A control group, with other neurological disorders (OND, n=18), and a cohort of Alzheimer's Disease (AD, n=20) patients were included in the study. In PD and control group exclusion criteria were: cognitive impairment (MMSE<24), systemic diseases and serotonergic medications. In PD, LP was performed following three days of therapy withdrawal, to vanish the effects of prolonged released dopamine agonists. Clinical motor impairment was quantified by the Unified Parkinson's Disease Rating Scale part III (UPDRS-III). Depression was assessed through the Beck Depression Inventory, apathy through the Apathy Evaluation Scale and nocturnal sleep disturbances by the Pittsburgh Sleep Quality Index.

*Results:* The PD group showed significantly reduced CSF levels of both 5-HT and 5-HIAA compared to control subjects (p=0.015 and p=0.002) or AD patients (p=0.02 and p=0.001). However, no correlation emerged between 5-HT/5-HIAA concentrations and UPDRS-III (r=-0.12), disease duration (r=-0.1), age (r=-0.27) and MMSE (r=0.11). Further, low CSF 5-HT levels did not differ for gender or motor phenotype (i.e. non-tremor/tremor dominant subtype) and did not correlate with the presence of depression, apathy or sleep disturbance.

*Conclusion:* 5-HT impairment is a cardinal feature of stable PD, probably representing a hallmark of diffuse Lewy bodies deposition in the brainstem. However, clinical relevance remains uncertain. Given these findings, an add-on therapy with serotonergic agents seems questionable in PD, or should be individually tailored, unless severe depression is present.

**P60****Low Frequency Transcranial Magnetic Stimulation with H-coil for Levodopa-induced dyskinesias in Parkinson's disease: an open label pilot study**

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*Background:* Repetitive transcranial magnetic stimulation has been proposed as a potential treatment for Parkinson's disease. H-coils, inducing deeper and wider magnetic fields characterized by widespread and bilateral involvement of cortico-subcortical circuits, may be potentially useful in PD. LID are severe motor complication in advanced PD patients. The neural mechanisms involved in LID are not clear, and it is apparent that both an excessive decrease in internal pallidus firing and a modification and overactivation of cortical motor and premotor areas are involved in its pathogenesis.

*Objective:* To determine whether low-frequency deep-TMS over primary motor (M1) and prefrontal regions (PF) may ameliorate LID in PD patients.

*Methods:* 15 non demented (MoCa score >24) PD patients suffering from peak-dose dyskinesias underwent 12 rDTMS sessions over 4 weeks at inhibitory (1Hz) frequency over primary motor and prefrontal regions during the off-state. Intensity and frequency of LID was scored using UDyRS performed in ON-state at baseline, 1 day after the last session and 2 weeks after the end of the study. Antiparkinsonian therapy and other drug treatments were not modified during the study.

*Results:* All 15 patients (mean age  $64 \pm 6.8$ , mean disease duration  $12 \pm 3.4$ , mean UPDRS part III  $23.72 \pm 21.3$ ) concluded the study. No adverse events were recorded. We observed that 1 Hz rDeepTMS induced a slight reduction of intensity of LID (UDyRS before:  $36.4 \pm 28.3$  UDyRS 1 day after last session:  $34.7 \pm 28.7$ ), without causing motor deterioration, but these beneficial effects were transient (UDyRS 2 weeks after last session  $35.8 \pm 28.7$ ).

*Conclusion:* These results suggest that 1 Hz rDeep TMS can lead a slight and transient reduction of intensity of LID . Further placebo-controlled, randomized studies are warranted.

**P61**

**Rotigotine effect on early morning akinesia. Gait Analysis study**

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*Objective:* The present study focuses on the assessment of the efficacy of rotigotine on the amelioration of gait in the morning in a group of moderately advanced Parkinson's disease patients (H&Y:>2) suffering by "early morning akinesia". Further, the study evaluates by specific clinical scales the time/daily spent in ON and the amelioration of quality of life.

*Subjects:* 25 PD suffering for Idiopathic Parkinsons Disease (H&Y stage > or = 2) with unsatisfactory control by on-going pharmacological therapy (Levodopa, COMT & MAO-inhibitors), characterized by an incomplete control of motor signs, in particular presence of early morning akinesia.

*Methods:* Gait analysis was performed always in the morning (8.30-9.30 am.) twice, at the beginning (V1) and after at least two week of stable administration of 16 mg of rotigotina system (V5), no changes of previous antiparkinsonian therapy were made.

The kinetic variables, except gait velocity, were evaluated considering The More affected Body side (Mabs) and the Less affect body side (Labs).

Variables Spatio-temporal variables: gait velocity (m/s), stride length (m), stance, and swing and double stance percentages with respect to the stride phase.

*Results:* Significant improvement gait velocity (m/s), stance, and swing and double stance percentages with respect to the stride phase.

*Conclusion:* Our data, by a validate tool as is Gait Analysis, indicate the efficacy of rotigotina transdermal system for relieve the morning extrapyramidal signs and support the importance of long lasting action of dopaminergic stimulation.



## P62

**Mucuna pruriens in Parkinson's disease: a kinetic-dynamic comparison versus Levodopa standard formulations**

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*Introduction:* Mucuna pruriens is a popular Indian plant used in Ayurvedic medicine for treating Parkinson's disease (PD). Levodopa (LD) is found in large quantities in Mucuna seeds (4-7%). Data on LD bioavailability and related therapeutic effects of Mucuna preparations in PD patients are scanty.

*Objective:* We aimed to compare LD kinetic-dynamic profile of a fixed dose of LD/benserazide (BZ) or carbidopa (CD) vs a nominally equivalent dose of a commercial Mucuna preparation in two PD patients chronically assuming LD standard combined with self-prescribed Mucuna formulations.

*Methods:* Patients were challenged with a fasting morning dose of 100 mg LD/BZ or CD and 100 mg LD from Mucuna tablets in two different sessions, after a 12-h standard LD formulations' wash-out. They underwent kinetic-dynamic LD monitoring based on LD test dose intake and simultaneous serial assessments of plasma LD concentrations and motor test performances, every 15 min for the first 90 min, then 30 min apart, up to 3 h post-dosing. Quali-quantitative analysis of Mucuna tablets was also performed.

*Results:* LD bioavailability was markedly lower after Mucuna test dose compared with LD/CD or BZ: in patient (pt) 1, peak plasma LD concentration (C<sub>max</sub>) decreased from 2.0 (LD/CD) to 1.0 mg/L and area under the plasma concentration time curve (AUC) from 137 to 62 (mg/L) x min; in pt 2, C<sub>max</sub> was 0.7 mg/L after LD/BZ and nearly undetectable after Mucuna. In pt 1, LD finger tapping motor response decreased from > 180 min (LD/CD) to 120 min after Mucuna. In pt. 2, no significant subacute tapping response was observed in either condition. Quantitative analysis of Mucuna tablets confirmed the 100 mg LD content.

*Conclusion:* Our data show an impaired LD bioavailability of Mucuna preparations and possible matched therapeutic response, as expected by the lacking dopa decarboxylase inhibitor co-administration. These preliminary results could explain suggested Mucuna lower dyskinesic potential compared with standard LD formulations.

**P63****The differential effect of STN-DBS on impulsivity and impulsive-compulsive behaviour in Parkinson's disease: a 2-year longitudinal study**

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*Introduction:* The effect of deep brain stimulation (DBS) of the subthalamic nucleus (STN) on impulsive-compulsive behavior (ICB) in Parkinson's disease (PD) is controversial.

Although STN-DBS has been associated to increased impulsivity in psychophysical studies, two short-term longitudinal studies demonstrated that ICB might improve after STN-DBS.

*Objective:* In this 2-year prospective study, we evaluated the effect of bilateral STN-DBS on behavioral and neuropsychiatric complications of PD, including ICB, apathy, anhedonia, anxiety, depression.

*Methods:* A consecutive series of 17 PD patients were evaluated longitudinally before surgery and 6, 12, 24 months after bilateral STN-DBS. Clinical, cognitive and behavioral assessments were performed at all time points. Behavioural evaluation included the following scales: apathy scale (AS), Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), punding rating scale, Barratt Impulsiveness Scale (BIS), Snaith-Hamilton Pleasure Scale. A visuo-analogue scale was also employed to rate severity of each ICB and a composite score for ICB severity was created. The Iowa Gambling Task (IGT) was employed to assesses the pattern of decision making under risk.

*Results:* 12/17 patients presented at least one ICB at baseline. At last follow-up, drug abuse disappeared in 6/7, gambling in 6/6 and compulsive shopping in 6/7. Binge eating did not significantly modify after STN DBS. None of the patients with past ICD developed any ICD after DBS. Improvement of ICB was correlated to magnitude of decrease of dopamine-agonists after STN-DBS. Impulsivity and decision making under risk by IGT did not significantly modify after DBS at all follow-ups.

*Conclusion:* Our data demonstrated that successful STN-DBS is efficacious in treating behavioral symptoms associated to PD, through a decrease of dopaminergic medications.

However, impulsivity and decision making under risk are not changed by stimulation nor medications decrease, supporting the concept that increased impulsivity might not exclusively necessary to develop ICB in PD.

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**Desmopressin and Parkinson's disease: a "new" approach to treat nocturia**

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Different dosages of desmopressin sublingually administered are able to control nocturia in about 70% of patients in the short term follow up, without any serious adverse effect.

To date no consistent informations exist on use of desmopressin in patients affected by Parkinson's disease (PD). We investigated the effects of desmopressin in the treatment of nocturia in PD patients, in a short term follow up. 33 PD patients were included in this prospective open label study. After a baseline evaluation including a 7 day voiding diary, serum chemistry and Nocturia Quality of Life questionnaire (N-QoL), patients underwent treatment with desmopressin 60 µg sublingually administered at bedtime for 7 day.

Patients with 50% or greater reduction in nocturnal voids at day 7 continued assuming the same drug dosage for 12 weeks. Patients who did not report such a response to treatment, after the first week changed to desmopressin 120 µg for the whole observation time. The same evaluation were repeated after 1 week and 12 weeks of treatment. Primary end point was the proportion of patients with a 50% or greater reduction in the mean number of nocturnal voids after treatment compared with baseline. Secondary end points: changes in nocturnal urinary volume, duration of the sleep period until the first nocturnal void, change in QoL, safety of treatment with desmopressin. At week 1 a (>50%) reduction in the mean number of nocturnal voids, mean nocturnal urinary volume, mean duration of the sleep period until the first nocturnal void and a significant increase in mean N-QoL total score were observed in 15 patients (41.9%). All the 15 patients continued assuming desmopressin 60µg for 12 weeks. Nine patients changed to desmopressin 120µg for 12 weeks. Nine patients discontinued treatment due to adverse effects, mainly nausea and diarrhea, and lack of efficacy. So at 12 weeks 24 patients (70.9%) reported significant effects in all the considered parameters and none of them presented with a serum sodium < 135 mmol/l.

## The effectiveness of a community intervention occupational therapy program with Parkinson's disease: "My Life in my hands"

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The main aim of this research was to implement a preventative community occupational therapy intervention developed by Palombi et al. [1] with individuals with Parkinson's disease and determine its effectiveness. Although some feasibility studies have shown positive trends, there is little to no recent literature which demonstrates the effectiveness of occupational therapy for individuals with Parkinson's disease [2,3].

Thirty eight community dwelling older adults with PD (5 drop out) were recruited for a single blinded, dual arm RCT. The experimental group received the preventative community OT intervention and the control group had no contact. There were three evaluation times, pre and post intervention (one month) and at 3 months after no contact. Outcome measure observed PD symptoms (UPDRS), disability levels (NUDS), quality of life (SF 36), daily activities (MBI), depression (BDII) and perceived performance and satisfaction of chosen occupations (COPM). The results demonstrated significant ( $p < 0.017$ , after adjustment) improvement in the experimental group compared to the control group in, motor symptoms, daily activities, decrease in disability and improved mental and physical health after one month intervention. Significant ( $p < 0.017$ ) improvement was also noted in levels of depression and perceived performance and satisfaction of chosen activities. Improvement was associated with high effect sizes ( $r = 0.5$ ). These gains were maintained in the experimental group in the three month period of no contact ( $p < 0.017$  after adjustment).

The result demonstrate that a preventative occupational therapy approach can improve quality of life and wellbeing and promote health in individuals with PD.

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## A psycho-neuro-endocrinological study about body weight gain after STN-DBS in Parkinson's disease

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*Introduction and Objective:* Subthalamic nucleus deep brain stimulation (STN-DBS) is an effective procedure for patients with advanced Parkinson's disease (PD). Early after STN-DBS it has been reported a moderate-to-marked gain in body weight (BW) [1-2]. The mechanisms underlying this phenomenon are still elusive: some groups reported an association with dyskinesias reduction, while others did not find such correlation, pointing to hormonal changes, daily energy-expenditure reduction and direct stimulation of near hypothalamic nuclei [1-2]. Our aim was to analyze neurological, psychological and endocrinological parameters in PD patients undergoing STN-DBS to better understand the causes of BW gain.

*Materials and Methods:* From 2005 to 2011 thirty-four PD patients underwent STN-DBS in our center. Twenty-eight patients were included in our analysis while six patients were excluded due to incomplete follow-up. Time of observation were at T0 (pre-surgery), after 6 and 12 months (T6, T12). We evaluated BW (Kg), UPDRS, electrodes voltage, levodopa-equivalent daily dose (LEDD), SF-36 scale, apathy evaluation scale, Beck depression inventory and hormonal status (gonadal, adrenal and thyroid-axis; prolactin).

*Results:* BW increased after STN-DBS (T0: 67.3±13.4; T12: 73.7±13.3; p<0,001). Improvement of UPDRS-III motor score (off-medication/on-stimulation state) was significant (35%, p<0.001). Hormonal laboratory tests: thyroxine decreased at T12 (p=0,006), prolactin was increased at T6 (p<0,001). Levodopa-induced dyskinesias (UPDRS-IV: items 32&33) significantly decreased (T0: 3.3±2.2; T12: 1.8±1.6; p=0,002), such as LEDD (T6: 725±388 Vs T0: 1088±374; p=0.013). BW gain was positively correlated with total electrodes voltage (left+right contacts) at T12 (p=0.038) and negatively correlated with levodopa-induced dyskinesias at T6 (p=0.033) and T12 (p=0.006).

