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Abstracts



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Comunicazioni Libere



C1

Tracking cortical changes throughout cognitive decline in Parkinson's disease: a longitudinal MRI study

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Introduction: Identification of biomarkers underlying cognitive decline in Parkinson's disease (PD) may facilitate the ongoing effort of identifying patients at risk of PD dementia (PDD).

Aims: To investigate longitudinal cortical thinning (CT) in patients with normal cognition (PD-CN), stable mild cognitive impairment (PD-MCIs), and patients who convert to MCI (PD-MCIC) and dementia (PD-Dc).

Methods: From a large sample of PD cases (n=236) and healthy controls (HC, n=123), we selected 114 patients with known cognitive outcome after 4 years of follow-up (37 PD-CN, 21 PD-MCIs, 36 PD-MCIC, 21 PD-Dc) and 39 HC, all age/sex-matched. Patients underwent up to four visits, including neuropsychological/clinical assessments and MRI scans. Baseline CT was investigated between patients and HC. In the PD sample, CT progression overtime was investigated within and between groups.

Results: At baseline, compared to HC and PD-CN patients, PD-Dc, PD-MCIC and PD-MCIs patients showed greater cortical damage in the entire parietal lobe, with additional involvement of the temporal cortex in PD-Dc group. Overtime, PD-CN and PD-MCIC accumulated the most damage in left frontal and parietal regions. PD-MCIs and PD-Dc showed similar pattern of thinning in the left temporal and parietal lobes, with involvement of the right side in PD-Dc. The posterior cingulate cortex (PCC) and the supramarginal gyrus were affected overtime only in the 'converter' groups. TimeXgroup interaction showed that (compared to the other patient groups): PD-Dc and PD-CN accumulated the least damage; PD-MCIC owned specific CT accumulation in PCC, supramarginal and parahippocampal gyri; PD-MCIs showed a widespread pattern of damage in fronto-temporo-parietal regions, bilaterally.

Conclusions: CT accumulation seems to be more prominent in the initial stages of PD cognitive decline. The involvement of specific temporo-parietal regions, only, is associated with the conversion to a more severe stage of cognitive impairment.

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C2

Neurophysiological correlates of bradykinesia in Parkinson's disease

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Introduction: Many neurophysiological abnormalities have been described in the primary motor cortex of patients with Parkinson's disease. However, it is unclear whether there is any relationship between them and bradykinesia, one of the cardinal motor features of the condition.

Aim: In the present study we aimed to investigate whether objective measures of bradykinesia in Parkinson's disease have any relationship with neurophysiological measures in M1 as assessed by means of transcranial magnetic stimulation techniques.

Methods: Twenty-two patients with Parkinson's disease and 18 healthy subjects were enrolled. Objective measurements of repetitive finger tapping (amplitude, speed and decrement) were obtained using a motion analysis system. The excitability of primary motor cortex was assessed by recording the input/output curve of the motor-evoked potentials and using a conditioning-test paradigm for the assessment of short-interval intracortical inhibition and facilitation. Plasticity-like mechanisms in primary motor cortex were indexed according to the amplitude changes in motor evoked potentials after the paired associative stimulation protocol. Patients were assessed in two sessions, i.e. 'OFF' and 'ON' medication. A canonical correlation analysis was used to test for relationships between the kinematic and neurophysiological variables.

Results: Patients with Parkinson's disease tapped more slowly and with smaller amplitude than normal, and displayed decrement as tapping progressed. They also had steeper input/output curves and a reduced response to the paired associative stimulation protocol. Within the patient group, bradykinesia features correlated with the slope of the input/output curve and the after-effects of the paired associative stimulation protocol. Although dopaminergic therapy improved movement kinematics as well as neurophysiological measures, there was no relationship between them.

Conclusions: Neurophysiological changes in primary motor cortex contribute to bradykinesia in patients with Parkinson's disease, although other mechanisms sensitive to dopamine levels must also play a role.

C3

Longitudinal cortical thickness changes in early Parkinson's disease patients with impulsive compulsive behaviors

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Introduction/Background: Numerous cross-sectional studies showed that occurrence of impulsive-compulsive behaviors (ICBs) in Parkinson's Disease (PD) is related to subtle changes in fronto-striatal and mesolimbic circuits. However, longitudinal brain atrophy in very early PD patients with ICBs is still poorly investigated.

Objective: To investigate the longitudinal changes of the cortical grey matter in patients with very early PD and ICBs.

Design/Methods: 110 patients in the initial stage of PD (Hoehn & Yahr 1-1.5) underwent clinical and neuropsychological evaluations and 3D T1-weighted MRI scans at baseline and once a year for 3 years. Twenty patients were diagnosed with at least one ICB on the initial exam or during follow up. From the initial cohort, we selected 35 patients who did not develop ICBs (PD-noICB) matched with PD-ICB cases for age, education, motor severity and cognitive status. 35 age-matched healthy controls were evaluated at baseline. The pattern of cortical thinning was investigated in PD patients relative to healthy controls at baseline and longitudinal cortical changes were assessed in the PD-ICB and PD-noICB patients, using FreeSurfer.

Results: Patient groups showed a similar pattern of motor, cognitive and psychiatric worsening over time. At baseline, PD patients did not show gray matter atrophy relative to controls and each other. Over time, both PD-ICB and PD-noICB patients showed widespread cortical thinning involving temporal, parietal and frontal regions. When analyzing the interaction group effect over time, the PD-ICB group showed a greater cortical thinning in the right rostral middle frontal, superior frontal and medial orbitofrontal regions of the right hemisphere relative to PD-noICB.

Conclusions: Our data suggest the importance of damage to the regions involved in inhibitory control for the development and maintenance of ICBs in PD.

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C4

Spread of dystonia in patients with idiopathic adult-onset laryngeal dystonia

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Introduction: Adult onset laryngeal dystonia (LD) can be isolated or can be associated to dystonia in other body parts. Combined forms can be segmental at the onset or can result from dystonia spread to or from larynx. Aim of this study is to identify main clinical and demographic features of adult onset idiopathic LD in Italian population.

Methods: Data were obtained from the Italian Dystonia Registry (IDR) produced by 37 Italian Institutions. Clinical and demographic data of 71 patients with idiopathic adult-onset LD were extracted from a pool of 1131 subjects included in the IDR.

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Results: 50 of 71 patients presented a laryngeal focal onset, remaining subjects had onset in other body regions and later laryngeal spread. The two groups did not show significant differences of demographic features. 32% of patients with laryngeal onset reported spread to contiguous body regions afterwards and in most of cases (12 of 16 subjects) dystonia started to spread within one year from the onset. LD patients who remained focal and those who had dystonia spread did not show other differences.

Discussion: data from IDR show that dystonic patients with focal laryngeal onset will present spread in almost one third of cases. Spread from larynx occurs early and it is directed to contiguous body regions showing similarities with clinical progression of blepharospasm. This study gives a new accurate description of LD phenomenology that may contribute to improve the comprehension of dystonia pathophysiology.

C5

Whole-Exome Sequencing for variant discovery in blepharospasm

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Blepharospasm (BSP) is a type of focal dystonia characterized by involuntary orbicularis oculi spasms that are usually bilateral, synchronous, and symmetrical. Despite strong evidence for genetic contributions to BSP, progress in the field has been constrained by small cohorts, incomplete penetrance, and late age of onset. Although several genetic etiologies for dystonia have been identified through Whole-Exome Sequencing (WES), none of these are characteristically associated with BSP as a singular or predominant manifestation. Here, we present WES of 31 subjects from 21 independent pedigrees with BSP. The strongest candidate sequence variants derived from in silico analyses were confirmed with bidirectional Sanger sequencing and subjected to co-segregation analysis. Co-segregating deleterious variants (GRCH37/hg19) in *CACNA1A* (NM_001127222.1: c.7261_7262delinsGT, p.Pro2421Val), *TOR2A* (NM_130459.3: c.568C>T, p.Arg190Cys), and *ATP2A3* (NM_005173.3: c.1966C>T], p.Arg656Cys) were identified in three independent multigenerational pedigrees. Deleterious variants in *HS1BP3* (NM_022460.3: c.94C>A, p.Gly32Cys) and *GNA14* (NM_004297.3: c.989_990del, p.Thr330ArgfsTer67) were identified in a father and son with segmental cranio-cervical dystonia first manifest as BSP. Deleterious variants in *DNAH17*, *TRPV4*, *CAPN11*, *VPS13C*, *UNC13B*, *SPTBN4*, *MYOD1*, and *MRPL15* were found in two or more independent pedigrees. To our knowledge, none of these genes have previously been associated with isolated BSP, although other *CACNA1A* mutations have been associated with both positive and negative motor disorders including ataxia, episodic ataxia, hemiplegic migraine, and dystonia. Our WES datasets provide a platform for future studies of BSP genetics which will demand careful consideration of incomplete penetrance, pleiotropy, population stratification, and polygenic inheritance patterns.

C6

Merging parkinsonism with dementia: application of a genetic panel in familial parkinsonism associated with cognitive impairment

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Background: A wide spectrum of genes may be responsible of familial parkinsonism associated with dementia as well as behavioural disturbances. Yet the prevalence and phenotypic spectrum associated to each relevant gene has never been thoroughly assessed in Italian cohorts.

Aim of the study: We applied a genetic panel targeting 34 genes known to be associated to either dementia and/or parkinsonism to 93 patients with parkinsonism and cognitive impairment reporting positive familial history for parkinsonism and/or dementia.

Methods: The gene panel was designed using SureDesign Tool (Agilent), libraries were prepared according to the HaloPlex Protocol (Agilent) and sequenced on a MiSeq platform (Illumina). Sequencing data underwent bioinformatics analysis and filtering with established pipelines. The potential pathogenicity of identified variants was assessed using bioinformatics tools (PolyPhen2, SIFT, MutationTaster, MutationAssessor, Provean), and their frequency was evaluated in genomic public databases (dbSNP, EVS, EXaC, 1000 Genomes).

Results: Ninety-three subjects underwent genetic analysis. Nine (9,6%) carried pathogenic variants (two Val717Ile APP, 1 Ala33Val SQSTM1+ Progranulin deletion, A382T TARDP, two N370S GBA, L444P GBA, R415C GBA, E365K GBA), while further 22 (23,6%) harboured novel, potentially pathogenic variants in different genes (PINK1, VCP, GRN, SMPD1, TARDP, APP, PSEN2, DCTN1, FUS, SQSTM1, MAPT, VPS13C).

Discussion: Our panel identified pathogenic or likely pathogenic mutations in about one-third of a cohort of subjects with phenotype of parkinsonism and cognitive impairment, and positive familial history for parkinsonism and/or dementia. The most frequently mutated gene was GBA followed by APP.

Conclusion: This study shows that a genetic diagnosis can be reached in a relevant proportion of patients with parkinsonism and cognitive impairment with positive familial history, with relevant implications for patients' management and for genetic counselling of the proband and relatives.

C7

Parkinsonism is associated with altered primary motor cortex plasticity in frontotemporal dementia

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Objective: Frontotemporal dementia (FTD) is characterized by frontotemporal lobe degeneration and heterogeneous clinical features. Among FTD variants, the behavioural variant (bv-FTD) and non-fluent variant primary progressive aphasia (nfv-PPA) affect frontal lobe networks involving premotor and motor areas leading to clinical symptoms including parkinsonism. In this study, we investigated long-term potentiation (LTP) and long-term depression (LTD)-like plasticity in the primary motor cortex (M1), in patients with bv-FTD and nfv-PPA, by using theta burst stimulation (TBS) protocol. We examined the possible pathophysiological link between parkinsonism and changes in LTP/LTD-like plasticity in M1 by comparing responses to TBS in FTD patients (bv-FTD and nfv-PPA), with and without parkinsonism.

Materials and Methods: We studied a total of 20 FTD patients (7 bv-FTD and 13 nfv-PPA) and [UW1] 18 age-matched healthy subjects. Diagnosis of FTD was achieved by using current consensus criteria. Cognitive and motor features were clinically evaluated by means of MMSE, a full neuropsychological battery and finally UPDRS part III. The diagnosis of FTD was also supported by brain MRI and FDG-PET. To test LTP- and LTD-like plasticity in M1, we applied two TBS protocols, intermittent TBS (iTBS) and continuous TBS (cTBS), respectively.

Results: In the whole group of FTD patients, TBS disclosed decreased M1 LTP/LTD-like plasticity compared to healthy subjects. However, when we compared responses to TBS in patients with and without parkinsonism, we found abnormal M1 LTP/LTD-like plasticity only in FTD patients with parkinsonism, regardless of the specific FTD variants (bv-FTD and nfv-PPA). Finally, when excluding patients with parkinsonism, responses to TBS were within normal range in patients with nfv-PPA and bv-FTD.

Conclusions: We here provide evidence for a direct association [UW2] between parkinsonism and abnormal M1 LTP/LTD-like plasticity in patients with FTD. Abnormal M1 LTP/LTD-like plasticity observed only in FTD with parkinsonism may reflect neurodegenerative processes occurring in cortico-basal ganglia-thalamo-cortical motor networks.

C8

Intrinsic functional connectivity correlates of anxiety in cognitively unimpaired drug-naïve patients with Parkinson's disease

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Background: Anxiety symptoms are common in Parkinson's disease (PD) and may affect both motor outcome and quality of life. Despite their clinical relevance, neural correlates potentially underpinning anxiety disorders in PD patients have not been completely clarified yet.

Objectives: Using resting-state functional MRI, we investigated intrinsic brain networks connectivity correlates of anxiety symptoms in a cohort of cognitively unimpaired drug-naïve patients with PD.

Methods: 3T MRI images of 41 drug-naïve PD patients (with and without anxiety), and 20 matched healthy controls (HC) were analyzed. Second-level Movement Disorders Society diagnostic criteria were applied to exclude PD patients with cognitive impairment. Anxiety presence and severity was assessed by means of a clinical interview and the Parkinson's Disease Anxiety Scale (PAS). Single-subject and group-level independent component analysis was used to investigate functional connectivity differences within the major neurocognitive resting state networks between patients sub-groups and HC. We also compared inter-network connectivity between PD patients with and without anxiety. Finally, linear regression analysis was used to investigate correlations between imaging and clinical data.

Results: Decreased connectivity within default mode (DMN) and fronto-parietal (FPN) networks as well as an increased connectivity within salience (SN) and executive control (ECN) networks were detected in PD patients with anxiety compared with those without. Moreover, PD patients with anxiety showed a disrupted inter-network connectivity between FPN and SN ($p < 0.05$). Anxiety severity was correlated with functional abnormalities within all these neurocognitive networks.

Conclusions: Our findings demonstrated that an abnormal intrinsic brain connectivity within and between the large-scale neurocognitive networks may represent a potential neural correlates of anxiety symptoms and severity in drug-naïve PD patients, even in the absence of cognitive impairment. We hypothesize that these divergent cognitive and limbic networks connectivity changes could be proposed as a potential biomarker of treatment response in clinical trial.

C9

Abnormal cerebellar connectivity in Parkinson's disease patients with freezing of gait

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Introduction: Freezing of Gait (FOG), is a disabling gait disorder that frequently occurs in Parkinson's Disease (PD) patients. The pathophysiology of FOG is still unclear.

Objective: To study the involvement of different cerebellar nuclei in the pathophysiology of FOG by analyzing both functional and structural connectivity of the cerebellum.

Methods: We recruited 15 PD patients with FOG, 16 PD patients without FOG (PD-nFOG) and 17 healthy subjects (HS). FOG was assessed using FOG Questionnaire (FOG-Q). Participants underwent a standardized 3T-MRI protocol. Cerebellar FC was investigated by analyzing resting-state functional-MRI data with a seed-based approach locating the seeds on the Cerebellar Locomotor Region (CLR), Fastigium Nucleus (FN) and Dentate Nucleus (DN). Cerebellar structural connectivity was investigated by analyzing fractional anisotropy (FA) and mean diffusivity (MD) along the superior (SCP), middle (MCP) and inferior cerebellar peduncles (ICP).

Results: PD-FOG exhibited increased FC of CLR and FN with several cerebellar areas as well as with the temporo-parieto-occipital cortex as compared to HS. The FC of the DN in the PD-FOG patients showed decreased FC with the frontal and temporo-parietal cortex, bilaterally, as compared to HS. Furthermore, PD-FOG patients showed lower FA values in the SCP and MCP than both PD-nFOG and HS. They also showed higher MD values in the SCP than PD-nFOG. In PD-FOG patients the increased FC of the CLR with cerebellar areas and parieto-occipital cortex positively correlated with FOG-Q. Moreover, FA values in the MCP and MD values in the SCP significantly correlated with FOG-Q scores.

Conclusions: Our results suggest that abnormal functional connectivity of the three cerebellar nuclei is altered in FOG patients and, in particular, the CLR may play a key role. WM damage of cerebellar peduncles may also contribute to the pathogenesis of FOG.

C10

Is idiopathic normal pressure hydrocephalus a unique disease? [123I]FP-CIT SPECT findings in relationship with cognitive impairment and cerebrospinal fluid markers

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Introduction: Idiopathic Normal Pressure Hydrocephalus (iNPH) is characterized by gait/balance disturbances, cognitive impairment, and urinary incontinence. Phenotypes overlaps with neurodegenerative dementia and parkinsonism can occur so it is not surprising to detect positive [123I]FP-CIT SPECT and Amyloid PET findings. In iNPH cerebrospinal fluid (CSF) beta-amyloid (A β)-42 has been showed reduced but total-Tau (T-tau) and phosphorylated-Tau (P-tau) are lower compared to Alzheimer's Disease.

Aims: To test the hypothesis of different iNPH subtypes, we matched the CSF markers results with the degree of cognitive impairment and with [123I]FP-CIT SPECT findings.

Methods: A β -42, T-tau and P-tau levels were analyzed in the CSF of 54 iNPH patients (M/F: 30/24, mean age: 75.5 \pm 4.7 years) who underwent diagnostic procedures prior to the surgical therapy. A complete neuropsychological evaluation was administered to all the patients. 36 out of 54 patients underwent [123I]FP-CIT SPECT.

Results: On the basis of the neuropsychological scores we subdivided the iNPH sample into three groups: no cognitive deficit (10 cases), mild (20 cases) and global impairment (24 cases) respectively. Groups were similar for age and duration of disease at the time to diagnosis. No significant difference was found among the three groups in T-tau and P-tau levels, while A β -42 levels were lower in the group with global cognitive impairment (ANOVA: $p < 0.006$). 30 out of 36 patients displayed a positive [123I]FP-CIT SPECT, among these 23 showed A β -42 levels within the normal range, while 7 had lower A β -42 levels (X^2 : 7.147, $p < 0.003$). 6 patients with negative [123I]FP-CIT SPECT presented lower CSF A β -42. The iNPH rating scale motor scores and MDS-UPDRS part 3 score have been found higher in patients with positive [123I]FP-CIT SPECT and normal CSF A β -42 (ANOVA: $p < 0.001$).

Conclusions: This report outlines two iNPH subtypes: the former with prevalent cognitive impairment and lower CSF A β -42 and the latter with prevalent motor involvement and positive [123I]FP-CIT SPECT.

C11

Gender differences in olfactory dysfunctions in Sardinian patients affected by Parkinson's disease

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Introduction: In the last years, several studies have identified the presence of gender-related differences in the burden of non-motor symptoms in patients affected by Parkinson's disease (PD) [1-2]. In this context, the role of specific gender-related patterns in olfactory dysfunctions of PD patients has not been clearly investigated.

Objective: To investigate the presence of specific gender-related patterns in olfactory dysfunctions among Sardinian PD patients, compared with age and sex-matched healthy controls.

Methods: Fifty-nine male and thirty-two female PD patients with a similar overall age and disease characteristics were recruited. Olfactory function was evaluated with the odor detection threshold, the discrimination, the identification tests of the Sniffin' Sticks (a psychophysical tool developed by Hummel in 1997 and widely validated) and their sum (TDI score). Cognition was evaluated with Montreal Cognitive Assessment (MoCA). Modified Hoehn and Yahr scale and UPDRS were used to assess motor symptoms. Forty-nine healthy controls matched for age were also enrolled.

Results: Male PD patients showed a significant greater impairment compared to female PD patients in odor identification (7.4 ± 3.6 vs 9.1 ± 2.7 ; $P \leq 0.01$) and TDI score (17.4 ± 7.7 vs 21.5 ± 6.0 ; $P \leq 0.01$), while a non significant reduction in male PD patients was noted also in the odor detection threshold and the discrimination. MOCA mean values among male and female PD were similar (21.4 ± 5.2 vs 21.4 ± 5.9 ; P not significant). No gender differences were identified in male and female healthy controls in any olfactory characteristic of the Sniffin' Sticks.

Conclusions: We identified a specific gender difference in olfactory dysfunctions in PD patients, with a more severe impairment in male PD patients with abnormal odor identification and decreased TDI score. These findings highlighted the possible role of gender differences in the development of associated PD non motor symptoms.

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C12

Diagnostic criteria for camptocormia in Parkinson's disease: a consensus-based proposal

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Background: There are no established diagnostic criteria for camptocormia in Parkinson's disease.

Methods: We performed a survey among movement disorders experts to identify camptocormia using images of patients with variable degrees and types of forward trunk flexion by fulcrum (upper and lower fulcra). We tested the subsequently generated diagnostic criteria in a sample of 131 consecutive patients referred for evaluation of postural abnormalities.

Results: Experts reached full consensus on lower camptocormia (L1-Sacrum, hip flexion) with a bending angle $\geq 30^\circ$ and upper camptocormia (C7 to T12-L1) with a bending angle $\geq 45^\circ$. This definition detected camptocormia in 9/131 consecutive PD patients (2 upper/7 lower) but excluded camptocormia in 71 patients considered to have camptocormia by the referring neurologist.

Conclusions: Strict criteria for camptocormia are met by 7% of patients with abnormal posture. The ascertainment of upper and lower camptocormia subtypes could improve the validity of epidemiological studies and assist future therapeutic trials.

Poster



P1

Diffusion tensor imaging of olfactory tract in Parkinson's disease

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Introduction: Olfactory dysfunction is recognized as one of the earliest indicators of developing Parkinson's disease (PD) and one of the major nonmotor symptoms with a significant impact on quality of life. In the present study, we investigated the possible relationships among olfactory impairment and alterations in diffusion tensor imaging (DTI) of olfactory tracts, comparing a cohort of PD patients and a matched control group.

Methods: Olfactory function of each subject was assessed using the Italian Olfactory Identification Test. Motor disability was assessed in all patients using Unified Parkinson's Disease Rating Scale-III part (UPDRS III) and Hoehn and Yahr rating scale (H&Y). Imaging was performed on a 3T Philips Achieva MR scanner. MRI pre-processing was performed by DTIPrep, DTI reconstruction and fiber tracking by DiffusionToolkit, tractography analyses using TrackVis. The following parameters were used for groupwise comparison: fractional anisotropy (FA), mean diffusivity (MD), tract volume and length.

Results: 17 patients with PD (mean age 64.9±7.6 years, UPDRS III 24.4±11.7, H&Y stage 1.9±0.5) and 9 controls (mean age 60.7±14.2 years) were recruited. Olfactory identification function of all PD patients was decreased. The region of interest analysis of the olfactory tract showed significant FA signal and volume decreases of the PD group when compared with the control group (P<0.05). Significant correlations were found between the MD values and the H&Y stage (r=0.60, P<0.01).

Discussion: DTI analyses of olfactory structures may be viable as a means of establishing cohorts of subjects with probable pre-clinical PD.

P2

Is avolition/apathy in Parkinson's disease associated with VTA dysconnectivity? A resting state functional connectivity study

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Introduction: Although avolition/apathy (a deficit of goal-directed behaviour) may be encountered at every stages of Parkinson's disease (PD) and may be a presenting symptom in a significant number of cases [1], there is lack of consensus regarding its neural substrates in PD [2]. Classical accounts suggest a critical role of the impairment of nigro-striatal projections to the prefrontal cortex, while the possible contribute of a dysfunction within the meso-limbic reward pathway remains poorly studied.

Objective: In the light of these considerations, we tested the hypothesis that avolition/apathy in PD may be (also) related to altered connectivity within dopaminergic neuromodulatory circuits involved in motivation processes.

Methods: Since dopamine input to these circuits derives mostly from the ventro-tegmental area (VTA), we investigated by functional magnetic resonance imaging (fMRI) the relationship between the resting-state functional connectivity (rs-fc) of the VTA and avolition/apathy scores (as measured by the Apathy Scale) in thirty idiopathic PD patients compared to thirty age- and sex-matched healthy controls (HC).

Results: The whole-brain seed-based analysis revealed that PD patients, in comparison to HC, showed significant dysconnectivity of the VTA from several key sub-cortical and cortical regions involved in motivational processes. In particular, significant correlations were found between avolition scores and rs-fc of the VTA with the right insular cortex.

Conclusions: Our results indicate that avolition/apathy in PD is linked to abnormal connectivity in the motivation-related circuits. A richer neurobiological understanding of the mechanisms underlying apathy should ultimately both promote and facilitate development of effective and tailored medical strategies for this disabling condition.

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P3

Microstructural changes preceding the development of impulse control disorders in patients with Parkinson's disease

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Background: Impulse control disorders (ICD) can be triggered by dopamine replacement therapies in patients with Parkinson's Disease (PD). Previous studies have identified several risk factors associated with ICD. Additionally, we have recently demonstrated, using functional MRI, that an abnormal intrinsic brain connectivity in the main neurocognitive networks can predict the development of ICD.

Aim: To investigate whole-brain white matter (WM) microstructural changes at baseline in a cohort of drug-naïve PD patients who successively developed ICD over a 36-month follow-up period (ICD+) compared with patients who did not (ICD-).

Methods: Baseline 3-Tesla MRI images of 48 drug-naïve PD patients and 20 matched healthy controls (HCs) were analyzed. The ICD presence and severity at follow-up were assessed by the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease Rating Scale. We used the diffusion tensor imaging (DTI) with tract-based spatial statistic (TBSS) analysis, to evaluate the WM integrity in 24 PD patients who developed ICD, compared to 24 PD patients who did not, and 20 HCs. We performed a TBSS analysis generating fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD) and axial diffusivity (AD) maps. The resulting statistical maps were thresholded at $p < 0.05$ corrected for multiple comparisons at a cluster level.

Results: Between-groups analysis revealed a statistically significant increase of RD of the main fasciculi of WM in ICD+ patients when compared to ICD- patients. In details, these differences were detectable, bilaterally, in thalamic radiations, cortico-spinal tracts, inferior longitudinal, superior longitudinal and uncinate fasciculi and in the splenium of corpus callosum.

Conclusions: In the present study we demonstrated, in PD patients who will eventually develop ICD, an altered WM integrity, at baseline, in several areas strongly involved in many cognitive and behavioural functions, with a central role played in the reward system and motor inhibition. The evidence of early axonal damage may represent a potential biomarker and an additional risk factor for the emergence of ICD in some PD patients.

P4

A Florbetapir [F18] amyloid PET imaging study in Parkinson's disease dementia: the influence of amyloid deposition on cognitive status and course of disease progression

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Introduction: The biological basis for dementia in Parkinson's Disease (PD) appears to be multifactorial. Although cortical Lewy bodies are the most robust correlate, the comorbid Alzheimer's Disease (AD) pathology has been also associated with PD-Dementia (PDD)[1].

The clinical significance of amyloid deposits (A β) in PD remains still a topic of active investigation.

Objective: To determine whether amyloid deposition, as assessed by PET imaging with the [18F]-Florbetapir, can distinguish PDD patients with respect to demographic and clinical parameters and to assess the regional patterns of amyloid deposition in PDD.

Methods: 21 PDD patients underwent standardized neurologic and neuropsychological examinations and Florbetapir-[18F] PET. The amyloid load was estimated on qualitative and semi-quantitative reading. Voxel-wise standardized uptake value ratio (SUVR) images were calculated using the whole cerebellum as a reference region.

Results: 8 of the 21 PDD subjects were rated as A β ⁺ in the visual assessment. Three further patients were categorized as A β ⁺ according to semi-quantitative measurements. A β ⁺ patients (11) showed a more rapid cognitive decline (yearly MMSE point loss of 3,15 versus 1,12 in the A β ⁻ group, p<0,007) and a poorer performance in the digit span forward (p<0,001) and phonemic verbal test fluency (p<0,018). No other significant group differences in demographic and clinical variables were observed. Comparing the two groups, increased A β binding was in the frontal pole, cingulate and paracingulate gyri, precuneus, temporal and lateral occipital cortices.

Conclusions: The A β -PET could be able to distinguish a group of PDD with a faster progression of dementia and a different cognitive profile [2]. The α -synuclein could promote amyloid deposition in selective brain regions, modifying the clinical phenotype of PDD patients. Unlike AD, in PDD the amyloid load appear to be related to the severity and type of cognitive impairment.

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P5

Cortical atrophy in Parkinson's disease with Mild Cognitive Impairment: a VBM study

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Objectives: Mild cognitive impairment (MCI) is common in Parkinson's disease (PD), but the underlying pathological mechanism has not been completely understood. Neuroimaging studies showed the presence of atrophy or abnormal networks involving several cortical and subcortical area in patients with PD and cognitive impairment. Voxel-based morphometry (VBM) is a fully automated quantitative magnetic resonance imaging (MRI) technique and could be used to reveal in vivo early neuropathological changes leading to MCI.

Materials and methods: Patients with diagnoses of Parkinson's disease according to the UK Brain Bank criteria were recruited from a larger cohort of PD patients of the PaCoS. Motor severity was assessed using the Unified Parkinson's Disease Rating Scale-Motor Examination (UPDRS-ME) and Hoehn-Yahr (H-Y) stage. Structural brain MRI data were acquired using a 3-D T1-weighted spoiled gradient (SPGR) echo sequence and each subjects underwent a complete neuropsychological evaluation. Patients were divided into PD with normal cognition (PD-NC) and PD with MCI (PD-MCI) according to the Litvan's criteria.

Results: One hundred and six patients with PD were enrolled (mean age 64.8 ± 9.5 years, mean UPDRS-ME score 29.6 ± 10.6 , mean H-Y stage 2.1 ± 0.5 , disease duration 2.8 ± 2.3 years). Forty patients were diagnosed with MCI and 66 were PD-NC. VBM analysis showed significant differences in several brain regions ($p < 0.001$ uncorrected). PD-MCI showed reduction GM density in left superior frontal gyrus, left precuneus, right superior parietal lobe (angular gyrus), bilateral temporal lobe, left cerebellum (lobule IV-V) and right cerebellum (lobule III). Analysis was also restricted to PD patients with a short disease duration (≤ 2 years) including 37 PD-NC and 25 PD-MCI. Early PD-MCI showed GM atrophy in bilateral medial frontal gyrus, right cingulate gyrus, left cerebellum (lobule IV-V), right paracentral lobule and left supplementary motor area.

Discussion: Main findings of this study is GM reduction in the frontal gyrus, precuneus, and angular gyrus. Previous findings, including fMRI and DTI studies, showed the involvement of these peculiar brain cortical areas in the development of MCI in PD patients in association with abnormal fronto-parietal connectivity and microstructural damage.

Conclusion: This study showed the presence of widespread anatomical changes in PD-MCI compared with PD-NC. The detection of frontal atrophy, even at an early stage of disease, could be used as an early marker of PD-related cognitive impairment.

P6

Use of quantitative susceptibility mapping for differential diagnosis between Parkinson's disease and atypical parkinsonisms

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Introduction: Despite the continuous improvement of clinical criteria and radiological tools, differential diagnosis between Parkinson's Disease (PD) and atypical parkinsonisms, mainly Multiple System Atrophy (MSA) and Supranuclear palsy (PSP), can still be challenging.

Objectives: Primary objective of the study was to compare relative susceptibility values of specific regions of patients with PD, MSA and PSP, to evaluate the potential utility of this new technique for differential diagnosis. Further objective was to search for possible correlations with clinical features.

Methods: Consecutive patients referring to the Movement Disorders Center of Pisa with a clinical diagnosis of PD, MSA or PSP according to current criteria, were recruited.

Of the 42 subjects, 23 were affected by PD, 8 by MSA and 11 by PSP. Each patient underwent both clinical and radiological evaluation with 3-Tesla-MRI, including Susceptibility Weighted Angiography (SWAN) sequences targeted on the whole region of basal ganglia and midbrain. For the quantitative analysis Quantitative Susceptibility Maps (QSM) were generated from SWAN images. Regions of interest (ROI) were drawn on substantia nigra (SN, whole and segmented), red nucleus (RN), globus pallidus, caudate, putamen and subthalamic nucleus (STN).

Results: QSM were obtained for 23 PD, 6 MSA and 10 PSP. The 3-group comparison showed significant differences in terms of relative susceptibility values of SN (especially the medial part), STN and RN in PSP patients, with a significant higher iron content at each level in PSP and high diagnostic accuracy (AUC between 0.788 and 0.957 in PD vs PSP). It was not possible to discriminate between PD and MSA. No significant correlations were found with clinical phenotype.

Conclusion: QSM could be a promising tool to discriminate between PD and atypical parkinsonisms, mainly PSP, since the early phases of the disease. Highest diagnostic accuracy for PSP was observed for STN and RN susceptibility values, according to early pathological involvement of these nuclei.