*Conclusion:* BW gain after STN-DBS is correlated with dyskinesia reduction and with total electrodes voltage. The latter finding could support a "central" direct effect of STN-DBS, accordingly to a recent study that has evidenced a strong inverse association between weight gain and electrodes distance from the third-ventricle wall [3].

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**Robotic Neurorehabilitation in Parkinson Disease: a neurophysiological approach**

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*Background and Objective:* Parkinson’s disease (PD)-related gait impairment represents one of the most disabling symptoms, often associated to an increased risk of falls, and loss of independence. The Lokomat is a gait robotic device that has been widely used for gait rehabilitation in several movement disorders.

Aim of our study was to evaluate the efficacy of an intensive robotic gait training on clinical and neurophysiological outcomes in patients affected by PD.

*Materials and Methods:* Six outpatients affected by PD entered our pilot study. All participants underwent motor and psychological scales, including UPDRS, MMSE, FAB, HRS-D and COPE, at baseline and after the Lokomat Training (consisting of 40 training sessions, 5 times a week for 8 weeks, of around 1 hour duration each). We also tested the following electrophysiological parameters: the resting and active motor threshold, the short intracortical inhibition (SICI), the short (SAI) and long (LAI) latency afferent inhibition. Then, we applied the paired associative stimulation (PAS) protocol for lower limb (Jayaram and Stinear 2008), in order to evaluate cortical synaptic plasticity within sensory-motor cortex.

*Results:* Nearly all the patients presented a significant improvement in the motor and cognitive function as well as the psychological well-being. Although at baseline there was no response to the PAS with a reduced SICI, SAI and LAI, after Lokomat-treatment the post-PAS MEP amplitude was increased and SICI and LAI were restored, but not SAI.

*Discussion and Conclusion:* Lokomat training is based on optimizing sensory inputs relevant to step training, repeated practice, and possible optimization of neuroplasticity thus leading to functional improvement.

Our pilot study indicates that active robotic training appears to be a promising way of facilitating not only gait and physical function but also the psychological and cognitive status in patients affected by PD, as also evaluated by means of a neurophysiological approach.

**Establishing health indicators for a local population of individuals with PD to inform an occupational therapy intervention***Sindy Banga*<sup>1</sup>, *A. Palombi*<sup>2</sup>, *A. Denaro*<sup>2</sup><sup>1</sup>University of Northampton, U.K.<sup>2</sup>Istituto Chirurgico Ortopedico Traumatologico, ICOT (GIOMI), Latina, Italy

Although some feasibility studies have shown positive trends, there is little to no recent literature which demonstrates the effectiveness of occupational therapy for individuals with Parkinson's disease [1,2]. The main aim of this research was to explore the key health indicators in a local community of individuals with Parkinson's disease (PD) in order to inform the development of an innovative occupational therapy (OT) intervention. Three methodologies were used to determine the effects of current service and patient experience. These were a retrospective chart review, a questionnaire and a secondary data analysis.

Chart reviews were completed of a 124 PD patients (Mean age =70.67 years) admitted from June 2007 till June 2008 in an Italian neuro-rehabilitation unit. The results found that 31% (n=38) of patients were admitted more than once a year and although demonstrated significant (P<0.001) functional improvement after rehabilitation, declined to baseline before the second admission. A questionnaire investigating patients experience of their hospital admission was sent by post (39% response rate, n=45). This revealed that social contact was an important factor for a positive hospital experience. Evidence from a secondary data analysis demonstrated that moderate and severe PD (Hoehn and Yahr III and IV) improved more than bilateral disease (Hoehn and Yahr II) with intense rehabilitation (p<0.001). This also showed that patients gave less priority to occupations which require social contact, when there is an increase in disability (p<0.05) and gave more priority to having control (p<0.01) over their occupations. This information together with a review of the literature which revealed the Lifestyle Redesign Programme developed by Mandel et al [3] for the Well Elderly Study I [4] and the Well Elderly Study II [5], resulted in the development of an innovative preventative community occupational therapy intervention. The original framework was modified taking into consideration the results of this research. The resulting new occupational therapy intervention is called "My Life in My hands".

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## Treatment of the motor and non-motor symptoms in Parkinson's disease according to cluster symptoms presentation

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The term Parkinson's disease has been changed in "Parkinson's diseases" to describe different clinical entities observed in several studies investigating the existence of PD subtypes. PD patients could be grouped based on clinical features. By considering only motor symptoms, we can classically distinguish two groups: "the tremorigen-form" and "akineti-rigidity-form" where resting tremor and akinesia/bradikinesia and rigidity are the most motor predominant symptoms, respectively. Non-motor symptoms (NMSs) are practically always present during the course of the disease and some of them (constipation, depressive status, hyposmia and anxiety) could even exist before the onset of classical motor symptoms. Many other NMSs and in particular hallucinations, cognitive impairment, sleep disorders and difficulty in swallowing strongly affect the advanced stage of disease, and represent a real therapeutic challenge when these symptoms are simultaneously present with different severity. If not adequately treated, they can increase the risk of hospitalization and admissions in nursing home, and profoundly and negatively influence the quality of life and participation in social activity of these patients. PD subtypes according to the combination of motor and non-motor symptoms have been recently proposed. This classification derives by cluster analysis which permits to identify statistically distinct subtypes of Parkinsonian patients according to the relevance of both motor and non-motor symptoms.

In this point of view, we propose a schematic therapeutic approach of motor and non-motor symptoms in Parkinson's disease according to cluster symptoms presentation (motor and no-motor symptoms) and using medications that act on multiple domains of PD symptoms.

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**P70****Importance of intestinal tube placement in Levodopa/Carbidopa intestinal gel (LCIG) therapy: a 5-year single-center hospital-based study**

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*Introduction:* In patients with advanced Parkinson disease LCIG has shown significant improvement in motor symptoms by reducing motor fluctuations and dyskinesias. Furthermore LCIG improves non-motor symptoms and quality of life.

Despite its effectiveness, procedural and device related problems are observed in 20-70% of patients where the most frequent complication is accidental removal/dislocation of the intestinal tube (IT), requiring device replacement.

LCIG is absorbed in the jejunal bowel tract. During IT placement procedure, Treitz tract can be difficult to reach and the tube is frequently placed in the second or third tract of duodenum where it reaches passively the jejunum.

*Objective:* The aim of the study is to compare the number of IT replacement occurred in patients with intestinal tube located immediately after Treitz-ligament with those in which the tube was left in the second or third portion of the duodenum.

*Methods:* We retrospectively analyzed in 26 LCIG consecutive patients the number of surgical procedures performed for accidental removal or dislocation of the IT. The UPDRS III e IV scores were also analyzed to verify the efficacy of LCIG treatment.

*Results:* In 13 patients (Group1) IT was placed in the second or third duodenal portion, whereas in the 13 remaining (Group2) it was located after Treitz-ligament. In Group1 4 dislocations (30,7%) occurred; ITs were replaced after the Treitz-ligament without occurrence of further dislocations. No dislocations have been observed in Group2.

No differences in LCIG efficacy have been observed in the 2 groups.

The PEG-j device has been replaced in 6 patients overall due to expected wear.

In this subgroup, IT was replaced after Treitz-ligament with a dislocation rate of 16.7% (1/6).

IT accidental removal or dislocation always occurred within the first few days after placement.

*Conclusion:* Our results suggest that the IT placement immediately after Treitz-ligament is preferable, reducing the frequency of IT accidental removal/dislocation.

## Anesthesia in orthopedic procedures of Parkinson's disease patients

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*Introduction:* Compromission of gait and postural stability in Parkinson's disease (PD) can result in an increased risk of falling and bone fractures requiring a surgical treatment.

*Objective:* To describe anesthesiological procedures in PD in use at an Orthotraumatologic Department.

*Methods:* Anesthesiological data sheet of 39 PD patients surgically treated during last three years are examined and described. The Authors focused their attention on types of anesthesia used, drugs and dosage and post surgical treatment with a particular attention to concomitant diseases.

*Results:* Examinations of data sheet shows in period considered:

Of 39 patients, 29 were female (74,36%) and 10 were male (25,64%).

The mean age was  $79,4 \pm 7,5$  years (F  $80 \pm 7,9$ ; M  $77,9 \pm 6,4$ ).

All procedure were elective and determined by a femur fracture in 27 case (F=19; M=8), humerus fracture (1 case), pelvis fracture (1 case), prosthesis in 10 cases (hip 7, knee 3; F=8; M=2). Concomitant disease were hypertension (27 cases, 69,2%; F=22, M=5); diabetes (13 cases, 33,3%; F=11, M=2); COPD (11 cases, 28,2%, F=10, M=2); anaemia (8 cases, 20,5%; F=7, M=1); arrhythmias (8 cases, 20,5%; F=6, M=2); CVD (6 cases, 15,4%; F=4, M=2); renal failure (4 cases, 10,3%, all female); previous myocardial infarction (3 cases, 7,7%; F=2, M=1).

Class of risk was 3 or 4.

All patients but three received a subarachnoid anesthesia.

Drug used were chinocaine 0,7% (20 pts, mean dose 1,72 mg; three received also fentanyl 25 mg); marcaine (11 pts, mean dose 1,51 mg); levobupivacaina (3 pts, mean dose 13,3 mg); bupivacaine (2 pts, mean dose 2,25).

One patient received local sedation by carbocaine.

Two patient received general anesthesia using propofol, nocumonio and remifentanil HCl.

All patients but two were in spontaneous ventilation and monitored for Sao<sub>2</sub>, HR, EKG, NI BP. During the intervention patients received liquid infusion ( $1554 \pm 405$  cc).

A blood transfusion needed in 17 patients (F=13, M=4, 5 of them were already anaemic).

All patient received analgesic treatment for pain relief after surgery: 24 paracetamole 3-4 a day, (17 in monotherapy, 4 with ketorolac, 3 with tramadole) 15 elastomeric pump with paracetamole, tramadole, ranitidine and antiemetic).

No intraoperative complication are shown.

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*Conclusion:* According to the literature, regional anesthesia is preferred to general anesthesia in patients affected by PD. Use of epidural anesthesia is a good option for many lower extremity procedures, such as knee replacements and femor fractures. In some case patients may also be sedated during the procedure, but it is usually not necessary to place a breathing.

Moreover regional anaesthesia has advantages over general anaesthesia, as it avoids the effects of general anaesthesia and the airway complications earlier as well as providing good postoperative analgesia and avoiding postoperative nausea and vomiting. Blood transfusion when needed and liquid infusion (balanced solutions of electrolytes: sodium, potassium, chloride and bicarbonate) are common. Pain relief after surgery procedure also is of significant benefit.

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**L-DOPA + carbidopa intestinal gel infusion and rehabilitation. Longitudinal study***Pietro Marano, M. Seminara*

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*Introduction:* Parkinson's disease is characterized by a chronic course, slowly progressive. The average age of onset is around 60 years, but about 10% of patients less than 50 years (Dodel 1998). Initially, the symptoms are unilateral, but become bilateral after a mean disease duration of 9 years. After about 10 years, patients require assistance in their daily activities, and after about 18 years they are likely to be confined to a bed or wheelchair. Also become frequent falls that often result in fractures, then surgery, then extended allurements, and risk of developing pressure sores, and increased health care costs.

Obviously Parkinson's disease has a great impact from a working point of view: in fact, after 5 years of 25% of patients the disease is no longer able to work and becomes 80% after 9 years of disease.

The advanced stage of Parkinson's disease then describes a clinical state of considerable gravity, characterized by severe limitation of mobility, impaired functional ability and progressive disabling condition of the patient to the loss of self. The disease progresses inexorably and motor disturbances are no longer controlled by conventional drug therapy oral Duodopa has been developed specifically for patients with Advanced Parkinson's disease is not well controlled by medication. L-DOPA + carbidopa intestinal gel is a suspension of L-DOPA. The objective is to obtain a more constant availability of L-DOPA, infuse it through a peristaltic pump directly into the small intestine through a jejunal feeding tube. The indication of L-DOPA + carbidopa intestinal gel is the advanced Parkinson's disease with fluctuations in state (On/Off).

The advanced stage of Parkinson's disease then describes a clinical state of considerable gravity, characterized by severe limitation of mobility, impaired functional ability and progressive disabling condition of the patient to the loss of self. The disease progresses inexorably and motor disturbances are no longer controlled by conventional drug therapy oral.

*Material and Methods:* We reported the experience of 27 patients with Hoehn & Yahr stage of initial 3:04. Neither of them had ever done before rehabilitation treatment. They were all treated medically with Levodopa + ID to medium dosages of 1200 mg / day and with a history of disease an average of about six years.

The program has provided, immediately before and during the test phase and immediately after implantation of the PEG/J with the final administration of L-DOPA + carbidopa intestinal gel in peristaltic pump, sessions three times a week rehabilitation day hospital treatment of various shapes specialist who then took turns during the period observation and therapy. In addition, the patient we decided to start his care giver in order also to prevent the execution of incorrect behavior which would inevitably lead to a worsening of the living conditions of the patient. The first patient was subjected to infusion therapy with physiotherapy in January 2007, while the last one currently in Croso. In place so we are not able to provide a true follow-up to well-defined, but we can only provide preliminary data. We reported the experience of 27 patients with Hoehn & Yahr stage initial 3-4. None of them had ever done before rehabilitation treatment. They were all treated medically with Levodopa + ID to medium dosages of 1200 mg / day and with a history of disease of approximately 8 years.



**P72 (segue)**

The program has provided, immediately before and during the test phase and immediately after implantation of the PEG-J with the final administration of Duodopa in peristaltic pump, three weekly sessions of rehabilitation in day hospital with treatment of various shapes so specialized that alternated during the period of observation and therapy. In addition, the patient we decided to start his care giver in order also to prevent the execution of incorrect behavior which inevitably led to a worsening of the living conditions of the patient. The first patient underwent therapy with Duodopa with physiotherapy in January 2007, while the last one currently in progress. In place so we are not able to provide a true follow-up to well-defined, but we can only provide preliminary data and certainly not definitive.

We finally made a rough calculation of how small it is stated the cost of this project, compared to the cost of each treatment administered to each patient. With great surprise we arrived at the determination that the project has made a net saving of about 20% on the total expenditure which is made on a complex patient as the patient's disease.

*Results:* The results can be discussed not only in economic terms but also and especially in functional terms. In fact, the sick Parkinson's as well as learn management from the point of view of ADL and IADL, was released from isolation continuous and constant within which it lives and island. The totality of patients with advanced Parkinson's disease treated not only with L-DOPA + carbidopa intestinal gel but also in DH rehabilitation have reported a reduction of at least one point in the scale of H. & Y., which constitutes a given absolutely positive if lays it all in terms of personal autonomy. Encouragingly, however, may be to continue the experience. A fundamental fact is constituted by the fact that the falls, measured with the scale of Tinetti, were reduced in all patients examined by more than 60%, reducing conspicuously therefore also the risk of fractures which was mentioned in materials and methods.

*Conclusion:* Each structure that takes care of rehabilitation in neurodegenerative diseases should develop a protocol adapted to better manage the disease in question, not only from a rehabilitative point of view, but also from a preventive point of view and pharmacological advanced. Also because advanced therapies are only apparent in a high cost of ownership, but in reality, in addition to improving the quality of life of the patient, avoid all the complications and sequelae that may cause such diseases. It therefore calls for greater cohesion of these structures that may give rise to these needs, making the necessary corrections.

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**Continuous subcutaneous apomorphine infusion therapy for Parkinson's disease: a retrospective cohort study**

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*Background:* Continuous subcutaneous apomorphine infusion (CSAI) can significantly improve motor fluctuations and off-period in patients with advanced PD. Actually, there is no clear definition of the best candidates for this therapy. Usually, the candidates are PD patients with a good response to l-dopa and inadequately controlled by oral therapy. Patients with cognitive impairment, severe systemic diseases, history of dopaminergic psychosis should be excluded.

*Methods:* We conducted a retrospective cohort study to investigate the selection criteria and clinical characteristics of candidates to help the clinician in choosing the most suitable option for their patients, the causes of drop out, stand over cognitive complications and identify the best treatment after the drop out. 147 subjects with PD who underwent to continuous subcutaneous apomorphine infusion and then dropped out were recruited. For all subjects we recorded age, age at onset, gender, phenotype, age since starting CSAI, switch to another therapy, time of treatment, 3 most important interruption causes. Furthermore, we recorded UPDRS part 3 and 4 and MMSE has been submitted for pre and post-treatment assessment of cognitive status.

*Results:* Subjects were recruited from Neuromed Institute between 1998 and 2012. The mean age of patients was  $68,98 \pm 10,41$  with a mean onset age  $48,35 \pm 9,91$ . They were underwent to CSAI for 27 months (min-6,max-108) and then dropped out for several reasons: most important interruption causes were dyskinesias (34%) and cognitive impairment (17%), while the most disabling symptoms for younger patient was orthostatic hypotension. Treatment after the drop out was deep brain stimulation for 35 patients, intrajejunal levodopa infusion for 16 and oral therapy for 96 patients.

*Conclusion:* CSAI is an effective therapy for off-episodes reduction and in management of several motor symptoms, but it is not devoid of side effects, such as cognitive impairment, so we conclude that could be a efficacy and safety therapy for a specific period or as a bridge towards DBS or intrajejunal levodopa infusion.

**P74****Hemorrhagic complications of deep brain stimulation: data from a large number of treated patients**

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*Objective:* To assess the incidence of hemorrhagic complications (HC) in a large series of deep brain stimulation (DBS) treated patients.

*Background:* DBS is an effective option for the treatment of movement disorders refractory to medication.

Despite its demonstrated safety, rare adverse events (AE), in particular HC, could result in potentially disabling outcomes. Intraoperative microelectrode recording (MER), age and hypertension increase the incidence of bleeding.

*Methods:* Data of all patients submitted to DBS at our Center between 1998 and 2013 were collected. MRI and stereotactic CT scans were performed prior to surgery. We use a single-track MER approach to the target, along a trajectory planned to avoid sulci and ventricles. Intraoperative microelectrode stimulation (MS) was also performed. If necessary, a second or even third track was performed. The definitive DBS electrode was placed along the best trajectory. We performed an immediate postoperative CT scan and a MRI one week after surgery. A single primary surgeon performed all procedures and bilateral implants were performed in a single-session.

*Results:* 442 definitive electrodes were implanted in 221 patients: 216 affected by Parkinson's Disease (130 M, 86 F), 3 by Essential Tremor (3 M), 2 by Dystonia (1 M, 1 F). Mean age at surgery was  $60.7 \pm 6.9$  years (M  $60.8 \pm 6.9$ ; F  $60.5 \pm 6.9$ ). A total of 590 MER tracks were performed. 42 (19%) patients were hypertensive. No HC occurred during intraoperative and postoperative period.

*Conclusion:* Hemorrhage is the most serious AE in functional neurosurgery, with an incidence of 5%. In our patients we did not observe HC, even though the population characteristics (age and hypertension percentage) were similar to those reported in literature. Moreover, we routinely performed MER, considered a bleeding risk factor. A careful patient selection and the application of standardized procedures performed by an experienced team can prevent high rate of hemorrhagic events.

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**The impact of Rotigotine on periodic leg movements and sleep quality in Parkinson disease: a three-case experience**

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*Introduction:* Sleep disturbances and impairment of the sleep-wake cycle are frequent non-motor symptoms and a prominent cause of disability in Parkinson Disease (PD) patients.

Periodic leg movements in sleep (PLMS) are a sleep-related phenomenon with periodic episodes of repetitive stereotypical movements of the lower extremities.

*Aim of the study:* In this study, we evaluated the efficacy of rotigotine treatment in three de novo PD patients showing reduced sleep efficiency (SE) and increased PLMS index (PLMI).

*Methods:* PD patients underwent clinic and neurological examination also counting the Unified Parkinson's Disease Rating Scale Motor Section (UPDRS-III) and the Parkinson's Disease Sleep Scale (PDSS). Two ambulatory polysomnographic (PSG) monitorings were performed through a dynamic 32-channel system polygraph (Somnoscreen; Somnomedics, Germany) before and after two month of rotigotine 6 mg/day treatment.

*Results:* Rotigotine markedly reduced PLMI (146.4/h vs 11.9/h; 41.4/h vs 6.5/h; 31.6/h vs 7.8/h) and improved the PDSS scores (96 vs 122; 98 vs 120; 101 vs 119) in all PD patients. On the other hand, as expected it markedly reduced the UPDRS-III scores (26 vs 9; 24 vs 7; 18 vs 6).

*Conclusion:* Rotigotine is a well-tolerated non-ergoline dopamine agonist with high affinity for the full dopamine receptors.

In our three case experience we have found that rotigotine markedly reduced PLMS improving the subjective sleep quality of patients. Since PLMS pathogenesis is related also to the dopaminergic system impairment, the efficacy of rotigotine on PLMI in PD patients may be due to the drug-related improvement of the dopaminergic transmission. Therefore, this report seems to suggest the efficacy of rotigotine in reducing PLMS in de novo PD patients.

However, in a more intriguing hypothesis, we may suppose that the significantly reduction of PLMS due to rotigotine therapy could ameliorate sleep in PD patients with high PLMI.

## Poetry and singing in Group Therapy for Parkinsonian patients

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Poetry is a valuable psychotherapeutic instrument [1] also in elderly [4]. Previous studies support the benefits of active music therapy [2] and singing [3] in patients affected by Parkinson's disease (PD).

A supportive therapeutic group formed by fourteen PD patients (mean age 75 years) and three caregivers was conducted by a skilled dedicated psychologist under supervision of a psychotherapist psychiatrist. Patients have attended weekly one hour group meetings for ten months. Meetings took place at Unione Parkinsoniani in Parma.

The innovative therapeutic pathway consisted of reading, analyzing and commenting poems written by famous authors (e.g. Goethe, Coleridge, Emerson, Kipling) about determination of action, non-judgmental acceptance, imagination in order to achieve an adaptive affective balance. The aim of psychological work was to develop skills of rhythmic expression of emotions suggested by poems.

Another effective approach was to change the lyrics of well-known songs (e. g. Stevie Wonder, John Denver) and to write new words about the group and their activities. To sing all together helped group members to feel empowered and on a positive path to growth and well-being.

Patients' satisfaction was high, as evidenced by an active and constant attendance. They perceived the group therapy as stimulating, engaging, and relaxing.

Positive outcomes were: improving communicative competence, emotional exploration and reflection, overcoming self withdrawal and social isolation, enhancing self-esteem, self-efficacy, self and group identity. The patients' trust of belonging to the group have been strengthened through democratic choices, mutual help and learning, and shared commitment of the entire group.

Our experience agree with Young-Masson [5]: "Singing for the joy of it, singing for hope, singing to heal: music and song improves lives of persons with Parkinson's disease".

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**MusicTherapy for motor and non-motor symptoms in Parkinson's disease: a 24-week, randomized, controlled, single-blinded study**

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*Background:* Parkinson's disease (PD) affects mobility, cognition and emotions. Music Therapy (MT) is considered an alternative neuro-rehabilitative technique for PD patients due to its action on motor and non-motor symptoms.

*Aim:* The aim of this prospective, randomized, controlled, single-blinded study is assessing the effectiveness of MT on motor symptoms, cognition and mood in PD patients.

*Methods:* 27 consecutive PD patients were enrolled and randomly assigned to MT or no treatment (NT). All patients were neither depressed nor demented, with mild/moderate PD (H&Y stage  $\leq 2$ ). At baseline and after 6 months, all patients were evaluated for quality of life (Parkinson Disease Questionnaire-39, PDQ-39) and underwent a detailed motor (MDS-Unified Parkinson's Disease Rating Scale; New Freezing of Gait – Questionnaire; Timed Up and GO test, TUG ( and neuropsychiatric assessment (Beck Depression Inventory and a neuropsychological exam evaluating executive function, attention, visuospatial skills, memory and language). MT sessions were held once a week for 24 weeks; each session lasted 90 minutes and consisted in production of music, singing and dancing.

*Results:* 10 patients were randomized to MT and 15 patients to NT. At baseline the two groups were comparable for demographic, quality of life and motor measures, whereas they differed on some neuropsychological tests, namely Raven test ( $p=0.046$ ), names denomination ( $p=0.025$ ), verbs denomination ( $p=0.042$ ) and Trial Making Test (TMT) A ( $p=0.011$ ). At follow up, MT patients showed significant improvement on PDQ-39 ( $p=0.03$ ), verbal fluency ( $p=0.03$ ), Stroop interference ( $p=0.03$ ), Rey delayed recall ( $p=0.02$ ); furthermore, MT patients showed improvement as a trend on TUG ( $p=0.06$ ) and TMT A ( $p=0.05$ ) and B ( $p=0.059$ ). At follow up, NT patients did not show significant difference on any motor and neuropsychiatric measure.

*Conclusion:* Our preliminary data suggest that MT might represent an effective tool for a holistic treatment of PD with a main effect on frontal functions.

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**Deep Brain Stimulation (DBS) in Parkinson Disease (PD): single-center experience from 2000 to 2013**

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*Background:* Deep brain stimulation (DBS) in different basal ganglia targets has been well established as a therapy for advanced Parkinson's disease. The technique has been refined throughout the years by improved imaging techniques, advanced neurophysiological recording possibilities, and advances in hardware and software technology.

*Aim:* To review our experience to identify differences in short- and long-term outcomes in order to find clinical predictors and management strategies able to improve good clinical outcome and reduce side effects development.

*Materials and Methods:* 200 PD patients treated with DBS from 2000 to 2013 were retrospectively evaluated. The cohort was divided in three timeslots: Ts1 (from 2000 to 2005), Ts2 (from 2005 to 2010) and Ts3 (from 2010 to 2013). Patients were divided in two groups: Idiopathic Parkinson disease (161) and Early Parkinson disease (39). Clinical variables of the two groups were matched with the timeslot to detect differences in clinical outcome and in side effect development.

*Results:* The target of choice was STN for 174 patients, GPi for 17 patients, and STN+GPi for 9 patients. 74% of the patients are still followed in our clinic, 26% were lost at follow up (LFU) after at least 3 years. In the over-all follow up period 21 patients died no one because of DBS-related causes. 5 patients develops acute after surgery complications, 2 of them are completely recover, 2 still manifests neurological sequele, 1 is LFU.

*Conclusion:* The preliminary analyses from our court show that the study group is reliable and the evaluations within- and between- groups and timeslots may help to define better clinical management strategy.

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**Parkinsonism-Hyperpyrexia Syndrome and Deep Brain Stimulation discontinuation: a case report**

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*Introduction:* Neuroleptic malignant syndrome (NMS) is a rare reaction to neuroleptics representing a movement disorder emergency; it encompasses autonomic instability, altered mentation and motor abnormalities. In parkinsonian patients the abrupt withdrawal of levodopa is occasionally associated to the development of acute akinesia mimicking NMS: in these cases it is termed "parkinsonism-hyperpyrexia" syndrome (PHS).

We report the case of a parkinsonian patient treated with subthalamic nucleus deep brain stimulation (STN-DBS) who developed PHS after battery depletion, despite regular assumption of oral dopaminergic therapy.

*Case Report:* A 63 year old man, with a 13-year history of Parkinson's disease and treated with bilateral STN-DBS and oral dopaminergic therapy, was hospitalized for the internal pulse generator (IPG) battery depletion.

Despite the dosage of dopaminergic drugs was increased to compensate the IPG switching off, the patient reported sudden severe axial and limb rigidity, upper limb tremor and anxiety and developed speaking and swallowing difficulties. At admission, he showed dyspnea and tachycardia, high blood pressure and fever. Blood tests demonstrated relevant increase of creatine-kinase (2.820 U/L) and white blood cells slightly higher than normal (10.000/ml); serum creatinine was normal (0.93mg/dl) while C-reactive protein was 50.1 mg/l.

Intravenous hydration, clonazepam and paracetamol were administered with partial relief of symptoms and normalization of vital parameters. Two days after hospitalization, IPG replacement was performed and the stimulation was switched on using the former parameter setting, causing a prompt and complete relief of symptoms: tremor and rigidity disappeared and the patient returned to his previous autonomy.