P7

Quantitative susceptibility mapping images for the parcellation of the subthalamic nucleus: a possible role for deep brain stimulation's targeting

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Introduction: Subthalamic deep brain stimulation is considered an effective treatment for Parkinson's disease (PD). The subthalamic nucleus (STN) has functionally been subdivided in three portions: the somatomotor part dorsolaterally, the associative part ventromedially and the limbic part in the medial tip. The goal of deep brain stimulation (DBS) is to preferentially stimulate the motor part of the STN to obtain optimal motor outcome. Histological studies have revealed an inhomogeneous iron distribution within the STN, which has been related to the subdivisions within this nucleus. Quantitative susceptibility mapping (QSM) is a novel magnetic resonance imaging (MRI) contrast mechanism that allows for detailed assessment of iron content in vivo.

Objectives: To investigate the iron distribution in STN in PD patients using QSM images.

Methods: Twenty-two PD patients were scanned using a 3T MRI and QSM images were generated starting from 3D-Gradient echo images. In QSM images we identified STN and we quantified susceptibility in 3 different part of the nucleus in the axial and coronal plane on both sides.

Results: We obtained the highest susceptibility values in the rostro-ventral part of the nucleus in the axial plane and in the rostro-medial part in the coronal plane, while we find the smallest susceptibility values in the dorso-caudal part in the axial plane and in the latero-caudal part of the nucleus in the coronal plane.

Conclusion: Using quantitative images we found the highest iron's concentration in the rostro-medial-ventral part of the nucleus and the smallest iron's concentration on the dorso-lateral-caudal part. Considering that the somatomotor part of the nucleus is dorsolaterally located and that the dorso-lateral part of the nucleus showed the smallest susceptibility values due to a lesser iron concentration, QSM images could be a promising MR technique to parcel the nucleus improving STN targeting for DBS in patients with PD.

P8

Cortical 123I-FP-CIT binding deficits are associated with mild cognitive impairment in Parkinson's disease

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Introduction: Severe deficits within dopaminergic striatal binding have been associated with early progression to dementia in Parkinson's disease (PD).

Objectives: The objective of the study was to evaluate the relationship between basal ganglia and cortical 123I-FP-CIT binding and early cognitive deficits in PD.

Methods: Sixty-seven PD patients (mean age 67.6 ± 10.7 years, mean disease duration 5.1 ± 4.2 years) entered the study and underwent 123I-FP-CIT imaging. An extensive neuropsychological evaluation (level II MDS definition) was performed, allowing the classification of patients into 33 with normal cognition (PDNC) and 34 with mild cognitive impairment (PD-MCI). The striatal tracer uptake was evaluated using BRASS software (Hermes, Sweden). The correlation between deficits within performances in specific neuropsychological tests and striatal dopaminergic binding were evaluated by multiple regression analyses. The whole-brain analysis was performed with Statistical Parametric Mapping (SPM). All the analyses were adjusted for the effect of age, sex, disease duration and presence of impulsive-compulsive disorders.

Results: No significant striatal binding differences were found between PD-MCI and PDNC patients by using adjusted BRASS analyses. Right caudate and right putamen binding correlated with MMSE and verbal fluency scores, respectively. PD-MCI patients showed a significant reduction of left precuneus tracer uptake compared to PD-NC (125 voxels, adjusted $p=0.001$, uncorrected).

Discussion: The development of cognitive deficits in PD may be related to early cortical 123I-FP-CIT reduction, even in absence of any difference in striatal binding. This might reflect a selective damage in PD-MCI of precuneus, classically impaired in early Alzheimer's disease. Alternatively, this might be secondary to a disconnection of bioaminergic striato- cortical projections. Multi-modal imaging and longitudinal studies are warranted in order to clarify this issue.

P9

Longitudinal cortical thickness changes in GBA-positive relative to GBA-negative Parkinson's disease patients with hemiparkinsonism

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Introduction/Background: Heterozygous glucocerebrosidase gene (GBA) mutations are the greatest genetic risk factor of Parkinson's Disease (PD). Compared with PD noncarriers (PD no-GBA) cases, PD-GBA patients are characterized by an earlier age of onset, a better response to L-Dopa and an increased likelihood to experience cognitive symptoms, neuropsychiatric disturbances, and autonomic dysfunction.

Objective: To investigate the longitudinal changes of the cortical grey matter in PD-GBA patients relative to idiopathic PD.

Methods: Eleven PD-GBA patients with hemiparkinsonism (Hoehn and Yahr 1.0 or 1.5) were compared with 24 PD no-GBA patients matched for age, sex, disease duration and severity and psychiatric and cognitive status. Patients underwent clinical and neuropsychological evaluations and 3D T1-weighted MRI scans at baseline and once a year for 3 years. 25 age-matched healthy controls underwent evaluations at baseline. The pattern of cortical thinning was investigated in PD patients relative to healthy controls at baseline and longitudinal cortical changes were assessed in PD-GBA and PD no-GBA patients, using FreeSurfer.

Results: At baseline, PD-GBA patients showed a greater cortical atrophy of fronto-temporo-parietal areas relative to both healthy controls and PD no-GBA. Overtime, PD no-GBA group showed a higher rate of cortical thinning relative to PD-GBA patients; however, the pattern of cortical thinning in PD no-GBA cases did not reach the severity shown by PD-GBA patients after 3 years.

Conclusions: PD-GBA patients showed a greater and earlier cortical thinning relative to PD no-GBA cases with the same disease duration and severity. Despite the slower atrophy progression over time, after 3 years, cortical damage was still greater in PD-GBA relative to PD no-GBA patients. Our findings in PD-GBA add to the existing literature by showing the strong contribution of GBA mutation to the progression of PD.

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P10

Functional brain connectome changes predict cognitive decline in Parkinson's disease

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Background: Cognitive impairment is one of the major extramotor symptoms in Parkinson's disease (PD). Up to date, there is still no reliable MRI marker to predict the onset of cognitive impairment in PD.

Objective: To investigate the functional connectome alterations associated with cognitive deterioration in patients with PD.

Materials and methods: We enrolled 87 PD patients and 41 healthy controls. At study entry, all subjects underwent clinical and cognitive evaluations, and MRI including resting state functional MRI. Patients were followed up clinically and neuropsychologically for 2 years and classified as cognitive progressors (from normal cognition to mild cognitive impairment [MCI], or from MCI to dementia) or non-progressors (stable cognition over two years). Global network metrics were measured using brain connectivity toolbox and differences in regional functional networks among groups were investigated using Network-based statistic.

Results: Thirty-one patients were classified as cognitive progressors (22 without [NCOG-evo] and 9 with MCI [MCI-evo] at baseline), 56 patients as non-progressors (23 without cognitive impairment [NCOG-noevo] and 33 with MCI [MCI-noevo]). Compared with controls, NCOG-noevo patients did not show alterations. MCI-noevo and MCI-evo groups showed altered global network metrics. In the regional analysis, NCOG-evo and MCI-noevo groups showed decreased functional connectivity covering a large fronto-temporo-parietal network including cingulate cortex, primary sensorimotor cortices, superior temporal and supramarginal gyri and insula bilaterally. MCI-evo patients showed similar alterations with more extensive involvement of frontal and temporal nodes. NCOG-evo, MCI-noevo and MCI-evo showed the same alterations present in the comparison with controls when compared to NCOG-noevo.

Conclusions: Functional connectome alterations at baseline are associated with the development or worsening of cognitive deficits in PD patients over two years. The study of functional connectome might open new perspectives in the identification of PD patients at-risk for cognitive impairment.

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P11

Ioflupane[123I] imaging and clinical phenotypes of Parkinson's disease

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Introduction: In order to provide the most effective treatment to patients, an accurate diagnosis for Parkinson's disease (PD) will require an understanding of the risk to develop nonmotor symptoms (i.e. cognitive and psychiatric disorders).

Objective: To evaluate the relationship of motor and nonmotor symptoms with striatal dopaminergic denervation in a cohort of symptomatic PD patients with positive ioflupane[123I] imaging.

Methods: Thirty-seven patients at onset with positive ioflupane[123I] were studied. Patients were divided into two groups depending on the evidence of dopaminergic denervation in putamina alone (PD-p) or in putamina and caudates (PD-pc). The two groups were compared in terms demographics, motor phenotypes, disease severity based on the MDS- UPDRS III score and presence of sleep, psychiatric and cognitive symptoms.

Results: Twenty-one patients entered in the PD-pc group (M/F=14/7; mean age 62.33 ± 8.65 years; mean disease duration 1.76 ± 1.09 years; mean UPDRS III 31.29 ± 8.16) and 16 patients entered in the PD-p (M/F=5/11; mean age= $64,31\pm 8,5$ years; mean disease duration 3 ± 2.68 mean UPDRS III 20.44 ± 5.96). Group did not differed in terms of age, gender and disease duration. PD-pc group showed significant worse UPDRS scores ($p<0.0001$). Rigid phenotype was found in 66,7% of PD-pc and 12,5% in PD-c ($p<0.0001$); tremolous phenotype was found in 4,8% of PD-pc and 56,3% of PD-p ($p<0.0001$); mixed phenotypes was found in 28.6% of PD-pc and 31.3% of PD-p (n.s.). At the time of onset in the PD-pc group 47.5% of patients presented premotor symptoms for at least 3 years (depression and different disorders in the anxiety spectrum), 71.4% of patients showed psychiatric symptoms (generalized anxiety, panic attacks, phobia, obsessive-compulsive disorder, moderate to severe depression) and 47.6% showed mild executive dysfunction at onset. In the PD-p group none of the patients had cognitive issues, 31.3% had psychiatric symptoms (mild depression and/or anxiety) and 12.5% had premotor symptoms (mild anxiety).

Conclusions: The evidence of early dopaminergic denervation in the caudates correlates with a more complex phenotype of PD.

P12

Progression of Parkinson's disease: 2-year longitudinal study of clinical and MRI changes in patients at different stages of the disease

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Introduction: MRI may improve monitoring of pharmacological and non-pharmacological therapies in Parkinson's disease (PD).

Objective: To investigate motor and cognitive/behavioural changes, cortical thickness abnormalities and white matter (WM) alterations over time in a large cohort of patients at different PD stages.

Methods: 143 PD patients were recruited: 83 early PD (Hoehn and Yahr [HY] 1-1.5) and 60 mild-to-severe PD (HY 2-4). Patients underwent clinical motor and neuropsychological evaluations and MRI at study entry and every year for 2 years. 66 healthy subjects performed baseline assessments. Cortical thickness measures and diffusion tensor (DT) MRI metrics of WM tracts were evaluated. Longitudinal changes of clinical, cognitive/behavioural and MRI data were assessed over 2 years.

Results: At baseline, motor disability was greater in mild-to-severe PD relative to early cases; however, cognitive/behavioural functions were similar in the two groups. Over 2 years, both groups showed a deterioration of motor skills, significantly in early PD, and a decline in depression, anxiety and apathy; mild-to-severe PD experienced a greater cognitive decline. At baseline, mild-to-severe PD patients showed a more severe and widespread cortical thinning relative to controls and early PD patients; on the contrary, early PD patients showed a significant cortical thinning over time relative to mild-to-severe PD. DT MRI at baseline showed focal WM abnormalities in early PD patients relative to controls; the group of mild-to-severe PD showed a more widespread damage than early PD involving also extramotor WM pathways. WM damage progressed over time in both groups of patients, involving both motor and extramotor circuits.

Conclusions: MRI may be a useful tool, if associated with clinical assessment, to monitor the progression of PD. Cortical thickness investigation is promising to evaluate the early phase of the disease, while the analysis of microstructural WM involvement may represent a potential biomarker for monitoring also advanced PD stages.

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Susceptibility-weighted imaging (SWI) MRI in parkinsonism: findings and clinical correlations

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Background: MRI is commonly used in clinical practice as an adjunctive test in the differential diagnosis of parkinsonism. Susceptibility-weighted (SW) imaging is sensitive to magnetic inhomogeneity effects, particularly due to iron accumulation. A disease specific target of MRI that has emerged recently is neuromelanin, a pigment expressed in high quantities in the substantia nigra and locus coeruleus. Neuromelanin is an iron chelator, which makes it visible to MR imaging due to its paramagnetic properties. SWI, enhancing iron bound to neuromelanin, can show differences between Parkinson patients and controls.

Aim of the study: The aim of the study was to assess the reliability of SWI sequences in the diagnosis of parkinsonism in a clinical setting and to identify clinical features associated with the severity of neurodegeneration.

Methods: This was a prospective observational cohort study of 30 patients presenting with a parkinsonian syndrome. A motor evaluation with UPDRS was done before the exam. Also, cognitive status (MoCA) and non-motor symptoms (NMSS score) were explored. 3T brain MR imaging with conventional and SWI sequences was performed. A neuroradiologist, blinded to the clinical evaluation, analyzed the images and gave a score based on the grade of degeneration of substantia nigra and basal ganglia. Mann-Whitney test was used to determine the correlation between variables.

Results: The included population had a mean age of 71,9 years old and mean UPDRS score was 57,8±18,3. UPDRS and age of symptoms onset were significantly higher in patients with a wide neurodegeneration. This group of patients showed also more bradykinesia than other subjects. Cognitive symptoms and hallucinations are negatively correlated with degeneration of substantia nigra (p=0.029 and p=0.009 respectively).

Conclusions: SW imaging is a promising technique in the differential diagnosis of parkinsonism. This study showed that there is a link between the severity of motor symptoms and the grade of neurodegeneration visualized with SW imaging.

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Cardiac metaiodobenzylguanidine (MIBG) SPECT in differential diagnosis of parkinsonisms: a ten-years retrospective study

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Introduction: Cardiac metaiodobenzylguanidine (MIBG) SPECT imaging provides a measure of cardiac sympathetic innervation and may be useful in differentiating PD from atypical parkinsonism. For this reason it has been recently included in the new diagnostic criteria for PD as a supportive feature even if its role as an important diagnostic tool remains controversial.

Objective: The aim of our retrospective study was to analyse the contribution of myocardial MIBG-SPECT in the differential diagnosis between PD and atypical parkinsonism.

Materials and Methods: Patients with parkinsonism, who performed a MIBG-SPECT from 2007 to 2016, in our Neurologic Unit were selected. Each case was reviewed by applying the new disease criteria for PD, MSA and PSP. Diagnosis at three different times (before and after MIBG execution and one year later) were established. Early and delayed H/M ratio and washout rate (WR) were analysed as cardiac SPECT parameters.

Results: 41 patients with parkinsonism were included in the study. At the follow-up evaluation we identified 15 PD, 15 MSA, 8 PSP, while 3 patients didn't receive a definite diagnosis, although an idiopathic Parkinson Disease was excluded. MIBG-SPECT was found abnormal in 12 (80%) PD patients while it was normal in 20 (77%) no PD patients. In PD and no PD groups respectively, mean values of early H/M ratio (1,46 vs 1,67), delayed H/M ratio (1,37 vs 1,64) and WR (56,54% vs 29,17%) resulted significantly different, while no differences were found comparing MSA and PSP patients. In 7 patients (17%) execution of MIBG-SPECT allowed us to improve the certainty level of PD diagnosis, according to the new diagnostic criteria.

Conclusions: Our study confirms the utility of MIBG-SPECT in distinguishing PD from atypical parkinsonism; in particular our data highlight how MIBG-SPECT may be a useful tool in identifying PD patients where other clinical criteria are lacking.

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Trans-cranial Magnetic Resonance-guided Focused Ultrasound Surgery (MRgFUS) integrated with a 1.5T scanner for treatment of essential tremor

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Background: Trans-cranial MR-guided Focused Ultrasound Surgery (MRgFUS) is an innovative technology that, via thermal ablation, enables noninvasive thalamotomy. Recent evidence demonstrated that thalamotomy of the ventral intermediate nucleus (VIM) performed by a MRgFUS system operating with a 3T MR was effective in alleviating medication-resistant tremor in patients with essential tremor (ET).

Objective: We evaluated safety and efficacy of the MRgFUS using a 1.5T MR unit in patients with ET.

Methods: Eighteen patients (13M/5F, mean age 65±13.02 yrs) with severe medication-resistant essential tremor were eligible to the treatment. Tremor was assessed before and after treatment, using the Fahn-Tolosa-Marin Tremor Rating Scale (TRS). Quality of life was measured using the Quality of Life in Essential Tremor Questionnaire (QUEST). The MRgFUS procedure was carried out using a 1.5T MRI scanner.

Results: Thirteen right-handed patients successfully underwent monolateral MRgFUS ablation of the VIM. In the other 5 patients treatment aborted mainly because of technical reasons (only one patient complained of sudden intense headache related to the high-intensity focused ultrasounds delivery). In all subjects we targeted the hemisphere corresponding to the dominant hand. In all treated patients, immediate cessation of tremor was observed in the dominant hand immediately after treatment. At a 3-month follow-up we observed a significant reduction in the TRS (from a mean baseline value of 40.2 to 17.3, $p < 0.0001$) and QUEST scores (from a mean baseline value of 35.09 to 17.09 $p < 0.0005$). No severe adverse effects were observed neither during sonication nor immediately after treatment. Though mild to moderate side effects were observed after treatment, e.g. gait ataxia or weakness of the contralateral side, no adverse event lasted beyond 3 months.