*Discussion:* PHS must be considered as a possible, severe presentation of the sudden switching off of STN-DBS devices. The increase of dopaminergic drugs could be ineffective, due to the levodopa-response modification occurring in DBS treated patients. The prompt replacement of IPG must be considered as an emergency in STN-DBS parkinsonian patients presenting with symptoms of PHS.



**Executive and visuo-spatial functions rehabilitation in Parkinson's disease: our experience**

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*Introduction:* Cognitive deficits, ranging from subtle dysfunction to dementia, affect 24% to 31% of PD patients [1]. Executive and visuospatial dysfunctions are present in up to a third of PD patients, even in the earliest stages, contributing significantly to disability, caregiver strain, and diminished quality of life over the course of the disease [2,3].

*Objective:* To evaluate the diagnostic accuracy of putative advanced MR biomarkers in the differential diagnosis of PSP and IPD.

*Methods:* 51 PD patients were extensively evaluated on memory, executive functions, logical reasoning, visuo-spatial processing, attention, language. Of them, 10 were diagnosed as being affected by MCI, involving only executive or executive and visuospatial domains. They received 24 one-hour treatment sessions over a three-month period (2 sessions/week). Treatment, performed by paper-pencil and computerized exercises, was tailored to each patient's needs. For each subject, pre and post-treatment scores by executive and visuo-spatial performances were compared using two-tailed Fisher's test.

*Results:* One patient discontinued treatment after a fall. As for the 9 subjects who completed treatment, significant improvement was observed in visuo-spatial praxis and visuo-spatial planning in 3 ( $p < 0.005$  for all subjects); in phonemic fluency in 2 ( $p < 0.005$ ); in working memory in 2 ( $p < 0.005$ ). Non-significant improvement in visuo-spatial planning abilities was observed in two additional patients.

*Conclusion:* This preliminary report shows that neurocognitive treatment may improve executive and visuospatial deficits in at least some MCI PD patients. These observations are promising, as systematic data on cognitive neurorehabilitation in PD are lacking. Their strength lies in the use of a homogeneous protocol in subjects who are relatively homogeneous from the cognitive viewpoint, which ensures the possibility to collect good quality data. Conclusions must remain tentative, however, due to small sample size, lack of a control group, and participant heterogeneity as regards non-cognitive parameters (age, years of illness and LED), and must be confirmed in a larger sample.

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**Peripheral neuropathy risk in Levodopa/Carbidopa intestinal gel treated patients**

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*Background:* Peripheral neuropathies (PN) have been described in Parkinson's Disease patients treated with oral dopaminergic therapies [1]. Some cases of PN have also been associated to levodopa/carbidopa gel infusion (LCIG) treatment, with the occurrence of chronic sensory-motor or even severe subacute PN [2]. This study reports clinical and electrophysiological (EP) data of 28 consecutive LCIG-treated patients followed-up for a mean of 30 months.

*Methods:* Patients underwent lower limbs nerve conduction studies, a battery of clinical scales for PN (ONLS, INCAT-SSS, MRCSS) and a serum vitamin work-up, before surgery and after a mean of 30 months.

*Results:* At baseline, 7/28 (25%) subjects presented EP signs of sensory-motor PN. Demographic, clinical and biochemical characteristics did not differ between normal and PN patients. One normal patient developed a severe subacute PN after 4 months of treatment: infusion was therefore interrupted. Data of 17 patients (13 from normal group/4 from PN group) were available at the 30-months evaluation. Patients with a pre-existing PN did not worsen significantly. Among normal patients at baseline, 23.0% (3/13) developed a new symptomatic neuropathy, 30.8% experienced EP alterations with PN signs but without symptoms, 30.8% had EP alterations without signs and symptoms, 15.4% did not reveal significant EP/clinical alterations. No differences were found between normal and neuropathic patients at 30 months concerning demographic and parkinsonian features. Despite a correct vitamin supplementation, symptomatic subjects showed a slightly higher prevalence of hyperhomocysteinemia.

*Conclusion:* This is the first prospective study reporting the evolution of EP characteristics in a large cohort of LCIG-treated patients over a period of 30 months. We observed a high prevalence of EP alterations and a moderate incidence of symptomatic PN (with one case of precocious subacute sensory-motor PN), higher than in previously reported data [1,2]. Our study underlines the importance of careful monitoring, prevention and treatment of PN in LCIG-treated patients.

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**P82****Effects of rasagiline on the severity of freezing of gait in patients with advanced Parkinson's disease**

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*Introduction:* Freezing of gait (FOG) is a disabling symptom in Parkinson's Disease (PD) that is usually observed in the advanced stage of the disease following long-term treatment with levodopa.

*Objective:* To evaluate the beneficial effects of rasagiline treatment 1 mg/day on FOG during on state (FOG-on) in patients with advanced PD [1].

*Methods:* This open-label study evaluated 7 patients with advanced PD and a recent history of FOG that were treated with rasagiline 1 mg/day for 2 months in the morning in add-on to a stable antiparkinson treatment. Patients were trained to walk on a standardized track and also to rotate on the right at 360° at baseline and at the end of treatment. Dynamic electromyography (EMG) was used to evaluate the effect of treatment on the steps phases and on the timing of muscular activation during normal gait and FOG. Scales administered at baseline and at the end of treatment were: Hoehn-Yahr scale, MDS-UPDRS Section III, Gait and Falls Questionnaire (GFQ) and FOG questionnaire (FOGQ) [2].

*Results:* Time and speed of walking significantly improved from baseline to end of treatment ( $p<0.05$ ). The mean number of episodes of freezing decreased and the mean duration of the time of freezing significantly decreased from baseline to endpoint ( $p<0.05$ ). There were no statistically significant changes in EMG during normal gait, while during FOG total duration of activity in the gait cycle at the right gastrocnemius muscle significantly decreased from baseline ( $p<0.05$ ), and onset of pre-swing activity and duration of activity at the beginning of the step at the right anterior tibial muscle significantly increased ( $p<0.05$ ) [3].

*Conclusion:* Rasagiline was effective in the treatment of FOG-on due to PD. Dynamic EMG is useful to evaluate the physiopathology of the main muscles of lower limbs and the effects of therapy in PD patients during FOG episodes.

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**Causes of withdrawal of duodenal Levodopa infusion in advanced Parkinson disease**

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*Introduction:* In the advanced Parkinson disease (PD) the burden of motor complications can be managed with device-aided therapies, such as deep brain stimulation (DBS), subcutaneous apomorphine infusions or duodenal levodopa infusions (DLI) [1]. There is insufficient information particularly on DLI, the most recently developed treatment [2]. We aimed to verify in a homogeneous group of patients the reasons and timing for DLI treatment withdrawal or discontinuation due to death.

*Methods:* We reviewed a series of 35 consecutive PD patients who underwent PEG tube insertion for DLI at the Carlo Besta Neurological Institute in Milan. The primary endpoint was to analyze causes of DLI withdrawal; the secondary was to evaluate the efficacy of DLI on motor complications.

*Results:* Mean age at PD onset was 54.4 ±9.4 years; DLI was started on average 12.3 ±3.9 years after onset and administered for 27.6 ± 22.6 months. At the end of the study, 21 patients (60%) were still on DLI, with a follow-up of 36.0 ±22.0 months. Efficacy analysis showed significant improvements for dyskinesia and off-period duration. Nine patients discontinued therapy, after a time lag of 11.3 ±15.7 months. The most common cause of withdrawal was peristomal infection. Five patients died, on average 17.4 ±9.1 months after implant, for different causes.

*Discussion:* These data confirmed that DLI allows a sustained reduction of off-periods and dyskinesia severity and duration, as documented previously [3,4]. The majority among the dropouts occurred within the first 14 months. Peristomal infection and worsening of dyskinesias were the most common causes, as noted in a previous work [5,6]. Dropout risk resulted independent from any of the variables considered. Nor strict selection criteria, excluding dementia, gastrointestinal disorders, insufficient level of compliance or accurate patient's management by a unique expert endoscopic surgeon team lowered the risk of adverse events in the post-operative phases.

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**P84****Double-blind, randomized, parallel group study to evaluate Peripheral Physical Neuro-Stimulation in Parkinson's disease**

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*Background:* Gait dysfunction is a cardinal feature of Parkinson's disease (PD) and significantly affects quality of life of patients. Previous studies showed that Peripheral Physical Neuro-Stimulation (PPNS) can improve gait performances of PD patients.

*Objectives:* The objectives of this study were to verify whether treatment with PPNS (GONDOLA®) is effective in reducing motor impairment in PD patients, and to investigate the effects of this treatment on Quality of Life.

*Methods:* 20 PD patients were included in our study and randomized in 2 groups: GONDOLA® therapy and SHAM GONDOLA. Every subject underwent a cycle of 8 stimulations with GONDOLA® or SHAM in 4 weeks (2 sessions per week). Clinical evaluations, that were performed at baseline (T0), after the 8 stimulations (T1) and after a washout period of 4 weeks (T2), included UPDRS part III, Hoehn and Yahr, Non Motor Symptoms Scale, Clinical Global Impression of Change Scale for Investigator (CGI-I) and Patient (CGI-P) and cognitive, quality of life, depression, gait performance assessments.

*Results:* Statistical analysis showed a significant improvement between T0 and T1 in UPDRSIII and Six Minute Walking test (6MWT) in the GONDOLA® stimulation group. No significant changes in UPDRSIII and 6MWT were found in the SHAM group. A statistically significant worsening of UPDRSIII score was found between T1 and follow up in the active stimulation group. No significant changes were found in the other clinical scales except for MoCA test and CGI-I.

*Conclusion:* The results of this pilot study show that PPNS improved Gait in PD patients. This treatment can implement rehabilitative procedures in PD. However, a multicentric study with a higher number of patients and Gait Analysis assessment of subjects is necessary.

**Effects of Tango dancing on spatiotemporal and kinematic gait parameters in Parkinson's disease: a Three-Dimensional Motion Analysis Study**

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*Background:* The basal ganglia may be selectively activated during rhythmic, metered movement such as tango dancing, which may improve motor control in individuals with Parkinson's disease. The purpose of this study was to compare the effects of tango, and no intervention on clinical and gait parameters of patients with Parkinson's disease (PD) by means of three-dimensional motion analysis study.

*Design:* This study employed a randomized, prospective, repeated measures design.

*Subjects/Patients:* Twenty people with mild-moderate PD participated.

*Methods:* Participants were randomly assigned to tango or no intervention (control) groups. After basal evaluation the study group attended 2-h classes once a week, completing 13 lessons in 13 weeks. Neurological status and spatiotemporal-kinematic gait parameters of the two groups were evaluated at study entry (t0) and at 13 weeks (t1, end of dancing training).

*Results:* At baseline evaluation the two groups did not differ on clinical features and gait parameters. At the end of dancing protocol, a significant improvement in both spatiotemporal and kinematic gait parameters and in UPDRS scores was observed in all treated patients as compared with baseline and controls.

*Conclusion:* Our preliminary findings showed that significant improvements in mobility and gait parameters of PD patients can be obtained through Tango dancing, with a parallel improvement in clinical status. As a consequence Tango may target deficits associated with Parkinson's and benefit locomotion. Quantitative motion analysis of gait pattern can be considered a useful tool to assess the efficacy of such motor interventions in patients affected by PD.

**Is it always convenient to start dopaminergic therapy in patients with Parkinson's disease immediately after the diagnosis? Case study about 10 patients never treated or treated with low doses of Levodopa with 10 years of follow-up**

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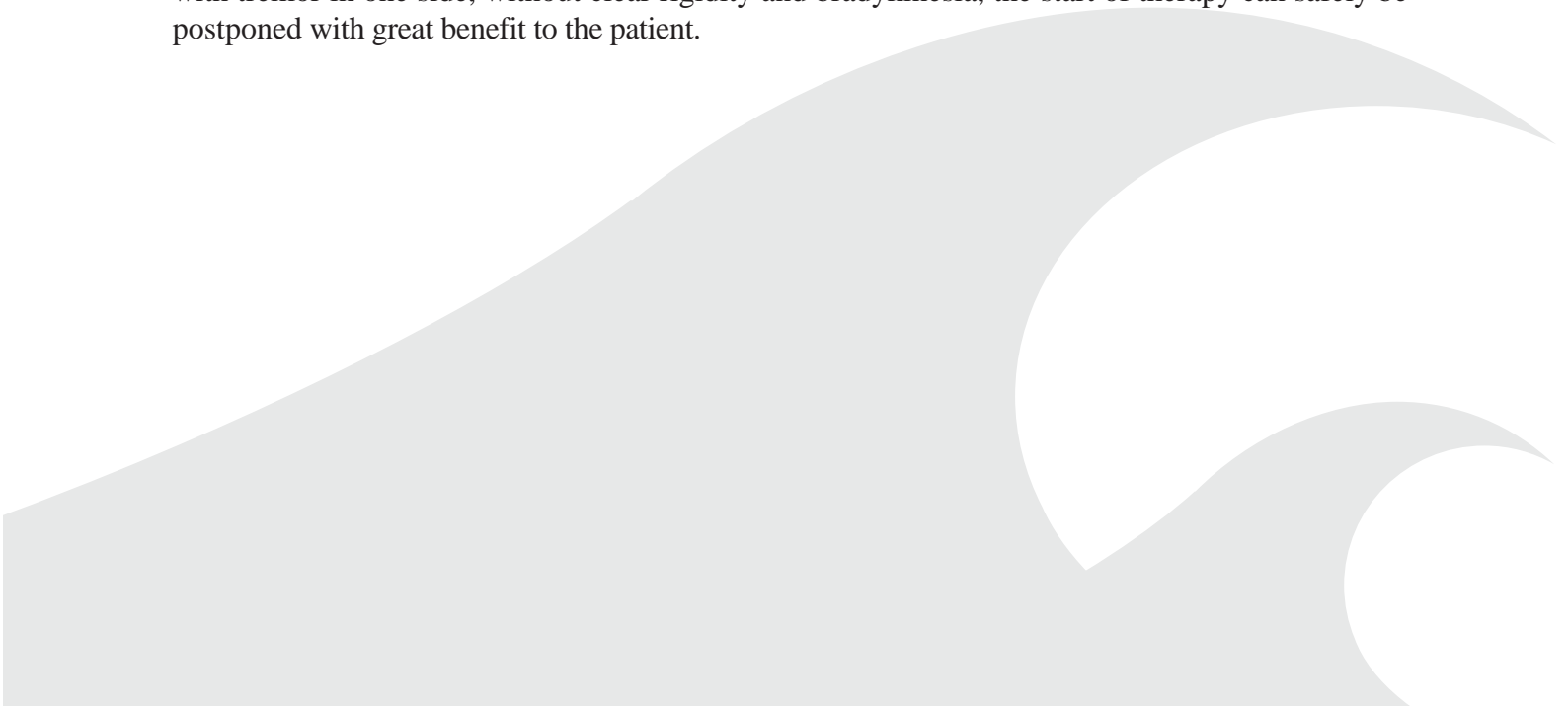
*Background:* It is now widely reported that patient suffering from Parkinson's disease (PD) should be treated with dopaminergic therapy immediately after the diagnosis.

*Design:* Although we consider this statement basically correct, based on our experience, we retain that this assumption is not always valid. Here we reported 10 PD patients never treated or treated only after several years with low doses of levodopa never exceeding in monotherapy 400 mg/day.

*Materials and Methods:* Among these 10 patients, 4 were females and 6 males, ranging between 63-82 years. At PD onset the degree of disability was between stage I and II of Hoehn/Yahr scale. None had psychiatric and/or cognitive disorders (MMSE = 24-30 range); SPECT was positive in four patients for an asymmetrical DAT deficit; four were positive for LRRK2 mutations. For all patients, the response to levodopa was clearly positive, six of these patients were treated with low doses of levodopa.

*Results:* After more than 10 years, none of these patients showed a significant progression of the disease (no one has slipped into a stage III H/Y scale); in the more aggressive forms only a slight increase of rigidity and bradykinesia in the affected side was observed. Nobody developed psychiatric and cognitive disorders (MMSE = 25/30). None of the patients treated with minute doses of Levodopa in monotherapy developed phenomena of wearing off, random on-off, dyskinesias and dystonia.

*Conclusion:* We are convinced that not all the parkinsonian patients must be treated since the first diagnosis with dopamine drugs, but that in some forms, which we think are benign, often occurring with tremor in one side, without clear rigidity and bradykinesia, the start of therapy can safely be postponed with great benefit to the patient.



**P87****Levodopa/Carbidopa intestinal infusion unusual complications: the experience of 3 Neurology Departments in North-West Italy***G. Gusmaroli<sup>1</sup>, M. Aguggia<sup>2</sup>, L. Scarzella<sup>3</sup>, K. Savio<sup>1</sup>, D. Barbagli<sup>1</sup>, P. Pastorello<sup>1</sup>, Mara Ravagnani<sup>1</sup>*<sup>1</sup>S.C. Neurologia, Ospedale degli Infermi, Biella, Italy<sup>2</sup>S.C. Neurologia, Ospedale Cardinal Massaia, Asti, Italy<sup>3</sup>S.C. Neurologia, Ospedale Valdese, Torino, Italy

*Introduction:* Levodopa/Carbidopa intestinal infusion represents one of the therapeutic options for advanced Parkinson's disease (PD) patients with motor fluctuations and dyskinesias unresponsive to other treatments. It relieves symptoms of advanced PD and it improves quality of life. The most common complications of levodopa/carbidopa intestinal infusion are related to the infusion device, especially intestinal tube dislocation, occlusion, kinking or looping. Other complications are peristomal infections, localized peritonitis, pneumo-peritoneum or hemo-peritoneum. Adverse events may be also related to levodopa/carbidopa infusion, such as acute psychosis, weight loss, polyneuropathy.

*Results:* Since 2007 72 patients underwent Levodopa/Carbidopa intestinal infusion in our Departments. Among complications, in our experience 5 patients had tube occlusion due to bezoars, one of them complicated by erosive duodenitis. One patient reported a mechanical injury due to camptocormia. One patients with sudden agitation, delusions of persecution, hallucinations, false recognition occurred, alternating with drowsiness, severe bradikinesia and then acute akinesia. Subclinical axonal polyneuropathy was present in over 60% of patients; in one case with weight loss of about 40 kg it was symptomatic and reversible.

*Conclusion:* Unusual and unexpected complications in course of Levodopa/Carbidopa intestinal treatment might be considered at the selection of candidates and during the follow-up.

**References**

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**Falls-related chronic subdural haematoma and acute intracranial haemorrhage in Sardinian parkinsonian and cognitively impaired patients: a retrospective study**

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*Objective:* Our aim was to determine, among a population with posttraumatic falls-related chronic subdural haematoma (CISH) or acute intracranial haemorrhage (AIH), whether patients affected by neurodegenerative disorders (parkinsonism and dementia) have a worse clinical outcome compared to age matched subjects.

*Methods:* Data of patients discharged from the Departments of Neurology/Stroke Unit/Neurosurgery/Intensive Care Unit at Brotzu General Hospital (Cagliari, Sardinia) between January 2010 and November 2013 and diagnosed with CISH and AIH, were reviewed. Patients with severe traumatism, evidence of spontaneous intracerebral bleeding or aged less than 40 years were excluded. Clinical status at admission and discharge was assessed by Modified Rankin Scale (mRS). We also calculate the time-lapse (days) between the trauma and the hospital admission.

*Results:* 286 patients were selected: 69 had a neurodegenerative disease (21 parkinsonism, 48 cognitively impaired). We found a significantly longer delay between trauma and time of diagnosis in patients with neurodegenerative diseases (X2 test  $p=0.00012$ ). This delay may account for the worse clinical conditions of neurological patients compared to controls at hospital admission (Mann-Whitney  $p<0.0001$ ). We also observed the lack of a significant variation in mRS score between admission and discharge in parkinsonian and demented patients (Wilcoxon test  $p=0,862$ ) unlike controls that showed a significant mRS score improvement during hospital stay (Wilcoxon test  $p=0.000$ ).

*Conclusion:* Parkinsonism and dementia are conditions that can significantly delay the diagnosis of CISH or AIH. Self-awareness patient's deficit and/or the potential overlapping between focal symptoms due to the intracranial bleeding and those of the pre-existing neurological condition are the main puzzling factors. The longer interval between the trauma and the hospital admittance may play a critical role in worsening the outcome of parkinsonian and cognitively impaired patients with respect to age-matched subjects after CISH or AIH.

**CSF biomarkers for the differential diagnosis and the evaluation of clinical impairment in idiopathic normal pressure hydrocephalus (iNPH)**

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*Introduction:* iNPH is characterized by dementia, gait disturbance and urinary incontinence associated to enlarged ventricular size with normal intracranial pressure. This classic phenotype may be mimicked by a subtype of Progressive Supranuclear Palsy (PSP); indeed autopsies revealed that a proportion of iNPH patients have other pathologies, as PSP or Alzheimer's Disease (AD).

*Objective:* Determining the CSF-biomarker profile of iNPH, to support the differential diagnosis among iNPH, PSP and AD and analyzing the relationship between the clinical features of iNPH and CSF-biomarkers values, to detect any markers of clinical impairment.

*Materials:* Four groups of patients: 15 iNPH, 12 PSP, 12 AD, 14 with non-neurodegenerative diseases (CTL) and corresponding CSF values of A $\beta$ 1-42, t-TAU and p-TAU.

*Methods:* CSF-biomarkers values were determined using an ELISA-assay and compared among the 4 groups. The iNPH patients have been rated with the MMSE, the domains for gait and continence of the iNPH scale, the Evan's Index (EI) for the ventricular enlargement; correlation values were obtained by comparing scores and CSF-biomarkers values.

*Results:* iNPH and PSP showed normal values of t-TAU and p-TAU, reduced levels of A $\beta$ 1-42. A $\beta$ 1-42 was indeed lower in iNPH, though in both diseases it was higher than AD. In iNPH, higher levels of t-TAU seem to have a correlation with lower MMSE scores. A significant correlation was found between EI and more severe gait impairment and cognitive decline, independently from the disease duration.

*Conclusion:* iNPH and PSP show a similar CSF profile of A $\beta$ 1-42, t-TAU and p-TAU, therefore, this panel of biomarkers is not useful in differential diagnosis between the disorders, that requires further diagnostic elements, to avoid unnecessary risks to patients candidates to a CSF-shunt. Our results also suggest that clinical impairment in iNPH is directly related to the ventricular enlargement rather than to CSF-biomarkers.

**Fahr's disease linked to a novel *SLC20A2* gene mutation manifesting with dynamic aphasia**

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*Background:* Idiopathic basal ganglia calcification (IBGC), also known as “Fahr’s disease”, is a rare disorder characterized by widespread cerebral calcifications, an autosomal dominant pattern of inheritance, clinical and genetic heterogeneity. The recently identified IBGC gene *SLC20A2* encodes for type III sodium-dependent phosphate transporter 2 and its loss-of function mutations may lead to the regional accumulation of inorganic phosphate in the brain, causing calcium phosphate deposition. The spectrum of *SLC20A2* mutations is limited with no clear genotype-phenotype correlations; moreover, no *SLC20A2* mutations have been reported in the Italian population so far.

*Objective:* To describe the clinical, neuroimaging and genetic findings in an Italian family with IBGC.

*Methods:* The family members underwent clinical and radiological examination in order to diagnose IBGC according to standard criteria, and screening for *SLC20A2* gene mutations. The affected subjects underwent also neuropsychological longitudinal assessments and functional neuroimaging investigations.

*Results:* The two affected family members harboured a novel missense mutation, G1618A, in *SLC20A2* gene, leading to gly540-to-arg (G540R) substitution in a highly conserved residue. This is the first *SLC20A2* gene mutation associated to fIBGC reported in the Italian population and is damaging according to all prediction programs. In the index case we observed a fair correlation between cortical areas with no calcifications but with significant hypometabolism at [18F]FDG-PET (inferior frontal premotor cortex) and the neuropsychological picture dominated by dynamic aphasia and buccofacial apraxia.

*Conclusion:* These findings expand the catalog of *SLC20A2* mutations identified to date and add dynamic aphasia to the spectrum of neuropsychological deficits reported in IBGC supporting the use of functional neuroimaging studies for better investigation of genotype-phenotype correlations.

**P91****The UP-TECH project, an intervention to support caregivers of Alzheimer's disease patients in Marche Region: preliminary findings on recruitment and caregiving burden in the baseline population**

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*Objective:* The paper describes recruitment results and characteristics of the UP-TECH clinical trial sample, including the level of care services use, informal caregiver burden and its determinants.

*Methods:* UP-TECH is designed to test innovative care solutions for community-dwelling patients with moderate stage Alzheimer's Disease and their caregivers in Marche Region. It aimed at randomizing 450 patient-caregiver dyads into three arms receiving different combinations of services, composed of case management interventions, nurse visits, assistive technology and educational brochures. The research nurses administered a questionnaire comprising an in-depth socio-demographic assessment and several clinical scales, such as Novak's Caregiver Burden Inventory. Analyses of baseline data were conducted using uni- and bi-variate statistics. Linear regressions were computed to identify de-confounded correlates of caregiver burden.

*Results:* 438 patient-caregiver dyads were recruited and randomized. In our sample, patients are predominantly women (71.5%), with an average age of 81.5 years and a mean Mini Mental State Examination of 16.2. Caregivers are mostly women (66.2%) and offspring (55.7%), with a mean caregiver burden score of 27.6.

They provide more than 50 hours of care/week, while receiving an almost negligible support from public services. Factors associated with caregiver burden are female gender, kinship and the patient's behavioral disturbances. The most important factor associated with lower burden is the employment of a live-in care worker.

*Conclusion:* The paper provides a comprehensive description of moderate stage Alzheimer's Disease patients and their caregivers, suggesting useful markers of caregiver burden. The well-balanced randomization assures the reliability of the study dataset for prospective evaluation of care strategies.

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**Treating apraxia in Corticobasal Syndrome: a transcranial direct current stimulation (tDCS) approach**

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*Introduction:* Corticobasal Syndrome (CBS) is a clinical entity characterized by higher cortical dysfunctions associated with asymmetric onset of levodopa-resistant parkinsonism, dystonia and myoclonus. One of the most typical and distressful features of CBS is limb apraxia, which is associated with parietal atrophy. Transcranial direct current stimulation (tDCS) is a non-invasive procedure of cortical stimulation, which represents a promising tool for cognitive enhancement and neurorehabilitation.

*Objective:* The aim of this study was to assess the effect of tDCS to the parietal cortex (PARC) on praxia abilities in CBS patients.

*Methods:* Fourteen patients with possible CBS and upper limb apraxia were enrolled. Each patient was subjected to three types of stimulation, i.e. tDCS over the right PARC, tDCS over the left PARC, and placebo tDCS, randomly performed. Anodal tDCs at 2 mA intensity, delivered for 7 minutes, was administered. Apraxia was assessed before and after each session using the De Renzi apraxia test.

*Results:* A significant improvement of De Renzi apraxia test score was observed after active anodal stimulation over the left PARC ( $P=0.0005$ ), while no significant effect was noticed over the right PARC ( $P=0.07$ ). By stimulating left parietal lobe, a significant improvement of praxis performances of both right (mean De Renzi improvement, real stimulation vs. sham,  $2.0\pm 1.6$  vs.  $-0.3\pm 2.9$ ,  $P=0.03$ ) and left ( $3.5\pm 2.8$  vs.  $0.1\pm 3.0$ ,  $P=0.01$ ) limbs was observed.

*Conclusion:* These results suggest that anodal tDCS applied over the left parietal cortex can modulate praxic abilities in CBS patients and might represent a promising tool for future rehabilitation approaches.

**Mapping regional grey and white matter damage in patients with progressive supranuclear palsy syndrome**

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*Introduction:* Progressive supranuclear palsy syndrome (PSPs) falls under the umbrella of frontotemporal lobar degeneration (FTLD) clinical spectrum. Pathological and neuroimaging studies revealed a severe white matter (WM) damage in syndromes with an underlying FTLD-tau pathology, such as PSPs.