Conclusions: MRgFUS VIM thalamotomy integrated with a 1.5T MRI magnet is safe and effective for treatment of ET patients with medication-resistant tremor.

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Quantitative sit-to-stand task analysis, in Parkinson's disease

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A complete method of detection of all the relevant features for the sit-to-stand task analysis, in Parkinson's disease (PD) patients and healthy subjects (H), has been proposed. A group of sixteen PD patients and thirteen H subjects have been analysed, using three magneto-inertial sensors, while the physician administers the MDS-UPDRS clinical scale. The PD group has been examined before and after the pharmacological therapy (respectively, OFF and ON phase), in order to monitor the different states of the PD, which implies changes in motor control. By calculating the features of this task, it has been possible to choose the most reliable indexes, already used in this task in order to identify differences in the score assigned through sensors. In addition to that, it has also been possible to find differences in the features' values which the clinical scale and the physician cannot identify. Results show how the use of sensors provides a higher sensitivity and specificity for the valuation of this particular task. Moreover, our study highlights how wearable motion sensors can detect statistically significant differences between OFF/ON phase and H subjects that the clinical evaluation cannot. We conclude that our method provides a complete analysis of the sit-to-stand task with a few number of sensors, allowing to check PD patient status, providing a method for home care monitoring.

P17

Information processing in Parkinson's disease with central fatigue: a P300 study

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Introduction: Fatigue has been reported to be a common and disabling symptom in Parkinson's disease (PD), worsening the patients' quality of life. It has been suggested that fatigue is associated to a dysfunction in the striato-thalamo-prefrontal loop, and could be related to the cognitive domain. The P300, the most studied event-related potential (ERP) component, is elicited by unpredictable, infrequent and salient changes in stimulus characteristics, the P3a being present when these changes are unexpected and novel, the P3b when they are task-relevant.

Objective: To explore the association between fatigue and information processing in patients with PD.

Methods: 24 non-demented PD patients without fatigue-PDnF, 12 non-demented PD patients with fatigue-PDF and 32 age-matched controls underwent a P300 novelty task. P3a, and P3b components were measured and amplitudes and latencies were analyzed separately by means of a mixed model rmANOVA.

Results: As regards the response to the target stimulus, the P3b latency was significantly longer both in PDF and PDnF respect to controls (PDF vs controls:p=0.006; PDnF vs controls:p=0.042). P3b amplitudes were comparable between groups.

As regards the response to the novel stimulus, the P3a latency was significantly longer in PDF alone, respect to both controls and PDnF (PDF vs controls:p=0.002; PDF vs PDnF:p=0.007). Similarly, P3a amplitude was significantly reduced in PDF alone, respect to both controls and PDnF (PDF vs controls:p=0.03; PDF vs PDnF:p=0.01).

Conclusions: PDF specifically showed a difficulty in the attentional switching to salient novel stimuli, which is related to functioning of the fronto/parietal brain areas and the ventral attention network, and mediated by dopaminergic activity. Instead, the ability to discriminate the significant target stimulus, that requires the integrity of the dorsal attentional network, is compromised in parkinsonian patients, irrespectively to the presence of fatigue. A more altered striato-thalamo-prefrontal loop may contribute to the pathogenesis of central fatigue in PD.

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**Is central fatigue in Parkinson's disease associated to an altered serotonergic central tone?
Data from Intensity Dependence of Auditory Evoked Potentials (IDAP)**

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Introduction: Patients with Parkinson's disease (PD) report a high prevalence of fatigue, which has a significant negative impact on quality of life. It has been suggested that fatigue is related to a dysfunction of the basal ganglia, especially in non-dopaminergic pathways. Reduced serotonin transmission could play a role in the occurrence of fatigue in patients with PD.

Objective: To evaluate serotonergic central neurotransmission in PD patients with and without fatigue, by means of the intensity dependence of the auditory evoked N1/P2- response, a reliable neurophysiological index of the central serotonergic function.

Methods: 30 non-depressed, non-demented PD patients (22 without fatigue-PDnF, 8 with fatigue-PDF) and 26 age-matched controls underwent a neurophysiological evaluation. Auditory evoked potentials were evoked by four runs of 250 stimuli. Tones (1000 Hz; 50 ms duration; rise-fall times: 10 ms) were delivered binaurally through earphones at four different intensities (60, 70, 80 and 90dB HL) in a pseudo-randomized order. N1 and P2 amplitudes were measured respectively between 50 and 150ms and between 120 and 200ms post-stimulus, and the N1/P2 ASF slope was calculated as the linear amplitude/stimulus intensity function slope for block averages ($\mu\text{V}/\text{dB}$).

Results: IDAP was significantly higher (meaning a lower serotonergic tone) in patients, as a whole, than controls ($U=220$ $p=0.020$).

Analyzing patients separately according to the presence of fatigue, a significant difference in IDAP values still emerged between groups (univariate ANOVA: $F_{2, 50}=3.29$; $p=0.045$). However, after Bonferroni correction, IDAP resulted comparable between the two groups of patients (PDF vs PDnF $p=1.00$), while a difference still emerged between patients and controls.

Conclusions: Our results point to a reduction of central serotonergic tone in PD, even in absence of depression and in early stages of the disease. Central fatigue in PD does not seem to be related to the reduced serotonergic neurotransmission, especially in non-depressed patients.

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Brain functional substrate of gait observation in Parkinson's disease

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Background: Gait disorders are extremely frequent in Parkinson's disease (PD). Action observation training (AOT) represents a promising tool for treatment of gait impairment in PD. However little is known about the neurophysiological substrate of observation of gait and its possible correlations with gait performance in PD patients.

Aim: The aim of the study was to investigate the neural correlates of gait observation in PD patients, in relation to gait performance.

Methods: 30 PD patients (10 females; mean age, 62.5±8.3; mean UPDRS III, 24.5±4.1; mean disease duration, 7.8± 5.0) and 21 gender and age-matched healthy subjects (HS; 13 females; mean age 64.6±13.5) were enrolled in the study. Patients underwent a clinical evaluation, gait analysis and MRI, including functional imaging recorded during the observation of a video showing a human during walking. Spatiotemporal kinematic parameters of gait were recorded during normal walking through a sensorized mat (GaitRITE®).

Results: fMRI showed increased recruitment of supplementary motor area (SMA) during action observation of gait in PD patients with respect to HS. Further, in PD patients, stride length and stride length variability correlated with activity of the inferior parietal lobule (IPL) during action observation. Precisely, worst gait performers (reduced stride length and increased variability) showed increased activation of IPL.

Discussion: Since the basal ganglia-SMA loop is believed to be associated with self- initiated gait, the over-activity at the level of SMA in PD patients could be interpreted as a compensation mechanism. In addition, IPL is involved in monitoring motor function based on visuo-spatial information and abnormal function of IPL has been associated to gait disorders in PD. Correlation between gait performance and IPL activity during AO of gait suggests that AO training could theoretically induce plastic changes in deficient cortical areas thus contributing to gait improvement.

P20

Transcranial direct current stimulation of dorsolateral prefrontal cortex improves dual-task gait and obstacle crossing in Parkinson's disease

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Background: Inefficient ability to walk under dual-task and obstacle negotiation in PD has been related to impaired gait mechanisms and ineffective attempts to compensate via higher-order cognitive functions. These cognitive functions are mediated, to a large degree, by the dlPFC. tDCS is a non-invasive brain stimulation method that can modulate cortical excitability. A recent study showed that tDCS targeting the left dlPFC improved gait performance under dual-task condition in healthy controls.

Aim: To explore the effects of dorsolateral prefrontal cortex (dlPFC) neuromodulation via Transcranial Direct Current Stimulation (tDCS), on gait performance during dual-task and obstacle crossing in Parkinson's disease (PD).

Methods: Sixteen patients with PD in stages II-III on the Hoehn and Yahr scale were recruited for this study. Gait performance was evaluated immediately before and after a 20 min session of either real or sham tDCS (1.5 mA) targeting the left dlPFC. Gait speed was recorded (i) during normal walking performance, (ii) during cognitive dual-task, consisting in a serial subtraction of numbers and (iii) during obstacle crossing through a sensorized mat (GaitRITE®).

Results: Comparing real and sham tDCS, we found that real tDCS led to a reduction of dual-task cost for gait speed, step time and double support time in patients with PD. Related to obstacle crossing, crossing velocity and crossing step length increased after real tDCS. Sham tDCS had no effect on gait parameters during normal, dual-task gait and obstacle crossing.

Discussion: These results showed that modulation of left dlPFC excitability might reduce the cost of performing a dual-task during gait in PD and improve obstacle crossing performance, suggesting that tDCS could be a potential additional tool for improving the effectiveness of rehabilitation in PD and for reducing the risk of falls.

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Electrocortical connectivity and non-linear quantitative analysis of EEG signal in PD-MCI

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Introduction: Mechanisms underlying cognitive decline in Parkinson’s Disease (PD) are not yet fully understood. There are few electrophysiological studies evaluating brain connectivity and potential markers of cognitive impairment in PD patients since its initial phases.

Objectives: To analyze electrocortical networks related with cognitive decline in PD patients with Mild Cognitive Impairment (PD-MCI) compared to PD patients with normal cognition (PD-NC).

Methods: From the PaCoS (Parkinson’s disease Cognitive Study) cohort of 659 PD patients, a sample of 102 subjects (46 PD-MCI and 56 PD-NC) was selected based on the presence of a comprehensive neuropsychological assessment and at least one artifact-free EEG recording. Diagnosis of PD-MCI was made according to the definition by Litvan et al. EEG signal epochs were analyzed using Independent Component Analysis LORETA. The Power Spectral Density (PSD) of site-specific signal epochs was also obtained together with the power law exponent β to estimate fractal-like behavior of site-specific signal.

Results: LORETA analysis revealed significant differences in PD-MCI patients as compared to PD-NC, with a reduced network involving alpha activity over the occipital lobe, an increased network involving beta activity over the frontal lobe associated with a reduction over the parietal lobe, an increased network involving theta and delta activity over the frontal lobe and a reduction of networks involving theta and delta activity in the parietal lobe. Quantitative EEG analysis showed a significant decrease of alpha PSD over the occipital regions and an increase of delta PSD over the left temporal region, with a significant β increase over the frontal regions in PD-MCI as compared to PD-NC.

Conclusions: Results suggest reduced occipital resting-state alpha rhythms and enhanced frontal low-frequency electrocortical networks associated with non-stationary EEG signals in PD-MCI as compared to PD-NC.

P22

Cluster analysis of selected kinematic parameters during Sit-to-Stand task in Parkinson's disease. Association with baseline motor characteristics

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Introduction: The ability to move from a sitting to a standing position during a Sit-to-Stand (STS) task is important to characterize overall functioning and motility in Parkinson's Disease (PD). Time to perform task is generally used to assess subject inability to perform this basic skill. Few data are available about other task components involved.

Objective: To test if performances during STS-task may be better characterized by integrated information including time to perform task and degree of axial displacement recorded by a motion transducer system in PD patients using a data-driven approach.

Methods: Forty-five patients with PD were recruited. All PD patients were tested at baseline motor conditions. Patients performed the STS-task wearing a portable motion transducer system. The device automatically detected task duration as well as patient axial flexion and extension amplitudes in the sagittal plan. Task was performed twice and measurements averaged to be analyzed. A non-hierarchical cluster analysis using k-means method was performed using average values of the three selected kinematic parameters for two cluster solutions. Differences in instrumental and clinical characteristics among detected clusters were evaluated.

Results: Cluster analysis identified two groups of N=17 (Group-1) and N=28 (Group-2) subjects. Task duration as well as axial flexion and extension amplitudes were higher for the Group-1 as compared to Group-2. Looking at clinical differences between the identified clusters, Group-1 subjects presented overall lower UPDRS motor baseline scores as compared to Group-2. Moreover, Group-1 had fewer patients with moderate to severe gait difficulties as compared to Group-2.

Conclusions: In PD, STS-task performances should be interpreted based on both task duration and degree of axial flexion-extension when tested in baseline conditions. Long task duration seems associated with better axial motility while standing and mild motor disability in PD. Compensatory mechanisms mainly acting on patients with mild disability could explain our findings.

P23

Instrumental assessment of Pull Test for postural instability using a wearable device. Applications for Parkinson's disease

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Introduction: The Pull Test (PT) is a common maneuver clinically used to assess postural instability in patients with Parkinson's Disease (PD). PT consists in observing the user response after providing a tug to the patients' shoulders, in order to displace the center of gravity from its neutral position. The validity of the test can be however compromised by nonstandard backward tugs provided to the patient.

Objectives: We evaluated feasibility of a wearable device to support and standardize PT.

Methods: The proposed solution consisted of a sensing unit positioned on the patient's chest allowing an instrumented estimation on the strength of the tug and a set of information extracted from the stabilogram useful for a further comprehension of the user response. Such information, processed by dedicated algorithms, were used to perform a reliable classification between stable and unstable behaviors.

Experiments to assess the system capability were performed in healthy subjects simulating typical behaviors observed in patients with different levels of instabilities. A large set of experiments to extract a set of features useful for the classification between stable and unstable behavior were then examined.

Results: Thirteen different parameters were investigated. A clustering of two classes of user's response was observed for a subset of the investigated parameters, thus suggesting the possibility to adopt a threshold based classifier. Results obtained demonstrate the validity of the approach proposed, with an average sensitivity of 0.9 and specificity of 0.8.

Conclusions: We propose the use of a portable low-cost sensing system while performing PT for the assessment of postural instability in PD patients and frail elderly subjects.

P24

Abnormalities of cortical neural synchronization mechanisms in subjects with mild cognitive impairment due to Alzheimer's and Parkinson's Diseases: an EEG Study

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Introduction: Today, disease monitoring of patients with Mild Cognitive impairment (MCI) due to Alzheimer Disease (ADMCI) and Parkinson Disease (PDMCI) is crucial since they have specific pathological causes and lesions and consequently require different treatments. This need boosts the development and validation of enhanced procedures to extract new clinical indexes and biomarkers. Among other biomarkers, resting state eyesclosed electroencephalographic (rsEEG) rhythms have extensively been studied as markers to assess the neurophysiological correlates of dementia.

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Objective: The aim of this retrospective and exploratory study was that the cortical sources of resting state eyes-closed electroencephalographic (rsEEG) rhythms might reveal different abnormalities in cortical neural synchronization in groups of patients with mild cognitive impairment due to Alzheimer's disease (ADMCI) and Parkinson's disease (PDMCI) as compared to healthy subjects.

Methods: Clinical and rsEEG data of 75 ADMCI, 75 PDMCI, and 75 cognitively normal elderly (Nold) subjects were available in an international archive. Age, gender, and education were carefully matched in the three groups. The Mini-Mental State Evaluation (MMSE) was matched between the ADMCI and PDMCI groups. Individual alpha frequency peak (IAF) was used to determine the delta, theta, alpha1, alpha2, and alpha3 frequency band ranges. Fixed beta1, beta2, and gamma bands were also considered. eLORETA estimated the rsEEG cortical sources. Receiver operating characteristic curve (ROC) classified these sources across individuals.

Results: Results showed that compared to the Nold group, the posterior alpha2 and alpha3 source activities were more abnormal in the ADMCI than the PDMCI group, while the parietal delta source activities were more abnormal in the PDMCI than the ADMCI group. The parietal delta and alpha sources correlated with MMSE score and correctly classified the Nold and diseased individuals (area under the ROC = 0.77-0.79).

Conclusions: In conclusion, the PDMCI and ADMCI patients showed different features of cortical neural synchronization at delta and alpha frequencies underpinning brain arousal and vigilance in the quiet wakefulness. Future prospective cross-validation studies will have to test these rsEEG markers for clinical applications and drug discovery.

P25

Quantitative EEG changes in de novo Parkinson's disease patients: preliminary findings

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Introduction: Search for disease biomarkers is essential to improve our knowledge on pathophysiology and treatment of Parkinson's Disease (PD). Quantitative EEG changes have been recently studied as possible potential predictors of dementia in patients with PD.

Objectives: The aim of our study was to evaluate quantitative EEG (qEEG) modifications in patients with PD, and to correlate qEEG changes to CSF biomarkers, motor impairment and neuropsychological assessment.

Methods: De novo PD patients underwent motor symptoms examination (UPDRS-III), neuropsychological assessment, CSF biomarkers analysis and qEEG. The panel of CSF biomarkers included phospho-tau, total tau and beta-amyloid(1-42). qEEG analysis considered, as reference parameter, relative power of EEG bands (delta, theta, alpha and beta).