*Objective:* To investigate the pattern of grey matter (GM) atrophy and WM microstructural damage in a patients with probable PSPs using MRI techniques.

*Methods:* We enrolled 21 patients (mean age:  $70 \pm 7.5$  years, 10 females) with probable PSPs and 21 age and sex-matched healthy controls. Patients underwent clinical and neuropsychological evaluation, and brain structural and diffusion tensor (DT) MRI. The regional patterns of brain GM atrophy and WM microstructural damage were assessed using voxel-based morphometry and tract-based spatial statistics, respectively ( $p < 0.05$  FWE).

*Results:* PSPs patients were in a moderate stage of disease (mean Hoehn and Yahr score: 3.3) and showed mild to moderate cognitive impairment involving especially attentive executive functions. PSPs patients did not show significant GM atrophy relative to controls. On the contrary, they showed a significant reduction of fractional anisotropy and a significant increase of mean, axial and radial diffusivities in the main WM tracts bilaterally, including body and splenium of corpus callosum, cingulum, inferior frontooccipital, superior longitudinal and uncinate fasciculi, anterior and superior corona radiata, corticospinal tract, and thalamic radiations. Superior cerebellar peduncles and internal capsules showed a significant increase of diffusivity values, but no FA changes.

*Conclusion:* In PSPs patients, WM microstructural damage is prominent compared to GM atrophy even in the moderate stage of the disease, suggesting that diffuse WM damage in tauopathies is not merely a function of disease severity. Regional differences in DT MRI metrics might reflect a different vulnerability of WM tracts. Our finding might provide new insight in understanding the pathophysiology of the disease and the clinical progression.

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**A rare case of neurodegeneration with brain iron accumulation**

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*Introduction:* Aceruloplasminemia is an autosomic recessive disorder of iron metabolism resulting from absence of ceruloplasmin (Cp) due to mutations of ceruloplasmin gene. Cp is a glycoprotein which carries copper and plays a crucial role in the mobilization of iron from tissues. Iron deposition is proposed to cause tissue injuries through the generation of free radicals. The classical clinical triad is diabetes, retinal degeneration and neurological disorder.

*Case Report:* A 50-year-old male outpatient was admitted in our hospital with a three years history of language disorder, gait impairment and mild parkinsonism. The patient's medical history was characterized by diabetes since 30 years old and sideropenic anemia. GRE T2\*-weighted MRI showed a severe hypointensity involving bilaterally midbrain, dentate nuclei and basal ganglia. Laboratory findings showed normocytic anemia; low serum iron and copper concentration; high serum ferritin; ceruloplasmin was undetectable. Sequence analysis of the CP gene has been performed. When the clinical diagnosis of aceruloplasminemia was established, treatment was initiated with deferasirox, during which time there was a mild improvement in the neurological symptoms and a significant reduction in ferritin levels.

*Conclusion:* Reports of single cases suggest that iron chelation therapy can slow the neurodegeneration in aceruloplasminemia. It seems rational to suggest that treatment should be started early in the course of the disease to remove iron before it induces neurodegeneration. Patients presenting with cognitive impairment, a movement disorder, retinal degeneration and diabetes should be screened for aceruloplasminemia by simple blood tests (blood count, Cp levels, and ferritin) and MRI scanning before molecular genetic testing.

**Subacute parkinsonism after correction of severe hyponatremia, without myelinolysis: description of a case**

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*Introduction:* Rapid correction of hyponatremia can be associated with non-inflammatory demyelination located in the pons (Central Pontine Myelinolysis-CPM) and/or in extrapontine regions (Extrapontine Myelinolysis-EPM). EPM is a rare cause of parkinsonism responding to dopaminergic therapy. MRI is the most useful examination for visualizing demyelinating lesions.

*Objective:* To describe the case of a patient who developed subacute parkinsonism after correction of severe hyponatremia but without evidence of CPM or EPM.

*Patient:* A 70-years-old woman was admitted to the Department of Medicine of our Hospital because of persistent vomiting. Blood examination showed severe hyponatremia (105 mEq/l).

The patient was treated with isotonic saline and, because of vomiting, only a vial (10 mg) of Metoclopramide was administered. Sodium concentration increased but, after a few days, she suddenly developed hypomimia, limb and axial rigidity, moderate bradykinesia, gait disturbances. UPDRS-Sez.III score was 29.

Brain MRI and [<sup>123</sup>I]FP-CIT SPECT were performed: [<sup>123</sup>I]FP-CIT SPECT showed decreased striatal dopamine transporter binding, but brain MRI did not show any extrapontine demyelination.

The patient was treated with levodopa 300 mg/day with rapid improvement of parkinsonism.

After a month the UPDRS-Sez.III score was 17 and after 6 months was 11.

*Discussion:* This case is interesting because:

1. *The subacute onset of parkinsonism is subsequent to development of hyponatremia and its rapid correction, but it's not related to evident EPM.*
2. *Hitherto only two studies investigated striatal presynaptic dopaminergic transporter in parkinsonism subsequent to hyponatremia (with EPM) using DaT-SPECT (with <sup>99c</sup>Tc-TRODAT-1 and [<sup>123</sup>I]IPT respectively).*

So some questions arise from the study of these case:

- Could hyponatremia have only highlighted an underlying PD?
- Could hyponatremia have all the same produced a damage of GB, unusually not detectable by MRI, but sufficient to lead to the onset of parkinsonian signs?
- Could the low dose of Metoclopramide administered have played a role in the onset of symptoms?



## Myocardial I-123 MIBG Scintigraphy in *Parkin* heterozygous and homozygous/compound heterozygous patients

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**Objective:** Myocardial I-123 metaiodobenzylguanidine (MIBG) scintigraphy has been usually reported abnormal in Parkinson's Disease (PD), suggesting a postganglionic sympathetic denervation.

Recently, it has been reported that MIBG uptake is normal in patients with *Parkin* gene mutations. Our aim was to evaluate cardiac autonomic innervation in *Parkin* compound heterozygotes or homozygotes (HOM) and heterozygous (HET) parkinsonian patients, in comparison to patients with idiopathic PD (IPD).

**Patients and Methods:** MIBG scintigraphy was performed in 4 HOM patients (3 M and 1 F), 5 HET patients (3 M and 2 F), 8 IPD (6 M and 2 F) and 9 control subjects (5 M and 4 F) by I-123 MIBG imaging. A 10-minute planar image of the anterior thorax was obtained 15 minutes (early image) and 3 hours (late image) after intravenous injection of I-123 MIBG. Myocardial MIBG uptake was semi-quantified by calculating heart-to-mediastinum (H/M) ratio after drawing regions of interest over the entire heart and upper mediastinum on early and late images.

**Results:** Early and late H/M ratio of I-123 MIBG uptake was normal in 3/4 HOM group (75%), in 2/5 HET (40%) and in 1/8 IPD (12%). Proportion of patients with normal I-123 MIBG uptake was higher in HOM cases ( $p = 0.06$ ).

**Conclusion:** Recent studies conducted in a few patients with *Parkin*-associated parkinsonism showed preserved cardiac MIBG uptake. This finding has been related to the absence of Lewy body pathology. To date, the role of heterozygous *parkin* mutations in the pathogenesis of PD is controversial and it is unclear if a single mutation represents a risk factor for the disease development or a coincidental finding. Our study confirms that cardiac I-123 MIBG uptake is normal in most HOM cases compared with IPD, whereas HET patients are in between. Extension of the study on a larger series of cases is needed to define if single *parkin* mutation carriers share a similar pathogenetic substrate of *parkin* patients.

## **Pallidal stimulation for acquired dystonia due to cerebral palsy: beyond five years**

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**Background:** There is increasing evidence that deep brain stimulation (DBS) of the globus pallidus internus (GPi) is effective in patients with idiopathic or inherited generalized dystonia.

There is comparatively less experience about the effects of GPi DBS on acquired dystonia, particularly dystonia due to cerebral palsy (DCP). Clinical and demographic outcome predictors for DBS in dystonia syndromes are also poorly defined. We aimed to examine the efficacy and safety of GPi DBS for the treatment of generalized DCP.

**Methods:** We studied 15 patients with DCP, up to 6.2 years after DBS surgery. Only mild limb spasticity or mild static brain MRI abnormalities were acceptable for inclusion. Dystonia severity and disability was assessed by the Burke-Fahn-Marsden dystonia rating scale (BFMDRS) and health-related quality of life by a validated Italian version of the medical outcomes study 36-item short-form (SF-36) general health survey questionnaire. The amount of energy delivered was calculated, adverse events and side effects were collected.

**Results:** At last FU, BFMDRS motor score improved on average by 49.5% and BFMDRS disability score improved on average by 30%; SF-36 improved in most patients. Age at implant, age at onset and disease duration did not correlate to outcome, while higher preoperative dystonia severity and occurrence of spasticity were associated to poorer outcome. The patients received a stable amount of energy after the first two years after the implant and throughout all the observation period. There were few serious adverse events or side effects.

**Conclusion:** In this series, GPi DBS provided a sustained improvement of motor symptoms starting from 2 years after implant. All the patients had severe dystonia without cognitive impairment and some had mild static brain MRI abnormalities. The outcome was encouraging in the majority of DCP patients, with a stable motor and functional outlook and a good safety profile.

## Fluctuating hemifacial spasm in Melkersson-Rosenthal syndrome

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*Introduction:* Melkersson-Rosenthal syndrome (MRS) is a rare neuro-mucocutaneous granulomatous disorder of unknown etiology, characterized by recurrent facial palsy (FP), fissured tongue, and orofacial edema with noncaseating granulomas on skin biopsy.

Comorbidities among those with facial edema included periodontal disease, allergic disease, Crohn's Disease, migraine headaches, and systemic lupus erythematosus [1].

*Case Description:* We report the case of a 50-year-old woman with right atypical hemifacial spasm (present for about 15 years, fluctuating, with long period of remissions), sub-continuous from 2 months prior to the admission to our Clinic. At the examinations orofacial edema and fissured tongue was present. Her medical history was positive for recurrent episodes of trigeminal neuralgia, peripheral FP, and migraine headaches. Results of routine hematologic tests were normal as well as the screening for autoimmune and infectious conditions. CSF analysis, brain MRI and MRA were normal, total-body CT showed reactive lateral cervical and submandibular lymphadenopathy. EMG showed right hemifacial spasm and conduction block of the left facial nerve. Labial skin biopsy showed infiltrating lymphocytes. The patient had already been treated with oral steroid therapy for 2 months. Carbamazepine (600 mg daily) was effective for HFS.

*Conclusion:* This is the first case of fluctuating HFS in patient with MRS. A progressive axonal degeneration can exert HFS due to abnormal reinnervation and episodes of demyelination [2].

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### Long-term evaluation of onabotulinum toxin A dosage in hemifacial spasm

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*Background:* Botulinum toxin A (BTA) is the first-choice treatment for hemifacial spasm (HFS). To date, only a small number of studies have monitored the amount of BTA treatment in HFS over time.

*Aim:* To evaluate the variability of BTA dosage required over time to achieve relief for 3 months in HFS patients.

*Patients and Methods:* In this retrospective longitudinal study performed in a neurological outpatient clinic, data were retrieved from patient files. Thirty-nine patients with HFS, who were treated for the first time with BTA injections, were followed up for 2 years (8 consecutive treatments). All patients received one treatment each 3 months, and both total dosage and number of treated muscles modified in time to obtain the best clinical result (relief from symptoms and no adverse reactions). The main outcome measures were the changes in effective total dose administered along 2 years treatment. A follow-up was performed by subjective (HFS-7 items) and objective (SMC grading system for HFS) assessment.

*Results:* 39 patients (mean age: 70,27 ys, 51,28% were male, mean disease duration: 9,81 ys) had the long-term evaluation. The mean HFS-7 and SMC remained stable during the follow-up and were 7,23 (0-21) and 2,85 (1-4) respectively. The mean dose changed from the first to the 8th treatment from 9,06 (4-15) U to 12,2 (5-25) U. A constant increase of the dose in time was also observed, with the minimum and maximum rate reached at the 6th (5,05%) and 2nd (22,38%) treatment respectively. The average number of sites changed from 6,08 (4-13) to 6,51 (3-10), with both minimum and maximum number of muscles injected at 4th treatment (2-13).

*Conclusion:* Our retrospective study showed an increase of the BTx dosage of 12.22% over two years to achieve 3 months of symptomatic relief.

**P100****Objective evaluation of Levodopa motor response in multiple system atrophy: a kinetic-dynamic approach**

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*Background:* A poor Levodopa (LD) response is a hallmark of probable Multiple System Atrophy with predominant parkinsonism (MSA-P), while a good response is diagnostic for Parkinson's disease (PD). However, attempts to quantify the extent of LD response in MSA-P compared with PD are scanty.

*Objective:* To evaluate Levodopa responsiveness in MSA-P vs PD patients under chronic LD therapy by a standardized kinetic-dynamic test.

*Methods:* Patients were challenged with a fasting morning dose of 100 or 125 mg of LD plus benserazide or carbidopa and underwent kinetic-dynamic LD monitoring based on simultaneous serial assessments of plasma LD concentration and finger tapping speed up to 3 hours post dosing. We evaluated LD pharmacokinetics (peak, time to peak plasma concentration and area under the plasma concentration–time curve) and pharmacodynamics (latency and duration of motor effect, maximum percentage increase in tapping speed over baseline values-TapI and the overall extent of tapping response by the area under the tapping effect–time curve-AUC<sub>TapE</sub>).

*Results:* 16 MSA-P (11 men) and 31 PD (20 men) patients matched for age, PD symptom duration and LD therapy duration were included in the study. LD pharmacokinetics did not differ between the two groups. A TapI > 20% was observed in all PD (range 21-94%) and in 4 MSA-P patients (range 20-40%). In the remaining MSA-P patients TapI was TapE value observed for PD (1900 taps/min). With the combined estimation of TapI and AUC<sub>TapE</sub> overlapping between PD and MSA-P was observed only for one MSA-P patient.

*Conclusion:* MSA-P patients may respond to a subacute low LD test dose but the overall extent of the effect is markedly lower compared with PD patients. The combined estimation of TapI and AUC<sub>TapE</sub> may help the clinician in the differential diagnosis between these diseases.