Results: 16 de novo PD patients were included in our study. We found a negative correlation between tau CSF levels and theta bands in frontal areas ($p < 0.05$). In addition, we documented a significant correlation between low performances in long-term memory test and reduction of cerebral EEG rhythms. Conversely, no correlation was found between qEEG and UPDRS-III.

Conclusions: In our study, we found significant correlations between qEEG changes and both lower long-term memory performances and tau CSF levels. Although preliminary, our data demonstrate the relevance of a complementary approach, requiring a larger cohort of de novo PD patients to be confirmed. In addition, they demonstrate that qEEG might represent an early biomarker of disease progression.

P26

UPDRS kinematic measures for telemedicine

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Background: Remote medical communications in the form of telemedicine is one of the challenges to Parkinson’s disease (PD) problems. We set up an experimental instrumentation to quantify selected items of UPDRS by a Kinect technology and body sensory-network (BSN), destined to an easy home-performance.

Methods: For automatic assignment of UPDRS scores, we studied on the whole 50 controls subjects and 110 PD patients. For finger-tapping, prono-supination, opening-closing UPDRS tasks, we propose an human-computer interface (Microsoft Kinect®) based on a RGB-Depth camera, a monitor and two light-weight gloves with coloured markers. For leg agility, sit-to stand and gait UPDRS tasks, we propose a BSN-based approach, composed of a few body-horn wireless inertial nodes. Movements are automatically translated in kinematic parameters and then classified by dedicated algorithms correlating with corresponding UPDRS clinical scores.

Results: The selected kinematic parameters show high correlation with the neurologists scores ($\rho > 0.7$). The average classifier performance is good (e.g. sensitivity 82%, specificity 66%) and consistent with the inter-rater agreements (Intra Class Correlation of 67%).

Conclusions: These results show that the proposed technology is an accurate, feasible and low-cost approach useful for at distance evaluation of PD patients. Moreover, our system has shown to discriminate even small changes in patient motor performance over the course of the day.

P27

Interoceptive processing deficit in Parkinson's disease

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Introduction: Non-motor symptoms in Parkinson's disease (PD), such as cognitive, emotional, autonomic and somatosensory alterations, are not ubiquitous but vary between the tremor dominant (TD) and postural instability/gait difficulty (PIGD) subtypes of the syndrome. Non-motor phenomena have been related to representation of autonomic and somatosensory sensations (interoception), and recent findings suggest interoceptive deficits in PD.

Objectives: The aim of the study was to test whether interoceptive processing is differently affected in TD and PIGD phenotypes, by assessing both interoceptive accuracy and sensibility in PD patients with TD and PIGD subtypes, and in healthy controls (HC).

Methods: Interoceptive accuracy was measured by the heartbeat perception task requiring participants to count their own heartbeats in a given time interval. A time-estimation, control task was also administered asking participants to count the seconds in a set period of time. Interoceptive sensibility was assessed by a questionnaire of subjective interoception. Finally, the patients underwent measures of anxiety, depression, apathy and anhedonia, and impulsive-compulsive disturbances.

Results: We found in TD patients reduced interoceptive accuracy and sensibility respect to both PIGD patients and HC. Reduced interoceptive accuracy of TD group was a reliable result since their performance on the time estimation control task was comparable to that of both PIGD patients and HC. Moreover, in PIGD patients, a higher interoceptive sensibility was related to higher severity of anxiety, impulse control disorders and anhedonia.

Conclusions: The present study revealed a deficit of interoceptive processing in TD patients, and a specific relation between emotional disorders and interoceptive sensibility in PIGD patients. The findings suggested that behavioural assessment of interoceptive processing can provide with a non-motor marker for subtyping patients, thus contributing to the clinical distinction between motor phenotypes of the PD.

P28

Cognitive correlates of apathy in Parkinson's disease: a meta-analytic study

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Introduction: Parkinson's Disease (PD) is characterized by motor and non-motor symptoms. Among them, apathy impacts negatively caregivers' and patients' quality of life. Several studies have investigated cognitive correlates of apathy in PD patients showing that apathetic PD patients had lower scores in global cognitive functioning, executive functions, visuospatial and memory tasks than non-apathetic patients. However, other studies failed to find significant differences between the two groups.

Objectives: To explore the cognitive correlates of apathy by means of a meta-analytical study.

Methods: An extensive search of published studies was conducted in online databases (PubMed, SCOPUS, PsycInfo). Studies were selected if they examined cognitive functioning in both apathetic and non-apathetic PD patients by a comparison between the two groups or by correlational analysis between apathy and cognitive tests scores. We considered the following outcomes: global cognitive function, memory (i.e. short term verbal memory, short term spatial memory, long term verbal memory, long term spatial memory), executive functions (i.e. general, shifting, abstraction ability/concept formation, inhibition, generativity), processing speed/complex attention/working memory, visuospatial and constructional ability, and language. Nineteen studies met inclusion criteria.

Results: Apathetic PD patients showed more severe dysfunctions on global cognitive functioning (Effect size= -0.49; $p < 0.001$), short term spatial memory (Effect size= -0.29; $p = 0.021$), long term verbal memory (Effect size= -0.61; $p < 0.001$), long term spatial memory (Effect size= -0.41; $p = 0.013$), processing speed/complex attention/working memory (Effect size= -0.44; $p < 0.001$), visuospatial and constructional ability (Effect size= -0.55; $p < 0.001$), language (Effect size= -0.46; $p = 0.004$) and executive functions than PD patients without apathy. As for executive functions, apathetic PD patients got significantly lower scores on general (Effect size= -0.99; $p < 0.001$), shifting (Effect size= -0.31; $p = 0.021$), abstraction ability/concept formation (Effect size= -0.61; $p < 0.001$), inhibition (Effect size= -0.57; $p < 0.001$) and generativity dimensions (Effect size= -0.53; $p < 0.001$). There were no significant differences between apathetic PD patients and non-apathetic ones on short-term verbal memory cognitive domain. A meta-analysis including only studies on non-demented PD patients confirmed the results regarding all cognitive domains, except for shifting outcome of the executive functions.

Conclusions: Apathy seems to have a pervasive effect on cognitive abilities. Apathy affects performances on global cognitive functioning, language, visuospatial abilities, memory and executive functions in PD patients with and without dementia.

P29

Psychiatric profile of motor variants of newly diagnosed drug-naïve Parkinson's disease patients

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Introduction: Parkinson's disease (PD) is a heterogeneous neurodegenerative disorder. It is well established that different motor subtypes of PD evolve with different clinical courses and prognoses. The complete psychiatric profile underlying these different phenotypes since the very early stage of the disease is debated.

Objective: We aimed to investigate psychiatric profile of three motor subtypes of PD (akinetic-rigid, tremor-dominant and mixed) in newly diagnosed drug naïve PD patients.

Methods: Sixty-eight drug naïve PD patients were enrolled. Based on different onset motor presentations of PD, patients were divided in three subgroups according to Kang et al. guidelines [1]: 1) AR (n=39), TD (n=22) and MIX (n=7). All patients underwent a complete assessment of psychiatric, cognitive, and motor symptoms. A Structured Clinical Interview for DSM-5 Disorders-Clinician Version for the identification of psychiatric disorders according to the DSM-5 criteria was applied. Psychiatric diagnoses were made by a senior psychiatrist. Moreover, the complete evaluation included: the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, the Snaith-Hamilton Pleasure Scale, the Toronto Alexithymia Scale-20 item and the Apathy Rating Scale for evaluation of depression, anxiety, anhedonia, alexithymia and apathy symptoms severity, respectively. Further, all participants underwent to a complete neuropsychological examination including: 1) MMSE; 2) the Mental Deterioration Battery, that includes: a) Rey's 15-word test Immediate Recall and Delayed Recall; b) Phonologic and Semantic Verbal Fluency tests; Copy of the Rey-Osterrieth picture and Delayed Recall of the Rey-Osterrieth picture; Wisconsin Card Sorting Test- Short Form; and Stroop Word-Color Test.

Results: No significant neuropsychiatric differences were found among groups.

Conclusions: Our results suggest that a differentiation on the psychiatric symptoms associated with specific motor subtypes of PD is not detectable in newly diagnosed drug naïve patients, therefore it emerges later along the disease progression as a consequence of the dopaminergic and non-dopaminergic damage increase.

References

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P30

Cognitive and psychiatric symptoms in early and classic-onset Parkinson's disease: two different subtypes of the same disease?

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Introduction: Non motor-dysfunctions are very frequent in Parkinson's Disease (PD). Among these, cognitive and psychiatric symptoms are prevalent. Patients with early onset of the disease show a wide spectrum of changes in neuropsychological and psychiatric performances compared to normal subjects of the same age.

Objective: We studied two populations of patients with PD, Early-Onset (EOPD) and Classic Onset (COPD). Although motor symptoms can be overlapping, we hypothesized that cognitive and psychiatric dysfunctions can be predominantly altered within each patient sample. We also hypothesized that motor deficits could affect the level of cognitive decline and mood depression in the two populations.

Materials and methods: We selected 20 patients (10 EOPD, mean age 53 years, and 10 COPD, mean age 69). Each group has been tested using validated cognitive scales (MMSE, MoCA), diagnostic criteria (DSM V) and scales for assessing the psychiatric disorder (Hamilton's scale). Results were matched and compared with statistical analysis.

Results: Cognitive disorders were very common in both patients with EOPD and COPD. The cognitive pattern of visual-working abilities is more compromised in the latter sample. The severity of depressive disorders is greater in the EOPD group and does not appear to be related to the degree of motor disability. A significant correlation between cognitive disorders and the level of motor symptoms was found, especially in the CODP sample.

Conclusions: From our analysis emerge significant differences in the cognitive and mood symptoms between the two groups with different onset of illness, which together with the motor variations allow us to support the hypothesis that the EOPD and the PD conventionally meant can represent two different subtypes of the same disease.

P31

Risky decision-making and affective features of impulse control disorders in Parkinson's disease

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Background: Impulse Control Disorders (ICDs) in Parkinson's disease (PD) are considered dopaminergic treatment side effects. Cognitive and affective factors may increase the risk of ICD in PD.

Aims: To investigate risky decision-making and associated cognitive processes in PD patients with ICDs within a four-stage conceptual framework. Relationship between ICDs and affective factors was explored.

Methods: Thirteen PD patients with ICD (ICD+), 12 PD patients without ICD (ICD-) and 17 healthy controls were recruited. Overall risky decision-making and negative feedback effect were examined with The Balloon Analogue Risk Task (BART). A cognitive battery dissected decision-making processes according to the four-stages conceptual framework. Affective and motivational factors were measured.

Results: ANOVA showed no effect of group on overall risky decision-making. However, there was a group X feedback interaction [$F(2, 39) = 3.31, p = 0.047$]. ICD+, unlike ICD- and healthy controls, failed to reduce risky behaviour following negative feedback. A main effect of group was found for anxiety and depression [$F(2, 38) = 8.31, p = 0.001$], with higher symptoms in ICD+ vs. healthy controls. Groups did not differ in cognitive outcomes or affective and motivational metrics.

Conclusions: ICD+ may show relatively preserved cognitive function, but reduced sensitivity to negative feedback during risky decision-making and higher symptoms of depression and anxiety.

P32

Orthostatic hypotension acutely impairs executive functions in Parkinson's disease

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Orthostatic hypotension is a frequent non-motor symptom of Parkinson's disease, with negative prognostic role on cognitive functions. Here we measured the acute effects of orthostatic hypotension of executive functions in Parkinson's disease patients devoid of hypertension, carotid artery stenosis and significant chronic cerebrovascular pathology. Measurements were carried out during regular visits in outpatient setting.

Twenty-four Parkinson's disease patients were recruited and studied along regular outpatient visits. They were divided into 2 groups (n=12 each) according to the presence or lack of orthostatic hypotension. This was diagnosed according to international guidelines. All patients were submitted to the Stroop's test and to the phonological and semantic verbal fluency tests after 10 min resting in supine position. Tests were repeated immediately upon standing in upright position.

In upright position, subjects with orthostatic hypotension displayed significantly worse performances at the Stroop's test (color naming and number of errors at interference section) as compared to those without orthostatic hypotension.

These results demonstrate that worsening of attentive function upon standing can be measured in Parkinson's disease patients with orthostatic hypotension during routine outpatient visits. These findings suggest that clinically asymptomatic OH in PD patients may produce transient neuropsychological sequelae with possible negative impact on daily functioning.

P33

Neuropsychological profile of patients with Parkinson's disease and Pisa syndrome

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Introduction: Pisa syndrome (PS) is a complex and disabling axial complication of Parkinson's disease (PD), affecting approximately 9% of the PD population. The pathogenesis of PS remains incompletely understood. It has been suggested that axial-dominant PD presentation can be associated with more severe cognitive impairment but literature data on the cognitive profile of PD patients with PS are still lacking. A recent study investigated for the first time the cognitive profile of PS patients, indicating an association between PS and worse performances in attention and posterior cortical function.

Objective: To evaluate whether PD patients with PS (PS+) have a different profile of cognitive impairment in comparison with clinically and demographically matched PD patients without abnormal postures (PS-).

Methods: Seven PS+ patients were matched with PS- patients for age, gender, PD duration, Hoehn and Yahr score and level of education. Both PS+ and PS- patients underwent an extensive neurological and neuropsychological assessment aimed to investigate six cognitive domains: reasoning, memory, attention, executive-functions, language and visuospatial abilities. Then, for each cognitive domain, we obtained a Cognitive Index (CI; score 0-3), corresponding to the average value of the related subtest. Descriptive statistics and nonparametric tests were used to compare neuropsychological performances in the two groups.

Results: PS+ and PS- groups outlined similar scores from measures of global cognitive status (MMSE: PS+ = 28.0±2.2; PS- = 29.0±0.82; p=0.456). PS+ group showed worse performances than PS- for attentional (CI: PS+ = 1.1±0.7; PS- = 0.0±0.0; p=0.004) and visuospatial abilities (CI: PS+ = 1.1±0.7; PS- = 0.0±0.0; p=0.004). No differences were found for the others cognitive domains.

Conclusion: Our preliminary results highlight a significant association of PS with altered attention and visuospatial skills in PD, possibly suggesting that PS may have a central pathogenesis, involving the visuospatial abilities and the perception of space.

P34

The ability of recognizing positive, negative and neutral facial expressions in Parkinson's disease is influenced by the presence of freezing of gait

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Background: Affective “Theory of Mind” (ToM) is the specific ability to represent own and others’ emotional states and feelings and can be assessed by means of the “Reading the Mind in the Eyes test” (RMET). A previous study by our group showed that this ability is impaired in patients with Parkinson’s disease, and particularly in patients with FOG. RMET stimuli can be divided, according to their emotional connotation, into positive, negative and neutral. So far it has not been investigated the impact of stimuli’s emotional connotation on RMET performance in PD patients.

Aim: We wanted to assess whether there are differences in the ability to recognize positive, negative and neutral emotional facial.

Methods: We evaluated ToM by means of RMET in 25 PD patients with FOG (PD- FOG+), 28 PD patients without FOG (PD-FOG-), and 35 healthy subjects (HS). All groups were matched for age and education level.

Results: Results confirmed that the ability to judge a person’s mental states was impaired in PD patients, and particularly in PD-FOG+. Regarding the valence stimuli, HS recognized better positive compared to neutral stimuli and neutral compared to negative stimuli. PD-FOG- performed better in recognizing positive stimuli compared to neutral and negative ones, but no differences emerged between neutral and negative stimuli. In PD-FOG+ no differences emerged between the three categories of stimuli. Particularly PD-FOG+ performance in recognizing positive stimuli was significantly worse than HS ($p=0.001$) and PD-FOG- ($p=0.045$). PD-FOG+ performed worse than HS also for neutral stimuli ($p=0.02$). No differences emerged between groups for negative stimuli.

Discussion: Our study showed that the ability to recognize positive facial expressions seems to be preserved in PD patients without FOG. On the contrary, patients with FOG showed at RMET test a widespread emotional processing dysfunction.

P35

Neuropsychological differences between Parkinson's disease, Multiple System Atrophy and Progressive Supranuclear Palsy

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Objective: Parkinsonian syndromes are characterized by a wide spectrum of non-motor symptoms. Whereas neuropsychological profile in Parkinson's disease (PD) has been widely investigated, a few studies explored cognitive deficits and neuropsychiatric symptoms in atypical parkinsonism. The study was performed to identify cognitive and neuropsychiatric differences between PD, Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) and to evaluate the influence of clinical features, depressive symptomatology and apathy on cognitive performances in the three groups.

Method: Fifty-five PD, 44 MSA and 42 PSP patients underwent cognitive tests assessing attention, language, memory, visuospatial and executive functions as well as scales assessing depression and apathy. Correlational analysis was performed between clinical, behavioural and cognitive parameters within each patients group.

Results: The main difference among the groups was on global cognitive status, verbal learning and short-term memory, executive functions, linguistic and visuospatial abilities, whereas no significant difference was found in long-term memory, buccofacial and ideomotor apraxia. Significant differences were found even on depression and apathy scales. Cognitive impairment and behavioural disturbances were more severe in PSP than in other groups. MSA group performed worse than PD group on tests assessing executive and linguistic abilities.

Conclusions: The present study underlined the pervasiveness of cognitive deficits, apathy and depressive symptoms in PSP, whereas little cognitive differences were found between PD and MSA. The findings indirectly supported that basal ganglia pathologies are characterized by common cognitive and behavioural disturbances and reinforced the pivotal role of altered basal ganglia and corresponding frontal deafferentation in their occurrence.

P36

Perception of verticality correlates with postural and balance deficits in patients with Parkinson disease

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Background: Perception of verticality is fundamental for postural stability that is often impaired in patients with Parkinson's Disease (PD) with severe consequence on independence. However whether these impairments might correlate with postural deficits has not been investigated so far.

Aim: The aim of the study was to assess verticality perception in a group of patients with PD in relation to postural and balance impairments.

Methods: 39 PD patients (23 women; mean age 72.87 ± 5.78 SD; range: 60 – 80) and 28 gender and age-matched healthy elderly (ELD, 16 women; mean age 69.16 ± 13.89 SD; range: 56 – 85) were enrolled in the study. The Pull test and the Activities-specific Balance Confidence (ABC) were used for evaluating balance performance, whereas measurement of posture was performed using the Physical Analyzer System®. For evaluating SHV, participants were instructed to provide their subjective vertical by manipulating with two hands a rod while standing with their eyes closed.

Results: SHV data showed that PD subjects had a greater deviation from the objective vertical respect to the controls ($p < 0.001$). As expected, a significant difference in balance performance (ABC and Pull test) and postural alignment was found between PD and ELD groups. Only in PD participants, SHV errors significantly correlated with (i) the lateral inclination of the trunk ($r = 0.618$, $p < 0.001$), (ii) pull test ($r = 0.519$; $p = 0.001$) and ABC ($r = 0.471$, $p = 0.002$) scores.

Discussion: Our results showed that the perception of verticality, driven by multimodal sensory integration, is defective in PD subjects compared to controls. Interestingly, deficits in SHV correlated with postural alignment and balance performances, independently from age, disease duration or cognitive decline. Our findings support that PD pathology is associated with a decline in haptic perception suggesting that perception per se might have a causal role in postural and balance deficits.

P37

Caregiver burden for informal caregivers of patients referring to the Memory Clinic of Bolzano

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Objectives: To measure the caregiver burden and the risk for psychosomatic problems among family carers of patients referring to the Memory Clinic at the Hospital of Bolzano for the diagnosis of neurocognitive disorders. We also analyze, in the subgroup with higher burden, which factors were related to the burden.

Method: From June 2015 to September 2017 913 patients came with the caregivers to undergo a diagnostic procedures for neurocognitive disorders, including clinical and neuropsychological evaluation, blood samples, and neuroimaging. To measure the burden, we used the BSFG (Burden Scale for Family Caregivers) a 28-item questionnaire validated for both Italian and German, since in our area there is a bilingual community. The level of the burden measured by the total score, can be divided into 3 levels:

- 0-35 no or minimal burden
- from 36-to-45: minimal to moderate burden
- score above 46 high burden

903 Caregivers who complete the self-administered BSFG were included. For this analysis a subgroup of 104 patients were considered (evaluated for 3 consecutive months from 20/2 until 20/4/2017). Disability was measured by BADL/IADL, comorbidity by the CIRS-index.

Results: The age of the patients ranged between 65-95 years (average age $79,81 \pm 6,27$ yy). 65% of the patients were women, 35% were men. The majority of the caregivers were female (60,6%), male were 35,6%, and in 3,8 % of the cases more caregivers were involved. 60% caregivers were children (including children-in-law); 27% were spouses (wives/husbands); 13% had other relations (sisters/brothers, cousins, grandchildren, nephews, nieces). The score obtained in the BCSF ranged between 0-77; the average score was 26. 13,5% caregivers showed high burden, 15,4% caregivers had minimal to moderate burden while and the majority of caregivers 71,1% showed no or minimal burden. In the subgroups with high-moderate burden, predictive factors were the presence of neuropsychological symptoms, high level of disability and high comorbidity.

Conclusion: Caregivers of family members with dementia are expose to depressive symptoms and physical problems. The burden of the caregiver can impact the quality of life of both patients and family members, and it is known to be associated with negative outcomes such as risk for institutionalisation, worse prognosis, higher social and health costs.

P38

Obsessive personality traits in patients with Parkinson's disease: an investigation by means of the Personal Meaning Questionnaire

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Background: Obsessive psychological symptoms and personality features has been largely described in Parkinson's disease (PD); however, this issue is still unsolved. The development of the Personal Meaning Questionnaire (PMQ) provided new insight to the concept of 'personal meaning organization' (PMO), within personality research. PMQ has been recently administered to neurological patients [1], even if it has never been applied to PD patients.

Objectives: Our work was aimed at investigating the presence of an obsessive PMO in PD patients and secondly, to better define depressive features of such neurological population.

Methods: 15 patients with probable or possible PD, 15 depressed subjects without neurological illness and 15 controls were recruited. Subjects underwent an extensive neurological investigation and the following psychological measures: PMQ, STAI-Form Y, BDI, SCL90 and SF-36. Non parametric statistics were applied.

Results: A tendency toward higher scores of obsessive PMO was observed in PD patients with respect to depressed and control participants ($p < 0.125$). A prevalence of phobic PMO in PD patients was detected with respect to depressive, obsessive and eating disorder organizations ($p < .003$). Positive and significant correlations emerged in PD patients between BDI somatic-performance subscale and UPDRS staging scale ($p < 0.007$), so as between obsessive PMO and UPDRS ($p < .01$). Specific patterns of depressive symptoms characterize PD patients and non-neurologically ill depressed patients, with higher values at the BDI somatic-performance subscale for the former and higher values at the BDI cognitive-affective subscale for the latter group.

Conclusions: Interesting differences were highlighted in depressive symptoms observed in PD and depressed non-neurologically ill patients. With regard to a specific PMO in PD patients, our results, even if not conclusive, show a tendency to experience the disease by means of cognitive and emotional patterns related to an obsessive personality organization.

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Diagnosis and management of schizophrenic-like psychosis in young-adults parkinsonian patients without dementia under ropinirole: schizophrenic co-morbidity, psycho-organic or drug induced psychosis?

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Background: The onset of psychiatric disorders of the schizophrenic spectrum (PDSS) is a very exceptional event in young-adults patients affected by Parkinson's disease (PD) without previous psychiatric disorders or cognitive impairment. In this regard the literature is extremely poor and has never expressed with clarity on their etiopathogenesis and their classification nosological definition. In fact, it is not clear if these psychoses may represent a co-morbidity of the schizophrenic spectrum, may descend from the organic base of the disease or, more simply, may be a iatrogenic psychosis.

Material and method: In about 3000 PD patients followed in our Center, we have observed five young-adults parkinsonian patients, all males (range: 42-52 years; Hoehn/Yahr I-III) without cognitive impairment who shortly after initiation of therapy with ropinirole (range from 3 months to 1 year) developed a florid subacute paranoid schizophrenic-like psychosis. Two of these patients were taking ropinirole 16 mg/daily and the remaining 24 mg/daily. No PDSS were observed with other dopaminergic medications.

Management: The first therapeutic measures were the rapid reduction/suspension of ropinirole, the sharing of the case with an expert psychiatrist, the introduction of clozapine at dosages variables. The clinical evolution was resolute for only 3 patients. Only two patients presented periodic resurgence of psychosis, confirming the possibility of a schizophrenic co-morbidity. The other patients proceeded with moderate doses of levodopa but still adopt clozapine or quetiapine.

Conclusions: Our observation documents that among the young-adults patients with first diagnosis of PD, 1.6/1000 patients can develop PDSS with initiation of therapy with ropinirole. In two of our patients, an hypothesis of schizophrenic co-morbidity may be legitimately supported, while for the other 3 the concept of "borderline subject" should be stressed. Male sex seems the most risk factor in PDSS onset, while high mean dosage of ropinirole appears the dopaminergic drug most at risk of inducing PDSS, while no PDSS were observed with other dopaminergic medications. We retain that the reciprocal interactions among PD and PDSS are far-off from to be well cleared representing an intriguing matter of search for the future.

P40

Validation of the Italian version of the questionnaire for impulsive-compulsive disorders in Parkinson's disease (I-QUIP)

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Introduction: The Questionnaire for Impulsive and Compulsive Behaviors (QUIP) is the only validated instrument specifically developed to evaluate Impulsive and Compulsive Behaviors (ICBs) in Parkinson's Disease (PD).[1] The aim of this study is to validate the Italian version of QUIP (I-QUIP), in order to obtain a screening tool for ICBs for Italian speaking PD patients.

Methods: 116 PD patients receiving outpatient care at our centre were consecutively enrolled in the study. After clinical data were collected, each patient underwent a quick interview to determine whether or not they were suitable for ICB diagnosis. Then I-QUIP was administered to all the patients. To test the reliability of the questionnaire, after a period of six months I-QUIP was re-administered to 36 patients from the original sample.

Results: A sensitivity value of 94%, a specificity value of 83%, a positive predictive value of 78% and a negative predictive value of 95% were found. Test-retest reliability was demonstrated.

Discussion: This study provides the validation of the Italian Version of the Questionnaire for Impulsive and Compulsive Behaviors (I-QUIP), a reliable instrument for the assessment of ICBs in Italian speaking PD patients.

References

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P41

Motor, behavioural, and cognitive correlates of fatigue in early, de novo Parkinson disease patients

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Introduction: Fatigue is one of the most common and disabling non-motor symptoms in Parkinson’s disease (PD). The objective of this study was to determine prevalence and motor, behavioural, and cognitive correlates of distressing fatigue in early, de novo PD patients.

Methods: Eighty-one consecutive de novo PD patients (64% men; mean age 65.73±8.26 years) underwent a comprehensive examination, including Parkinson’s disease Fatigue Scale (PFS), Epworth Sleepiness Scale (ESS), Parkinson’s Disease Sleep Scale (PDSS), Beck Depression Inventory (BDI), Parkinson’s Anxiety Scale (PAS), and Apathy Evaluation Scale (AES). Moreover, all patients underwent a detailed neuropsychological evaluation exploring attention and working memory, executive functions, memory, visuospatial abilities and language. Score of patients with or without distressing fatigue (defined as a PFS score ≥ 8) were compared by Student’s t test or Pearson’s chi-square test. Logistic regression analyses were performed to search for motor and non-motor features independently associated with presence of distressing fatigue.

Results: Twelve (15%) patients presented distressing fatigue. Logistic regression identified sleepiness ($p = .04$), “episodic anxiety” subscale of PAS ($p = .005$), and “cognitive apathy” subscale of AES ($p = .017$) as the main factors associated with distressing fatigue. No significant association was found between diagnosis of Mild Cognitive Impairment and distressing fatigue ($p = .745$).

Conclusions: In a sample of consecutive de novo PD patients, distressing fatigue is associated with episodic anxiety, cognitive apathy and sleepiness, but not with cognitive impairment. Our findings suggest possible shared pathogenic mechanisms underlying these non-motor symptoms and foster development of early combined therapeutic approaches.

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Quality of gait pattern is associated with physical activity levels in people with Parkinson's disease. Results from a 3-month monitoring

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Introduction: People with Parkinson's Disease (pwPD) are characterized by reduced levels of physical activity (PA), however it is unclear to what extent this phenomenon is associated with the quality of their gait patterns.

Objective: To analyze the existence of correlations between spatial-temporal parameters of gait and intensity of PA, objectively assessed using an activity tracker.

Methods: Eighteen pwPD (mean age 68.7, UPDRS 17.8, H&Y 1.9) wore a validated accelerometer (Actigraph GT3X+) on their non-dominant wrist for 3 consecutive months. At the end of the period of observation, spatial-temporal parameters of gait (i.e. speed, stride length, cadence, stance/swing phases duration) were assessed using 3D gait analysis, performed with a motion capture system. Accelerometric signals were processed using cut-points specific for pwPD in order to calculate steps count, Vector Magnitude Counts (VMC) and to classify the amount of PA spent at different intensity's levels. The correlations between gait and PA parameters were assessed with the Spearman's rank correlation coefficient r .

Results: The daily steps count was found positively correlated with swing phase duration and step length ($r = 0.588$, $p = 0.01$ in both cases). The VMC was found correlated with stride and swing durations ($r = 0.577$ and $r = 0.704$, $p < 0.05$) and negatively correlated with cadence ($r = -0.577$, $p = 0.012$). Stride length, swing phase duration and cadence, were also found moderately correlated with time spent at different gait speed and with the amount of time spent in sedentary, light and moderate-to-vigorous activity (r between -0.503 and 0.683). Step length was also found correlated with time spent in sedentary behavior ($r = -0.482$, $p = 0.043$).

Conclusions: In pwPD, continuous daily PA monitoring seems to be partly associated with gait's quality, thus suggesting a possible low-cost option for the physician to assess possibly gait worsening associated with the disease course.

P43

Parkinson's disease in older adults: clinical and epidemiological data from a single Italian centre

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Introduction: According to worldwide aging of populations, the incidence of neurodegenerative diseases, such as Parkinson's disease (PD), is expected to significantly increase in the next decade, with relevant socio-economic implications. Older patients with PD (OPD) indeed are extremely frail, presenting higher burden of comorbidities, multiple therapies and different sensitivity to medications. Despite the relevance of this matter, clinical-epidemiological studies are still lacking, although they are essential to drive public health's choices.

Objectives: To provide descriptive data on clinical features and therapeutic regimens of OPD from an Italian single centre.

Methods: This cross-sectional study retrospectively evaluated OPD patients afferent to a PD clinic of Tor Vergata University Hospital (Rome, Italy) from 2010 to 2017 that at last visit was older than 75 years. Data on age, sex, disease duration, Hoehn and Yahr (H&Y) score, presence of depression, cognitive decline, hallucinations, levodopa induced dyskinesia (LID) and current therapy were collected. Descriptive statistics, parametric test and regression analysis were performed.

Results: 916 PD patients were reviewed and 240 case have been included in the study (61% male) with a mean±SD H&Y score = 2.23±1. Prevalence of depression, cognitive decline, hallucinations and LID were calculated, resulting LID significantly more frequent in male. The mean±SD levodopa equivalent dose (LED) was 713±358 mg/day. Levodopa (LD) was the largest used medication (>95% of population); dopamine agonists (DA) were administrated in 39.3% and MAO inhibitors (IMAO) in 28.5%. Frequencies of either mono-/multiple therapies or single medication from DA and IMAO groups were calculated together with concomitant other therapies. No significant associations emerged between different therapeutic regimens and clinical complications.

Conclusions: This study provides preliminary clinical-epidemiological data on Italian OPD. Overall, they may constitute the background for future interventions aimed at improving the health status of a rapidly growing frail patient category.

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Cardiovascular autonomic neuropathy is an independent predictor of falls in Parkinson disease: a prospective cohort study

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Introduction: Falls represent one of the main complications of Parkinson Disease (PD), with a significant impact on patients’ mobility and quality of life. Cardiovascular autonomic neuropathy (cAN) is one of the key contributing factors to PD-associated falls. However, a direct quantification of its impact on the risk of falling in PD is still lacking.

Aim: To evaluate the association between falls and cAN in a 12-month prospective cohort study.

Methods: Fifty consecutive PD patients were evaluated with a standardized battery of autonomic testing including the assessment of heart rate variability and blood pressure changes during deep breathing, Valsalva maneuver, laying to standing. Clinical evaluations included UPDRS, push and release (P&R) test, timed up and go test, freezing of gait (FOG) questionnaire, and Montreal Cognitive Assessment (MoCA). The severity of dyskinesia and the presence/absence of REM sleep behavioral disorder (RBD) was additionally considered. Follow-up evaluations were conducted at 6 and 12 months.

Results: We observed a 38% prevalence of cAN (19/50 patients). At baseline, 36% of patients (18/50) reported at least one fall in the previous six months. This figure increased to 56% over the 12-month follow-up. After adjusting for age, disease duration, axial symptoms, MoCA score and dopaminergic treatment, cAN was associated with a 15-fold (OR:15.194; p=0.011) higher probability of falls; orthostatic hypotension (OH), the most common and recognizable expression of cAN, with a 10-fold probability (OR:10.702; p≤0.020). In addition, other clinical features emerged as independently correlated (p<0.05) with greater probability of falls, including P&R test (OR:14.021), RBD (OR:5.470) and FOG severity (OR:1.450).

Conclusions: This study provides evidence that cAN, including but not limited to OH, is a strong and independent predictor of falls in PD. Future research endeavors clarifying to what extent pharmacological and non-pharmacological treatments targeting autonomic dysfunctions might reduce the risk of falls in PD are warranted.