**P101****Rotigotine as a promising therapeutic tool in atypical parkinsonism syndromes: a 24 months pilot observational open-label study**

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*Introduction:* Rotigotine (RTG) is a non-ergot dopamine agonist developed as a new transdermal formulation, and it is indicated for use in early and advanced Parkinson's disease (PD). The potential advantages of the RTG patch include immediacy of effect onset, constant drug delivery, better tolerability avoiding drug peaks and easy of use, helping patient's compliance. Based on this, RTG patch appears to be a suitable candidate in the treatment of patients with atypical parkinsonism.

*Objective:* The present is an observational study to evaluate the efficacy and tolerability of RTG in patients affected by atypical parkinsonian disorders.

*Methods:* 61 subjects with diagnosis of atypical parkinsonian disorders were treated with transdermal RTG. Diagnosis was: Parkinson disease with dementia, multiple system atrophy parkinsonian type, multiple system atrophy cerebellar type, progressive supranuclear palsy, cortico-basal degeneration, Lewy body dementia and fronto-temporal dementia with parkinsonism. Patients were evaluated by UPDRS-III, NPI, MMSE and adverse events (AEs) were recorded.

*Results:* Patients treated with RTG show a overall decrease of UPDRS III scores without increasing behavioral disturbances. Main adverse events (AE) were hypotension (14 patients), nausea (13), vomiting (5), drowsiness (5), tachycardia (2) dystonia (3 patients, all treated with concomitant l-dopa). On the whole, 16 patients were affected by AE and 7 patients suspended RTG treatment due to AE (vomiting, tachycardia and sleepiness).

*Conclusion:* In our population transdermal RTG seems to be effective and well tolerated. Due to its system of drug delivery, RTG appears to be a suitable therapy in elderly patients as it has a good tolerability profile, improves patient's compliance and helps management of fragile patients.

**P102****Clinical and cognitive correlations of microstructural changes in progressive supranuclear palsy**

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*Introduction:* Progressive supranuclear palsy (PSP) is a late-onset neurodegenerative disorder characterized by motor and cognitive deficits. In patients with PSP, previous reports have shown a severe white matter (WM) damage involving supra and infratentorial regions including cerebellum. In the present study, we investigated potential correlations between WM integrity loss and clinical-cognitive features of patients with PSP.

*Methods:* By using magnetic resonance imaging and diffusion tensor imaging with tract based spatial statistic analysis, we analyzed WM volume in 18 patients with PSP and 18 healthy controls (HCs). All patients and HCs underwent a detailed clinical and neuropsychological evaluation.

*Results:* Relative to HCs, patients with PSP showed WM changes encompassing supra and infratentorial areas such as corpus callosum, fornix, midbrain, inferior fronto-occipital fasciculus, anterior thalamic radiation, superior cerebellar peduncle, superior longitudinal fasciculus, uncinate fasciculus, cingulate gyrus, and cortico-spinal tract bilaterally. Among different correlations between motor-cognitive features and WM structural abnormalities, we detected a significant association between frontocerebellar WM loss and executive cognitive impairment in patients with PSP.

*Conclusion:* Our findings, therefore, corroborate the hypothesis that cognitive impairment in PSP may result from both “intrinsic” and “extrinsic” frontal lobe dysfunction, likely related to cerebellar disconnection.

**P103****Syringomyelia and Arnold-Chiari type I malformation presenting with head tremor***Sonia Mazzucchi, E. Unti, F. Baldacci, U. Bonuccelli, R. Ceravolo*

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*Introduction:* A 53-year-old woman came to our attention complaining head tremor, appeared almost one year before and progressively worsening, more recently associated to left arm resting and action tremor. Her family history was positive for Parkinson's Disease. She did not complain of bradyknesia or gait disturbances.

*Methods:* Neurological examination was normal except for negative head tremor with minimal left head shift (lack of sensory tricks, no worsening with head movement) and slight rest and postural tremor involving left arm; muscle tone was normal. Serum PTH, copper, ceruloplasmin and thyroid function were normal. Electrophysiological recording demonstrated postural head tremor (7-8 Hz) associated to spontaneous firing of MUPs in the sternocleidomastoid muscles particularly in the right one. Her brain and cervical MRI demonstrated Arnold-Chiari type I malformation associated with a notable syringomyelia involving the spinal tract from C4 to D1 for which surgical correction was recommended. She was started on Clonazepam with partial clinical benefit. Syringomyelia, frequently associated to Arnold-Chiari I malformation, sometimes can cause involuntary movements; the largest case series in literature have reported movement disorders in 22% of patients affected by syringomyelia, mainly represented by arm/finger dystonia, hand tremor (uni/bilateral), torticollis, blepharospasm, myoclonus, athetosis, abnormal head, shoulder and arm postures. The main hypothesis is that a central spinal cord lesion could predispose to spinal motor neuron hyperexcitability leading to involuntary movements.

*Conclusion:* Our report confirms the importance to perform cervical MRI besides brain MRI in patients with head tremor to exclude secondary causes, particularly when electrophysiological recording suggests a possible dystonic pattern. To our knowledge this could be the first case of head tremor secondary to syringomyelia and Arnold Chiari type I malformation however, follow-up after surgery will be crucial to better understand the ethiological relationship between radiological findings and head tremor.



### Rotigotine in tetrahydrobiopterin deficiency: a case report

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Tetrahydrobiopterin (BH4) is a fundamental cofactor for the enzymatic hydroxylation of aromatic aminoacids. BH4 deficiency is a rare metabolic disorder, causing psychomotor development delay and parkinsonian symptoms. An early replacement therapy, including L-dopa, is a therapeutic milestone [1]. Recently, the use of dopamine-agonists has been proposed to reduce levodopa-induced complications [2].

We present the case of a 24-years-old male affected by BH4 deficiency, who came to our attention with the following treatment: BH4, 5-hydroxytryptophan, L-dopa/carbidopa 225/56.25 mg/day, entacapone 1000 mg/day, selegiline 7.50 mg/day. Two years before, he underwent pramipexole therapy, then withdrawn because of the occurrence of dyskinesias and dystonias.

Neurological examination showed postural/kinetic tremor, mild bradykinesia, sporadic dyskinesias and early-morning dystonia. MDS-UPDRS-III score was 12/8 (OFF/ON-condition). His DaTSCAN-SPECT was normal. In the attempt to arrange a more feasible therapy he interrupted entacapone and selegiline, starting a combined therapy with rotigotine extended-release 6 mg/day and L-dopa/carbidopa 100/25 mg/day, with an improvement of parkinsonian symptoms (MDS-UPDRS-III (ON-condition)=3), and a reduction of the early-morning dystonia. Three months later, he experienced painful dystonias and dyskinesias of right foot and trunk: rotigotine was interrupted and previous therapies restored, with a prompt resolution of side effects.

This first description of a BH4-deficient patient treated with rotigotine confirms previous efficacy data on pramipexole [2]. However, our patient developed the same complications already experienced with pramipexole.

The molecular mechanisms of dyskinesias in parkinsonian patients involve aberrant synaptic plasticity and loss of dopamine storage capacity [3,4]. Nevertheless, our patient had normal dopamine storage capacity and an intact anatomical substrate. Despite being on long-term L-dopa therapy, he never experienced motor complications, except for mild dyskinesias. Both pramipexole- and rotigotine-induced dyskinesias/dystonias could be explained by an overstimulation of D3 receptors [5] and by the additive effect of dopamine-agonists and L-dopa, which could enhance motor complications [6], especially on a receptor pool imbalanced by long-term L-dopa treatment.

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**P105****Subacute and reversible progressive supranuclear palsy-like phenotype in a patient with pontine/extrapontine myelinolysis**

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*Background:* The so-called "osmotic demyelination syndrome" unifies the classical definition of "central pontine myelinolysis" and "extrapontine myelinolysis" and refers to several clinical scenarios, included extrapyramidal involvement. A PSP-like phenotype due to osmotic demyelination syndrome has never been described.

*Methods:* A 64-years old woman was admitted to the Emergency Department of S. Camillo de Lellis Hospital complaining the subacute appearance of gait impairment with imbalance and generalized slowing of movements. She was regularly taking acetazolamide for glaucoma and during the preceding week had suffered for a flu-like syndrome with fever, vomit and constipation, treated with domperidone and sodium picosulphate. General examination and vital signs were normal. Neurological evaluation revealed a severe rigid-akinetic symmetric parkinsonism with marked axial and mild appendicular involvement, impairment of attention, hypomimia, dysarthria, hypophonic and monotonous speech, paralysis of downgaze and resting tremor of tongue. No pyramidal or cerebellar signs were observed. Consciousness was preserved. Brain CT was normal. Blood exams revealed severe electrolyte imbalance (sodium 103mEq/L, potassium 1.9mEq/L, chlorine 72mEq/L, phosphorous 1.1mEq/L), instead general parameters were normal. Although the recommendation of a slow correction, sodium imbalance was rapidly normalized. MRI revealed DWI/ADC lesions in cerebral cortex and FLAIR hyperintensity in pons and bilateral putamen and caudate. Neurological condition gradually improved and after several days patient was discharged, reporting mild hypomimia, moderate axial bradykinesia, tremor of tongue and an apathetic syndrome. Six months later, neurological examination revealed only slight cogwheeling at the elbows while RMN showed slight FLAIR hyperintensity of pons and precentral gyri.

*Conclusion:* Flu-like syndrome and iatrogenic effect together produced the electrolyte imbalance and as a consequence the osmotic state, responsible for the cortical and subcortical demyelination. A subacute PSP-like phenotype could be caused by osmotic demyelination syndrome. The severity of this condition requests an extremely careful clinical management.

**P106****Social cognition and oxytocin in Huntington's disease: evidences from a preliminary study**

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*Introduction:* Impaired social behavior, partly related to altered perception of emotions, is commonly reported in Huntington's disease (HD). Over the past few years the role of oxytocin (OT) as social hormone has been proposed and it is supported by the improvement of recognition of the expression of the faces after administration of intranasal OT.

*Objective:* To investigate social cognition in HD and to evaluate the role of OT in mediating this cognitive domain.

*Methods:* 13 patients with symptomatic HD and 11 controls, matched for age and educational level were investigated for social cognition. The basal levels of OT were analyzed in the whole cohort of subjects and the relationship between the basal levels of OT and social cognition was also investigated.

*Results:* HD patients, with respect to controls, showed cognitive impairment expressed by Montreal Cognitive Assessment (MoCa) and Frontal Assessment Battery (FAB) ( $p < 0.01$ ), lower performance in social cognition particularly in Faux pas test and Strange Stories, and in recognizing negative emotions from face expression (KDEF scale) and verbal emotions ( $p < 0.05$ ,  $p < 0.01$ ). Better cognitive performance, assessed by the MoCa, well correlates in patients and in controls with better performances on social cognitive tests. OT levels did not differ in the two populations, however with a trend for lower values HD (average  $9.9 \pm 7.2$  controls,  $6.5 \pm 2.4$  HD). Regression analysis showed that the model constituted by MoCa scoring, and blood OT levels was able to explain 54% about the variability of KDEF in the general population ( $p < 0.05$ ) and 74% in HD population ( $p < 0.01$ ).

*Conclusion:* The present study, albeit limited by small sample size, shows a clear impairment of social cognition in HD, particularly represented by difficulties in perception of face expressions, which resulted dependent on both cognitive impairment and blood OT levels.

**P107**

### **Different clinical presentation of intracranial calcifications**

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*Objective:* To report different clinical phenotypes of patients with intracranial calcifications (IC) of various aetiology.

*Background:* IC can be due to Fahr's disease, a neurodegenerative disorder with involvement of both basal ganglia and dentate nuclei, or be secondary to hypocalcemia, SCA20, coeliac disease, MELAS, MERRF and cerebral infections.

*Methods:* Three patients with basal ganglia and cerebellar calcifications on CT scan were reviewed. Blood tests and genetic analyses were carried out.

*Results:* Patient 1, an 81-year old woman, presented with acute onset confusional state and visual hallucinations. Neurological examination revealed cognitive impairment, disorientation and confusion. The patient showed short stature, also observed in her daughter and her 22-year old nephew, whose CT scan at age 20 also showed IC despite being clinically unaffected. Genetic analysis revealed a heterozygous mutation in exon 10 of *SCL20A2* gene (c.1765G>A; p.G589R). Other family members are currently being tested. Patient 2, aged 79, presented with syncope and had a history of thyroidectomy with post-surgical hypoparathyroidism on chronic calcium replacement therapy. Neurological examination revealed mild bradykinesia in the left upper limb and a mild ataxic gait. Blood tests revealed severe hypoparathyroidism consistent with imaging findings (severe basal ganglia and cerebellar calcifications). Patient 3, aged 31, complained of short-lasting generalized dystonic attacks since age 13, triggered by sudden movements or prolonged physical exercise, worsened in the last years with spreading to tongue muscles. Hypocalcemia (5.8 mg/dl) was detected on blood tests and hormonal assessment was consistent with pseudohypoparathyroidism. Therapy with Carbamazepine 200 mg/day abolished the attacks. Genetic analysis for *SLC20A2*, *PRRT2*, *MR1* revealed no mutations.

*Conclusion:* IC can present with variable age at onset and clinical phenotypes including paroxysmal movement disorders. A possible new phenotype of Fahr's disease due to *SLC20A2* mutations including short stature and late onset neuropsychiatric symptoms is herein reported for the first time.

**P108**

**Cardiovascular autonomic testing is useful in differentiating MSA-P from PD at an early stage**

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*Background:* Differential diagnosis between MSA-P and PD is challenging for prognosis and treatment and arduous before the appearance of other features diagnostic for MSA. Early occurrence of autonomic failure would suggest the diagnosis of MSA but previous studies showed that cardiovascular tests do not differentiate MSA-P from PD.

*Objective:* To evaluate whether a battery of cardiovascular autonomic tests (Ewing's battery, EB) is useful in differentiating multiple system atrophy with predominant parkinsonism (MSA-P) from Parkinson's disease (PD) at an early stage of the disease.