P45

Parkinson's disease and Microbiota: the experience at the University of Rome "Tor Vergata"

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Introduction: Dysbiosis of gut microbiota, in Parkinson's disease (PD) patients, may affect any disease stage and influence clinical features and prognosis. So far, few reports have provided a consistent analysis adjusted for confounders (such as medication regimen).

Objectives: Here we present preliminary data obtained from the collaboration between the Dept. Biology (Prof. Desideri) and Parkinson Centre (Prof. Stefani), at University Tor Vergata.

Methods: Idiopathic PD patients afferent to our PD clinic, fulfilling the UK Brain bank criteria, and not afflicted by severe co-morbidities, were enrolled. Special care was taken for acquiring complete data on life and dietary habit, utilizing questionnaires adapted to Italian customs. 16 rRNA amplicon sequencing was performed using the Illumina MiSeq technology from DNA extracted from patient's and control's stools. Sequences were classified to taxonomic rank through a bioinformatic analysis. For identifying differential abundant species between controls and patients, statistical analysis was performed taking into account the effect of potential confounders (age and sex, medication regime, diet, etc).

Results: On the first 40 samples, we show that neither age (Mann-Whitney p-value = 0.913) nor gender (Fisher exact test p-value = 0.19) can be considered potential confounder. At least 17 taxa were found significantly different when comparing PD to controls. We are currently promoting a large extension study on at least 200 subjects, in order to confirm, in Italy, the possible correlation with specific profile (i.e. abundance of Enterobacteriaceae in association with postural instability or peculiar non-motor spectrum).

Conclusions: This study promises to provide original findings on the microbiota of an Italian PD population. We believe that it may contribute to identifying patients at risk for severe complications and to tailoring individual therapy.

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PIGD and Akinetic-Rigid subtypes of Parkinson disease are not the same: debunking a myth

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Introduction: Parkinson’s disease (PD) is a heterogeneous disorder. One of the earliest proposal categorized PD into three subtypes: 1) tremor-dominant (TD1); 2) postural instability and gait disorder (PIGD); and 3) indeterminate subtype. Subsequently, an alternative classification system [e.i., TD2; 2) Akinetic-Rigid (AR), and mixed subtypes] has been proposed. Semantically, the concepts of PiGD and AR are not the same. However, since in both classification systems those patients who do not have tremor as a marked feature are contrasted to the TD subtype, PiGD and AR subtypes have been constructed to be somewhat equivalent.

Objective: We sought to examine: 1) whether PiGD and AR are identical subtypes; and 2) the temporal stability of both PiGD and AR subtypes over a 4-year follow-up.

Methods: 103 de novo PD patients were evaluated and classified as TD1/PiGD or TD2/AR at baseline, 2- and 4-year.

Results: At baseline 46 (44.6%) were classified as TD1; 39 (37.9%) as PiGD; and 18 (17.5%) as indeterminate. Alternatively, 14 (13.6%) were classified as TD2, 81 (78.7%) as AR, and 8 (7.7%) as mixed. There was no association between the two classification systems at either time evaluation ($\chi^2 < 0.87$; $p > 0.05$). Prospective data were available for 61 patients. As to the TD/PiGD classification, at 2Y about 35% and 25% of the original TD1 and PiGD, respectively, shifted category. A slightly lower rate of shift was observed from 2Y to 4Y. Analogously, 22.2% of the original TD2 subtype and 70.0% of the original AR subtype remained stable at 2Y, while 49.2% of the entire cohort shifted category at 4Y.

Conclusions: Our results contrast with the common knowledge that the PiGD and AR are identical subtypes and argue for a temporal “instability” of both TD/PiGD and TD/AR classification systems. It is perhaps time to revisit the motor subtypes of PD.

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“PD or not PD? That is the question”. Unravelling the diagnosis of MSA

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Background: In the recent past increasing attention has been paid to the non-motor symptoms in Parkinson’s disease (PD), sometimes minimizing the diagnostic red flags. Differentiating Multiple System Atrophy (MSA) from PD is difficult in the early stage and important given the prognosis of MSA. MSA is an adult-onset, sporadic neurodegenerative disease characterised by parkinsonism, cerebellar ataxia, autonomic failure, urogenital dysfunction, and pyramidal symptoms.

Aim: To describe two cases diagnosed as early onset PD later reclassified as MSA.

Case Description: Patient A, a 46 year-old woman, came to our attention for progressive rigidity on her left leg then arm, with onset four years before. She was on levodopa (250mg/die), rasagiline (1mg/die) and rotigotine (10mg/die). Patient B was a 54 year-old woman with two-year history of frozen shoulder, she complained of pain and rigidity in her left arm and later tremor. She was treated with levodopa (150mg/die), rasagiline (1mg/die) and ropinirole (16mg/die). Both patients suffered from early urinary problems: the first has urinary retention treated with auto-catheterization; patient B from urge incontinence. In both cases neurological examination revealed rigidity and bradykinesia with axial and distal distribution (more on the left side), rest and postural hands tremor and brisk deep tendon reflexes with left side prevalence. Patient B also had intentional tremor on her left hand. MRI scans were unremarkable. 123I-FP-CIT SPECT scans showed bilateral severe reduction of tracer uptake in the putamen resulting in an “egg shaped” caudate. A diagnosis of possible MSA according to consensus criteria (ref) was made. Patients A and B underwent 123I-MIBG myocardial scintigraphy that revealed preserved cardiac uptake suggestive for atypical parkinsonism.

Conclusions: Even though urinary problems are compatible with the diagnosis of PD, as are the alterations of 123I-FP-CIT SPECT (“egg shape”), the timing of their presentation is important in their weight as red flags.

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Accuracy of MDS-UPDRS section IV for detecting motor fluctuations in Parkinson's disease

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Introduction: We recently validated the UPDRS part IV version 3.0 using a 12-hours waking-day motor assessment (WDMA) as gold standard, obtaining a high sensitivity (>80%) and low specificity (<45%) for detecting motor fluctuations. No data are still available for the MDS-UPDRS.

Objective: We validated the MDS-UPDRS part IV, especially items 4.3 and 4.5, using a WDMA as gold standard.

Materials and Methods: PD patients who underwent a WDMA for therapeutic purposes, were consecutively enrolled in the study. Motor impairment was evaluated using the motor section of the MDS-UPDRS. Presence or absence of motor fluctuations and the type of motor fluctuation were assessed by four blinded raters, expert in movement disorders, by evaluating the graphical representations of the WDMA. Motor fluctuations were also evaluated by the MDS-UPDRS part IV.

Results: Fifty-two PD patients were enrolled in the study. According to the raters evaluation 35 (67.3%) out of the 52 patients were classified as having motor fluctuation. On the contrary, according to the item 4.3 of the MDS-UPDRS section IV, 31 PD patients (59.6%) reported to spend time in the OFF state giving a sensitivity of 83.9% (95%CI 66.3-94.6) and a specificity of 57.1% (95%CI 34-78.2); meanwhile a sensitivity of 70.4% and specificity of 64% was found for the item 4.5.

Discussion: Our data suggest an improved specificity of the part IV of the MDS-UPDRS with respect to the old version (even if a slightly lower sensitivity has been detected) likely due to better and detailed instructions for patients and raters.

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Parkinson's disease prevalence in a cohort of Gaucher's disease patients

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Background: Gaucher's disease (GD) is a lysosomal storage disorder caused by GBA mutations with a large range of phenotypes. Type 1 GD is the most frequent. GBA mutations are by far considered the major genetic risk factor for Parkinson's disease. Although only a minority of GD patients develop PD, characterization of these patients may help to elucidate the mechanisms underlying this association and potential prognostic indicators.

Objective: To investigate the prevalence and describe clinical and genetic aspects of PD and parkinsonian features in a cohort of 34 type 1 GD patients.

Material and Methods: After signed informed consent, we evaluated 34 genetically characterized GD patients. We performed an extensive interview especially focused on non-motor symptoms and a neurological examination.

Results: The mean age at examination of GD patients was 46 years. Eighteen (53%) had familiarity for PD. Neurological manifestations were present in eighteen patients (53%), fourteen (41%) of which showed parkinsonian features, including reduced upper limbs swinging, tremor, rigidity and bradykinesia. Thirteen patients (38%) showed non-motor symptoms, especially RBD (n=11; 32%), constipation (n=7; 21%) and depression (n=6; 18%). Four patients (12%) fulfilled PD diagnostic criteria (Queen Square Brain Bank criteria). The genotypes of GD-PD were N370S/L444P, N188S/N188S, N370S/N370S, and N370S/R163X. The mean age of onset of PD in GD-PD patients was 52 years.

Conclusions: Although the majority of patients with GD1 are not likely to develop PD during their lifetime, its incidence among them is significantly increased compared to general population. Almost half of the cohort show motor and/or non-motor parkinsonian symptoms, which could represent prodromal clinical markers of PD in type 1 GD. This suggests that GD population represents a very interesting cohort for identifying potential biomarkers and neuroprotective therapies for PD.

P50

Alternative splicing as a potential biomarker for Parkinson's disease

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Introduction: There is a compelling need for biomarkers for the diagnosis, staging and treatment of PD. In the extensive field of biomarkers, transcriptomic profiling has been showing encouraging results: however, only few studies have focused so far on the role of aberrant alternative splicing (AS) events as PD biomarkers, and research on such biomarkers in peripheral blood is particularly lacking.

Objective: The aim of this pilot study is to investigate the potential role of alternative splicing as a biomarker of dementia development in PD patients, by analyzing leukocyte-derived RNA.

Materials and Methods: Blood leukocyte samples were collected from 4 early PD patients (EPD), 4 advanced PD patients with dementia (PDD), 4 patients with Alzheimer's disease (AD), and 7 age-matched healthy controls (CTR). RNA was extracted from the leukocytes and then analyzed by using quantitative PCR (qPCR). Firstly, we assessed the overall expression levels of SNCA, PARK2, and LRRK2 genes; successively, we investigated the AS pattern on three other target genes (ATXN2, HSPH1, LRRFIP1), which recent studies have found to be altered in a group of PDD patients.

Results: We found no significant differences in the expression levels of SNCA, LRRK2, and PARK2 between PD patients and controls. Similarly, AS quantitation did not show any significant difference in the splicing pattern of ATXN2, HSPH1, and LRRFIP1 genes. Our data, however, suggest that PARK2 might be poorly expressed in PDD patients as compared to the other subject groups; also, there are some indications of abnormal exon skipping events, with regard to exons 18-19 of the LRRFIP1 gene, observed in PDD patients.

Conclusions: Our preliminary results provide interesting clues as to possible gene expression and splicing alterations in PDD patients. These findings will be further investigated in the next phase of the study, through deep RNA sequencing.

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Neuroinflammation in Parkinson disease: exploring the role of P2X7R-NLRP3 inflammasome complex in de novo patients and healthy controls

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Introduction: The P2X7 receptor (P2X7R)-NLRP3 inflammasome complex is part of the innate immune system; its activation, through caspases, leads to the release of mature proinflammatory cytokines, promoting neuroinflammation. Recently, an involvement of inflammasome-mediated pathways in neurodegenerative diseases has been suggested. Lewy bodies, hallmark lesions of degenerating neurons in Parkinson's disease patients (PDP), are mainly composed of the protein-synuclein, which seems to play a role in NLRP3 inflammasome activation.

Objective: Aims of this study were to compare the expression of the P2X7R-NLRP3 inflammasome in PD patients and age-matched controls (CTL), and to evaluate the potential impact of therapies on the systemic expression of such platform in PDP at baseline and after one year of dopaminergic treatments.

Subjects and Methods: Nineteen consecutive, neo-diagnosed, drug naïve PDP were studied at baseline (T0) and after one year of dopaminergic therapies (T1). Nineteen age and sex-matched subjects served as controls. P2X7R, NLRP3 and caspase-1 were determined by real-time PCR in peripheral lymphomonocytes. The alternative pathway NFkB was also explored. Motor clinical features were assessed by UPDRS and H&Y and cognitive impairment by MMSE, relating scores to inflammatory markers.

Results: P2X7R and NLRP3 baseline expression was significantly higher in PDP than CTL (Median:1.80 IQR:1.14-2.44 vs 0.96,0.67-1.54 T/R p:0,01 and 3.0,1.19-7.24 vs 1.31,0.77-3.05 T/R p:0,049); CASP1 expression differed too, although not significantly. After 12 months of treatment, PDP showed a significant reduction in P2X7R (1.80,1.14-2.44 vs 0.91,0.34-1.97 T/R p:0,01), NLRP3 (3.0,1.19-7.24 vs 1.62,1.04-3.17 T/R p:0,03) and CASP1 (4.02,2.82-6.43 vs 2.93,2.05-5.09 p:0,01) compared to T0. No difference was observed in NF-kB expression, confirming the specific involvement of the P2X7R-mediated pattern.

Conclusions: An involvement of the P2X7R-inflammasome complex in the development of PD provides an alternative mechanism underlying this neurodegenerative disorder; dopaminergic treatment improves symptoms also through the modulation of such pathway. These preliminary results require confirmation.

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Identification of novel candidate genes for Parkinson's disease in a family from Trentino

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Introduction: Parkinson's disease (PD) is generally sporadic with unknown aetiology, even though familial cases are not rare. In the last 20 years several genes have been associated with PD. The identification of the majority of these genes has been due to the study of large pedigrees with multiple affected members. In this view, we collected several families affected by typical PD and one of them underwent in-depth genetic analysis.

Objectives: To identify the genetic cause of PD in a large pedigree with three cousins affected.

Methods: Neurologists with expertise in movement disorders collected familial and clinical history and performed neurological examination of the affected relatives. Mutations in known causative genes for PD were excluded. Seven members of the family (three affected and four unaffected) were genotyped with Infinium OmniExpressExome-8 v1.4 BeadChip. Affected family members underwent Whole-exome sequencing (SureSelect Human All Exon V6). Linkage analysis was performed with Allegro software. Exomic variants were filtered with Enlis Genome software.

Results: Three peaks were detected by linkage analysis, mapping on chromosomes 6, 9 and 13. We performed WES of three affected family members and subsequently selected all shared variants located within the identified loci, with allele frequency less than 1% and predicted impact on protein or transcript. We obtained twelve variants which were characterized in terms of protein function, in-silico predicted pathogenicity, tissue expression and conservation among orthologues. Three variants located in three different genes were found to be of particular interest and we propose them as possible novel candidate genes for PD.

Conclusions: We found three novel candidate genes for PD using a combined approach of linkage analysis and WES. These findings can give an insight into molecular mechanisms underlying the pathogenesis of PD and may provide novel targets for innovative therapeutic approaches.

P53

Dyskinesia-hyperpyrexia syndrome in Parkinson's disease patients during levodopa-carbidopa enteral infusion and seasonal heatwaves

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Objectives: In the last years some reports have emerged describing the occurrence of dyskinesia hyperpyrexia syndrome (DHS), in patients with advanced Parkinson's disease (PD). The few studies so far published emphasize the role of high doses dopaminergic therapy and complex concomitant polytherapy in the pathogenesis of the disorder.

Our aim was to better define any additional pathogenic factors that have so far been poorly explored.

Patients and Methods: We report three cases of patients with advanced PD in levodopa-carbidopa intrajejunal gel (LCIG) who developed DHS during a seasonal heatwave and review other cases reported in the literature.

Results: Our study highlights the pathogenic role of extremely high ambient temperature and the high dosage of dopaminergic therapy by intrajejunal infusion.

Conclusions: In this context of climate warming, the population of PD patients, especially those treated with high amounts of LD (even more if through LCIG), represents a cohort at risk of DHS. In case of heatwaves, the onset of fever and the appearance/worsening of severe dyskinesia must be evaluated with the utmost care in order to prevent a DHS emergency.

P54

Non-motor symptoms and CSF alpha-synuclein correlate in a population of patients with Parkinson's disease

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Introduction: Non-motor symptoms (NMS) often precede motor signs (MS) and progress along the disease course, leading to severe disability and poor quality of life in patients with Parkinson's disease (PD). Therefore, the early recognition together with a better comprehension of underlying biological bases of NMS are both crucial to conceive effective treatment strategies. CSF proteins reflect main pathological alterations of the brain, thus representing reliable biomarkers for diagnosis and prognostic clustering of patients with neurodegenerative diseases.

Objectives: In this prospective study we correlated a panel of CSF neurodegeneration-related proteins to "gold standard" clinical scores for both MS and NMS aimed at clarifying clinical-biochemical associations and identifying useful biomarkers for stratification of PD patients.