*Methods:* Ninety-nine patients with a parkinsonian syndrome of uncertain diagnosis, who performed EB during the first assessment and were subsequently evaluated at least once a year during the disease course, were included. Thirty-four patients were eventually diagnosed with MSA-P (disease duration =  $3.2 \pm 2.0$  years; follow-up =  $3.5 \pm 2.3$  years), 65 with PD (disease duration =  $2.9 \pm 2.3$  years; follow-up =  $6.2 \pm 4.9$  years). Thirty-eight controls matched for age and sex were also included. EB consisted of: head-up tilt test, Valsalva manoeuvre, deep breathing, and sustained handgrip performed according to standardized procedures. Correct execution and results were checked and obtained automatically. Test results were compared between controls and patients. Discriminant analysis was performed for each test and for the whole battery to identify MSA-P or PD patients.

*Results:* Orthostatic hypotension was found in 22 patients with MSA-P and 3 patients with PD. Autonomic indices of cardiovascular reflexes were significantly more affected in MSA-P compared to PD ( $p < 0.0001$ ) and controls. Milder differences were also found between PD and controls. The EB allowed us to correctly identify 31/34 MSA-P and 61/65 PD patients.

*Conclusion:* EB classifies correctly 91% of MSA-P and 94% of PD before a diagnosis with current consensus criteria is achieved, suggesting that EB might improve the accuracy of current diagnostic criteria in the differential diagnosis between MSA-P and PD.

**P109**

**A subtle mimicker in emergency department: acute drug-induced dystonia**

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*Objective:* To report two cases of acute oro-mandibular dystonia, resulting from haloperidol occasional intake, misinterpreted in emergency room (ER).

*Case Reports:* A 49-year-old woman was referred to the ER because of sudden appearance of severe involuntary tongue protrusion. After two minutes of continuous tongue protrusion, spastic masseter contraction appeared for one minute. These clinical features recurred several times during the examination. The disorder was interpreted as dystonia and was successfully treated with diazepam 10mg i.v.. The day after admission to the ER, patient finally revealed that a few hours before the onset of dystonia she had felt anxious and had taken unspecified dosage of haloperidol prescribed to her mother. She reported to have taken haloperidol also before the onset of a similar episode occurred eighteen months before, spontaneously resolved and interpreted in ER as tongue angioedema. A 29-year-old man affected by anxious depressive syndrome, referred to the ER with painful and involuntary masseter spasm with gnashing of teeth and jaw involuntary closure, appeared during dinner with his family. The psychiatrist interpreted the clinical features as a manifestation of conversion disorder. In those days, patient had presented paranoid delusions. Therefore, in the 24-hours prior to ER admission, he had taken haloperidol (2% 10+10+30 drops), prescribed by the specialist of the mental health center. The neurologist diagnosed acute drug-induced dystonia, haloperidol was stopped and treatment with diazepam 10mg i.v. and chlorhydrate-bipéridène 4mg daily led to healing.

*Conclusion:* These are two examples of acute drug induced oro-mandibular dystonia, both subsequent to occasional haloperidol intake. Approximately only 10% of acute dystonias appears in the first hours after treatment, 90% within the first three days. In the management of acute dystonias an accurate drug history is necessary. Acute dystonic reaction represents a serious challenge for ER because of the high probability of misdiagnosis, which may delay intervention.

**P110****Primary lateral sclerosis can mimick atypical parkinsonisms: two case reports***Giovanni Palermo, C. Del Gamba, S. Gori, R. Ceravolo, U. Bonuccelli*

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*Introduction:* Primary lateral sclerosis (PLS) is a rare variant of motor neuron disorders, characterised by spasticity, hyperreflexia and mild weakness, due to upper motor neuron degeneration. The symptoms onset can be so slowly progressive and insidious that it can occasionally results in misdiagnosis of PLS as an atypical parkinsonism.

*Materials and Methods:* We describe two cases initially suggestive for an atypical parkinsonism and subsequently found to have features consistent with PLS. In both, unilateral limb slowness or clumsiness was the initial complaint, associated with impaired balance and falls. At onset, on the basis of the asymmetrical presentation of a prevalent limb stiffness and slowness with hand clumsiness in one, and the presence of pyramidal signs and autonomic dysfunction in the other, associated to an ineffective trial of dopaminergic treatment, it was proposed a diagnosis of CBD (case 1) and MSA (case 2), respectively. Both developed dysarthria, dysphagia and urinary urgency and, eventually, they revealed brisk reflexes with spasticity, extensor plantar response and ankle clonus. Neither atrophy nor fasciculations were observed. Finger tapping was slow but without decrement or fatiguing. Lumbar and cervical somatosensory evoked potentials were normal as well as nerve conductions studies, EMG (limbs, tongue), brain and cervical spine MRI and DaTSCAN. In case 1, FDG-PET showed decreased glucose uptake in the fronto-parietal regions, especially in the precentral gyrus. In both motor evoked potential showed marked reduction in amplitude in arms and legs, bilaterally.

*Conclusion:* The diagnosis of PLS was based on a clinical picture of a progressive pyramidal syndrome, previously excluding other secondary causes. Slowness of movements and postural instability can sometimes mislead clinicians suggesting a parkinsonian syndrome, while we have to consider them as a possible presentation of spasticity. Our report confirms the possibility that motor neuron disorders can mimic an atypical parkinsonism.

**P111**

### **Memantine vs Rivastigmine in Parkinson's Disease Dementia**

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The involvement of cholinergic deficits in Parkinson's disease dementia (PDD) has been established, and cholinesterase inhibitors could play a beneficial action improving the clinical courses by lowering the choline degradation. Not all patients respond or can tolerate cholinesterase inhibitors. On the other hand Memantine seems to be better tolerate and can be useful acting on the glutamate level.

To compare Memantine and Rivastigmine over global cognitive performances and behavioural features in PDD patients during chronic treatment.

We analysed 70 PDD outpatients, from 2010 until 2013. The diagnosis of PDD followed the clinical diagnostic criteria for dementia associated with Parkinson's disease as outlined in the 2007 MDS-Task Force publication. 40 patients at the time of diagnosis of Dementia (baseline) began treatment with Rivastigmina 4.6 mg/24 transdermal patch (group 1), the other 30 were treated with Memantina 10 mg b.i.d. (group 2). The evaluations were performed at baseline and then at least at one year after the beginning of treatment. All the patients underwent a neuropsychological assessment based on five cognitive domains: attention and working memory, logical executive, language, memory, and visuospatial functions. The global cognitive functioning (GCF) was also assessed with Mini Mental State Examination, while the behavioural changes were assessed with the MDS-UPDRS Part I, in particular question n. 2 (Q2. visual hallucinations). Clinically evaluation of nocturnal sleep quality was performed with an ad hoc questionnaire to detect presence and variation in confusional arousals, RBDs and overall sleep quality.

Both treatments were well tolerated at this dosage; no side effects were reported. From the preliminary analyses, an overall amelioration was present for both treatments in all GCF, behavioural and sleep evaluations. A more detailed analyses is needed to detect if differences exists between treatments. However this preliminary data showed that both treatments could be useful in clinical practice to improve behavioural symptoms especially at late stage of disease.



**P112**

**A good response to selegelina in primary writing tremor**

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*Background:* Task specific tremor is a form of action tremor that occurs only when a person is performing a specific skilled task and the most frequently form is primary writing tremor (PWT). Actually there are no specific therapy, sometime there is a response to propranololo, primidone, anticholinergics or botulin toxin treatment.

We present a case of PWT with a good response to selegelina.

*Case Report:* A 80 years old man presented to our observation with 20 years history of PWT, worsened in the last period. By some months appeared gait instability, a propensity to backward fall, progressive motor slowing. Neurological examination revealed a extrapyramidal syndrome with predominantly axial component, absence of postural reflexes, decreased walk bilaterally synkinesis, hypomimia, difficulty in rapid alternating movements more on the left side, no resting or postural tremor, only specific task tremor, vertical supranuclear gaze palsy.

Brain Magnetic Resonance Imaging showed cerebellar and brainstem atrophy and DatScan SPECT revealed a bilateral activity reduction in the striato, more evident on the right side (non congruo con il PWT). Diagnosis of degenerative parkinsonism (progressive supranuclear palsy-PSP) associated with task specific tremor was reached; he began Ldopa therapy, with a poor response; amantadine, clonazepam, triesifenilina were ineffective.

The administration of selegeline 5 mg gave immediate good response on task specific tremor, for which the patient is able to write correctly. No improvement on the extrapyramidal syndrome.

*Conclusion:* Actually there are no randomized controlled therapeutic studies involving patients with PWT, but there are single report of responses to propranololo or anticholinergics.

This patient has both a PWT for many years, both a parkinsonism (PSP type) L Dopa non responsive. The addition therapy with selegelina has improved the PMW, without clinical effect on the axial and extrapiramidal syndrome.

Probably the involvement of different networks in parkinsonism and PWT may explain the effectiveness of the therapy only in the PWT.

**P113****Ultra-high field MRI of the substantia nigra in patients with atypical parkinsonisms**

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*Introduction:* Recently, by using high resolution three-dimensional Susceptibility-Weighted Angiography (SWAN), the Ultra High Field anatomy of the Substantia Nigra (SN) has been described, and the loss of normal aspect allows to distinguish PD from healthy subjects (HS) on an individual basis with high accuracy [1].

*Objective:* To evaluate 7 Tesla MRI anatomy of the SN in patients with atypical parkinsonisms.

*Methods:* Fourteen patients with atypical parkinsonism (6 Multiple System Atrophy, 4 Corticobasal Degeneration and 4 Progressive Supranuclear Palsy) were enrolled in the study (mean age 68,2±7,8; mean disease duration 3,3±0,9). All patients underwent 7T MR examination by using 3D-GRE multi-echo susceptibility weighted image targeted. According to recent evidences, SN was defined normal if hyperintense laminar or oval shaped area could be detected into the larger hypointense area, abnormal if the SN appeared as a homogeneous hypointense structure.

*Results:* Ten out of fourteen patients exhibited bilateral abnormal SN, 4 patients showed bilateral normal aspect of SN. Particularly in 1 patient with Progressive Supranuclear Palsy and three with Corticobasal Degeneration the hyperintense area previously attributed to the nigrosome1 [2] was still detectable. In patients with Corticobasal Degeneration the hyperintense oval shaped area still bilaterally present, was larger in the side omolateral to the clinically affected side.

*Conclusion:* Our data demonstrate heterogeneous aspect of the SN in patients with atypical parkinsonism. In patients with Multiple System Atrophy SN was always abnormal in susceptibility weighted imaging consistently with pathological evidences suggesting iron deposition. Our report of no alterations in SN area in corticobasal degeneration is consistent with SN sparing previously described [3], and confirm that heterogeneous pathology might underlie corticobasal syndrome presentation.

**References**

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**P114**

**Paraneoplastic cerebellar ataxia associated to tongue cancer**

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*Introduction:* Paraneoplastic neurological disorders are broadly defined as neurological signs and symptoms associated with malignancy, which are not explained by direct tumor invasion, metastasis, or iatrogenic causes such as chemotherapy or radiation. Some movement disorders, i.e. chorea, opsoclonus-myoclonus, cerebellar ataxia, can be associated to cancer.

*Methods:* We observed a 75 year-old woman that developed a subacute onset of cerebellar ataxia. Family history was negative for hereditary ataxia.

*Results:* In the diagnostic tests, serum antibodies reactive against neural tissue antigens have been investigated, and the anti-Yo antibody was positive. Computerized tomography scan of chest, abdomen and pelvis was negative for an underlying tumor. In the face of the presence of a predictive antibody, whole body fluorodeoxyglucose positron emission tomography (FDG-PET) has been considered that showed an abnormality in the lingual region. A surgical procedure was effected and revealed tongue cancer.

*Conclusion:* In case of a rapid onset of a movement disorder, if routine imaging is negative, in the face of high clinical suspicion of a paraneoplastic syndrome or the presence of a predictive antibody, whole body fluorodeoxyglucose positron emission tomography (FDG-PET) should be considered. These disorders typically appear well before cancer is discovered, hence the initial diagnosis of PND is made by the neurologist rather than the oncologist.



**P115****Occurrence of Takotsubo syndrome in a patient with Parkinson's disease after entacapone add-on**

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Takotsubo syndrome (TTS) is characterized by clinical suspicion of an acute myocardial infarction without significant coronary stenosis, and its pathophysiology may involve a sudden catecholamine surge leading to a usually reversible myocardial dysfunction.

Cardiac catechol-O-methyltransferase (c-COMT) activity promotes the removal of catecholamines during both physiologic and pathologic conditions and, consequently, the inhibition of c-COMT activity with entacapone increases norepinephrine, epinephrine, and dopamine bioavailability. We report the first case of TTS in a patient with Parkinson's disease (PD) after starting treatment with levodopa/carbidopa/entacapone.

A 68-year-old woman with a 18-year history of PD came to our attention for recent worsening of parkinsonian with motor fluctuations onset. She was taking levodopa/carbidopa, rasagiline and ropinirole. Entacapone (Stalevo©) was added due to mild motor fluctuations onset. After 4 days, she had a sudden acute chest pain at rest lasted for about 90 minutes, with mild and transient serum troponin elevation was observed, no electrocardiographic abnormalities. The echocardiogram showed a normal-sized left ventricle (LV) with an apical and distal septal akinesia together with a ballooning pattern and a moderate impairment of global function (LV ejection fraction 35%).

A coronary angiography performed 2 hours after the onset of pain demonstrated normal epicardial vessels. Pheochromocytoma was excluded. Antiparkinson therapy was withdrawn after the onset of chest pain and reintroduced 12 hours after the acute clinical picture had resolved, with the exclusion of entacapone.

A second echocardiogram performed about 24 hours after the acute episode showed a recovered LV function (ejection fraction 61%).

In our case, we suggest a possible relationship between TTS and entacapone intake, which could be supported by the manifestation of TTS shortly after entacapone administration. An increased bioavailability of catecholamines promoted by COMT inhibition in the presence of a hypothesized adrenergic receptor upregulation could have been the mechanism triggering the transient myocardial dysfunction.

Our case adds another piece of evidence to the puzzle, and prompts prospective clinical trials about the possible protective usefulness of beta-blockers in PD patients requiring DA agonists, COMT inhibitors, MAOI-B or any combination of them.

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