Methods: Demographic, biochemical and clinical data were prospectively collected from 48 PD patients and compared to 36 healthy controls (CTL). CSF quantitative analysis included total alpha-synuclein (a-syn), amyloid-beta-42 (Ab42), total and phosphorylated tau (t-tau, p-tau), Ab42/p-tau, p-tau/t-tau, t-tau/a-syn+Ab42, p-tau/a-syn+Ab42 ratios. In PD group, clinical assessment consisted of anamnesis collection, Mini Mental State Examination (MMSE), Unified PD Rating Scale (UPDRS) pars 2-3, NMS scale (NMSS, total and subitems scores), levodopa equivalent dose (LED) calculation. Parametric and non-parametric tests were conducted to evaluate differences between the groups. Spearman' test and subsequent linear regression analysis (using age, disease duration and LED as covariates) were applied to test the association between biomarkers and clinical scores.

Results: a-syn and t-tau levels were lower in PD than age/sex matched CTL. a-syn was inversely related to NMSS, either total or items 3(mood/cognition) – 9(miscellaneous) scores; also p-tau was inversely related to NMSS, either total or items 3-4(Perceptual problems/hallucinations) scores.

Conclusions: Our findings show that NMS may directly correlate with synuclein-related degeneration of neuronal networks, apart from dopaminergic system. Therefore, we preliminarily suggest that CSF levels of a-syn can predict and/or monitor the burden of NMS.

P55

Minimal clinically important change in levodopa-response detecting motor fluctuations in Parkinson's disease patients: usefulness of base-peak evaluation in clinical practice

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Background: The progressive change in response to levodopa represents the crucial element determining the inadequate control of motor condition in the advanced stages of PD. Early detection of motor fluctuations could provide physicians with the possibility of optimizing the clinical and therapeutic management of parkinsonian patients. Since the single evaluation either in practical OFF or ON-state during the medical counselling could just partially reflect the actual motor status and responsiveness to levodopa therapy, the assessment of Minimal Clinically Important Change in levodopa dose-response through a base-peak evaluation might be useful to investigate the emergence of motor fluctuations in clinical practice.

Methods: Two independent samples of PD outpatients (exploratory population N=26, testing population N=139) were evaluated at baseline and two hours after the administration of levodopa by using the UPDRS part III. Motor fluctuations were defined by the UPDRS-IV. We quantified the magnitude of motor variation as absolute (Δ) and percentage ($\Delta\%$) change in UPDRS-III scores. Optimal cut-offs for each index assessing motor fluctuations were calculated on the exploratory population, then verified in the testing one.

Results: The optimal cut-offs defining the presence of motor fluctuations were an absolute change in UPDRS-ME scores of 6 points and an improvement from baseline condition of 18.4%. When we studied the identified cut-off scores on the testing population, the two response indices showed a sensitivity and specificity of 93.8% (95%CI: 89.7 to 97.8) and 91.2% (95%CI: 86.5 to 95.9) for the Δ and 83.3% (95%CI: 77.1 to 89.5) and 86.8% (95%CI: 81.2 to 92.4) for $\Delta\%$, respectively. In particular, our indices and their cut-offs showed a higher accuracy in distinguishing stable patients from fluctuating ones compared to the single evaluation either in ON or OFF-state.

Conclusions: The base-peak evaluation represents an accurate method for evaluating the presence of motor fluctuations in PD patients.

P56

Weight loss in Parkinson's disease patients under levodopa/carbidopa intestinal gel infusion treatment

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Introduction: Weight loss (WL) has been suggested to be a biomarker of disease progression for Parkinson's disease (PD). WL is reported as a frequent adverse event among PD patients under levodopa/carbidopa intestinal gel (LCIG) treatment. However nor its prevalence neither its causes have been systematically evaluated.

Objectives: To evaluate the WL occurrence since LCIG onset and nutritional status of PD patients.

Methods: A retrospective and cross-sectional studies were performed, among all the PD patients who were under LCIG treatment at our Center, for at least six months. Weight/body max index, MDS-UPDRS, Mini Mental State Examination, Beck Depression Inventory Scale, Hoehn Yahr (HY) Stage and levodopa equivalent daily dose (LEDD) were evaluated before LCIG onset (T0), by means of a retrospective analysis, and during the last visit (T1). At T1 the Mini Nutritional assessment (MNA) and Schwab and England ADL Scale (SE) were also assessed.

Results: We recruited 44 patients out of the 55 PD patients treated with LCIG. Patients' age, disease duration and LCIG treatment duration were respectively, mean \pm SD, 71 \pm 6, 18 \pm 6 years and 50 \pm 27 months. 75% of the patients presented a WL, being more than 10 kg among 9 patients who had a bad nutritional state as per the MNA. WL showed positive correlations with UPDRS IV score, dyskinesia duration/disability (UPDRS item 32-33), a history of device complications/granuloma and MNA score, while no correlations were found with disease duration, LEDD/Kg, dysphagia and disease severity (MDS.UPDRS III, HY and SE). At a multiple linear regression analysis, corrected for LCIG therapy duration, the only variable that kept significance was "dyskinesia duration" (p= 0.023).

Conclusions: WL is a common event among PD patients treated with LCIG with implications on patients' nutritional status. Dyskinesia duration seems to be the most related factor for WL occurrence.

P57

Taste assessment in Parkinson's disease by a new sensitive tool: the Flavor Test

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Objective: Olfaction impairment represents the most common sensory disturbance in Parkinson's Disease (PD). The gustatory perception has been poorly explored so far. As the previously used methods are heterogeneous and often not validated, we developed a new standardized tool, named "Flavor Test" (FT). The aim of this study is to examine olfactory and gustatory senses in PD patients in comparison with healthy control subjects (HC).

Material and Methods: We enrolled 40 patients and 39 HC comparable for sex, age and education. All subjects underwent: the Sniffin' Sticks Test (SST), whose results are included in the composite TDI score; the basic gustatory test (BGT), evaluating the four basic tastants; the FT, assessing the identification of 21 aromatic extracts.

Results: We found lower scores for TDI ($p < 0.001$), BGT ($p = 0.045$), and FT ($p < 0.001$) in PD patients compared with HC. No correlation was evident between SST, BGT or FT scores and: age at exam, age at onset, disease duration, MMSE, and l-dopa dose. The FT score was positively correlated with the TDI score, whereas the BGT score resulted negatively correlated with UPDRS-III score and HY scale.

Conclusions: As expected, the olfaction was impaired in PD regardless of disease duration and severity. The BGT showed that PD patients are less able to identify the four basic tastants than HC, but the loss of this ability appears late in the course of the disease. The taste perception and discrimination assessed by FT were dramatically lower in IPD than in HC. The difference in FT score between IPD and HC was more remarkable than that observed for the BGT, suggesting that the FT might be a more sensitive tool in identifying the gustatory dysfunction in PD, even in the early stage and regardless of the disease severity.

P58

Taste disturbance and non-tasting genotype in Parkinson's disease

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Background: The few studies that have evaluated taste function in Parkinson's disease (PD) have shown inconsistent results. The inherited ability to taste the bitter compound of 6-n-propylthiouracil (PROP) has been considered to be a paradigm of general taste perception. PROP taste perception is mediated by the TAS2R38 receptor, and reduced PROP sensitivity has been associated with a number of diseases not typically related to taste function disruptions.

Objectives: Here we evaluated, in PD patients and healthy controls (HC), the PROP taste perception and the TAS2R38 gene as genetic risk factors for the development of PD.

Methods: PROP taste perception was assessed by testing the responsiveness, and the ability to recognize, PROP and sodium chloride. Subjects were classified for PROP taster status and genotyped for the TAS2R38 gene.

Results: A significant increase in the frequency of subjects classified as PROP non-tasters and a reduced ability to recognize taste quality were found in PD patients, compared with HC. Results also showed that only 5% of PD patients had the homozygous genotype for the dominant tasting variant of TAS2R38, while most of them carried the recessive non-taster form, and a high number had a rare variant.

Conclusions: Our results show that PROP taster status and the TAS2R38 locus are associated with PD. The PROP test may therefore represent a novel, simple way to identify increased vulnerability to PD. Moreover, the presence of the non-tasting form of TAS2R38 in PD may further substantiate that disease associated taste disruption may represent a risk factor associated with the disease.

P59

Effects of probiotic bacterial strains on peripheral inflammation in Parkinson's disease

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Background: Parkinson's disease (PD) is characterized by loss of dopaminergic neurons and intraneuronal accumulation of alpha-synuclein, both in the basal ganglia and in peripheral sites, such as the gut. Recent findings demonstrate that PD patients display a pro-inflammatory phenotype. In this context, the present in vitro study was focused on the direct effects of probiotic bacterial strains on inflammatory pathways in PD patients.

Methods: We enrolled 40 PD patients and 40 matched controls. Peripheral Blood Mononuclear Cells (PBMCs) were isolated and cultured with the following bacterial strains: *Lactobacilli* (*salivarius*, *plantarum*, *acidophilus*, *rhamnosus*) and *Bifidobacteria* (*breve* and *lactis*). The modulation of the in vitro release of the major pro- (Tumor Necrosis Factor-alpha and Interleukin-17A) and anti-inflammatory (Interleukin-10) cytokines by PBMCs was investigated, as well as the production of free oxygen radicals (ROS). To provide a surrogate marker of inflammatory profile, we expressed cytokine data as Th1/Th2 ratio.

Results: All strains were able to inhibit inflammatory cytokines and ROS production in both patients and controls. The most striking results in patients were obtained with *L. salivarius*: 55 and 94% reduction of Th1/Th2 ratio and ROS compared to baseline. A relevant decrease of Th1/Th2 ratio was provided by *L. plantarum* and *B. breve* (39 and 38%), whereas ROS production was reduced of 85 and 77% by *L. plantarum* and *L. acidophilus*.

Conclusions: Probiotics exert promising results in modulating the release of cytokines towards an anti-inflammatory profile and in counteracting oxidative stress. Further data are mandatory to confirm the role of bacteriotherapy in PD.

P60

Pisa syndrome in Parkinson's disease: evidence for bilateral vestibulospinal dysfunction

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Introduction: Pisa Syndrome (PS) is a postural complication of Parkinson's Disease (PD). Yet, its pathophysiology remains unclear, although a multifactorial component is probable. Cervical Vestibular Evoked Myogenic Potentials (cVEMPs) explore vestibulospinal pathway but they have not yet been performed in PD patients with PS to assess a potential vestibular impairment.

Objective: To assess vestibular integrity in PD patients with PS (PDPS) and without postural abnormalities compared to healthy controls (HC).

Methods: We enrolled 15 PD patients, 15 PDPS patients and 30 healthy controls (HC). They underwent neurological examination and were assessed with Unified Parkinson's Disease Rating Scale II-III (UPDRSII- III), audio-vestibular work up and cVEMPs recording. Data were analyzed with Chi-square, one-way ANOVA, multinomial regression, non-parametric and Spearman's tests.

Results: Normal cVEMPs were significantly reduced in both PD and PDPS compared to HC (respectively $p < 0.001$ and $p < 0.001$). The pattern of cVEMPs abnormalities significantly differed between PDPS and PD ($p < 0.0001$), with PDPS showing lower normal responses ($p < 0.05$) and more frequent "bilateral absence" ($p < 0.0001$, 40% vs 6%); otherwise "unilateral absence" was more common in PD than PDPS ($p < 0.05$, 26% vs 12%). No clinico-neurophysiological correlations emerged.

Conclusions: cVEMPs are a non-invasive and inexpensive test exploring vestibulospinal tract, a crucial pathway for postural control. In our cross-sectional analysis of cVEMPs among PDPS, PD patients without PS and HC, we demonstrate that PD patients, compared to HC, have significantly abnormal vestibular evoked responses, consisting in unilateral or bilateral loss of cVEMPs. Furthermore, our findings indicate that the neurophysiological profile differs between PD patients with and without PS. PD group mostly exhibits the unilateral absence of cVEMPs, whereas PDPS group shows prevalently bilateral loss of responses. These data may thus reflect the progression of vestibular dysfunction and brainstem neurodegeneration along disease course, with a progressive worsening in advanced stages, when postural complications are more frequently observed.

P61

Dysphagia predicts poor outcome in late-stage Parkinson's disease

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Background: Parkinson's disease (PD) disability milestones emerge in an exponential manner at a late stage disease. Few data exists on the rate of clinical progression and prognostic factors for patients who have entered a very late stage of disease.

Objective: To evaluate the clinical progression and prognostic factors of a late-stage PD (LSPD) population.

Methods: 50 LSPD patients (Schwab and England ADL Scale <50 or Hoehn Yahr Stage >3 in MED ON) and 17 advanced (AD) PD patients matched for age at disease onset underwent an acute levodopa challenge test and an extensive cross-sectional clinical assessment for motor, non-motor symptoms (NMS), quality of life (QoL) and caregiver burden. LSPD patients were also assessed at one-year follow-up.

Results: Mean (SD) age was 71.5 (5.3) and 77.5 (5.9) years for ADPD and LSPD patients, respectively. LSPD patients present a more severe clinical picture, with prominent axial and NMS, that negatively influenced QoL. LSPD and ADPD patients' MDS-UPDRS-III score significantly improved after levodopa (p<0.001) respectively 18% and 53%. The magnitude of levodopa response significantly correlated with motor complications in LSPD. After one-year, 20% of LSPD patients have died.

Overall, at follow-up there was still clinical worsening of motor symptoms and NMS (worsening of MDS-UPDRS-III mean±SD 7.7±10.3, of Non-Motor Symptoms Assessment Scale 19±46 and of Neuropsychiatric Inventory test 6±13), although heterogeneous. Nevertheless, motor fluctuations and dyskinesias improved.

Functional independence worsened. At a multivariate analysis dysphagia severity at baseline was the only significant factor for negative outcome (death, institutionalization or HY 5).

Conclusions: LSPD patients still present a significant, although heterogeneous, progression in the motor and non-motor features. Acute response to levodopa does not seem to predict outcome. Dysphagia severity was the single factor associated to progression for additional disability milestones.

P62

The Italian version of the Munich Dysphagia Test-Parkinson's disease (MDT-PD): translation and cultural validation

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Objective: to perform linguistic and psychometric validation of the Italian version of the MDT-PD.

Background: Oropharyngeal dysphagia (OD) can contribute to serious respiratory complications including aspiration pneumonia, the leading cause of death in patients with Parkinson's disease. Early detection of OD is challenging due to heterogeneity of screening instruments with low specificity and sensitivity. The German MDT-PD developed and validated in 2014 was the first OD screening tool specifically for early detection of OD and aspiration risk in the PD population.

Methods: Translation and cultural adaptation of the MDT-PD was done according to international guidelines for this procedure. The Italian language version underwent a linguistic and psychometric validation on 30 continuous patients having coming to our center and having been diagnosed with Parkinson's disease. Inclusion criteria: males/females aged between 40 – 80 years, Hoehn & Yahr 2.5 – 4, stable therapeutic response for at least one month. These patients participated only in this phase of the project and were not included in the larger sample selected for the subsequent clinical validation of the Italian version. The interclass coefficient correlation and Cronbach's alpha limit (set at 0.80) were evaluated. The repeatability of the instrument was assessed using the Pearson r correlation statistic, and the comprehension of each item on the scale was evaluated by an expert interviewer (neuropsychologist).

Results: Linguistic validation: Psychometric evaluation revealed a highly significant score for both reliability and repeatability ($\alpha = 0.876$ $p=0,01$; $r=0,969$ $p=0,01$).

Conclusion: The linguistic and psychometric evaluation of the Italian version of the MDT-PD indicates that the questionnaire is a viable, non-invasive, easy to administer screening tool for detecting subclinical or early-stage dysphagia and aspiration risk in Italian PD patients. The results of this project phase enabled us to select our sample and complete our clinical/diagnostic validation of the Italian version. Paper in submission

P63

Characteristics of a population of patients referred to a secondary Parkinson's disease centre of Azienda Sanitaria Locale Roma 1

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Introduction: The prevalence of Parkinson's Disease (PD) is estimated to be 0.3% in the general population. Very few studies have reported data on consultations and referrals of such patients in tertiary PD centres and, at the best of our knowledge, there are no reports on secondary PD centres.

Objective: We retrospectively analysed the first 3 years of activity of our outpatient's clinic dedicated to PD, and all available clinical data collected at the first visit. We also compared total referral numbers of PD patients to those of the Headache Centre of the same outpatients' clinic.

Methods: Clinical records collected from 3rd October 2014 to 3rd October 2017 were analysed, the main clinical data collected and the statistics of referrals for Parkinson's disease and headache obtained from the Centro Unico Prenotazioni. Diagnosis and treatment were done following the Parkinson's disease guidelines of the Italian National Institute of Health (ISS) of 2013.

Results: Eighty-three patients were referred specifically to the Parkinson's outpatient clinic, 442 to the headache clinic and 1233 to general neurology consultations.

Clinical data of 129 patients were available for analysis, 66 males and 63 females, mean age $74 \pm 9,5$ years (range 43-92); more frequent diagnosis at first consultation were as follows: PD 74 patients, LBD 7, Parkinsonism 20, Essential Tremor 17. The 74 PD patients were 36 females and 38 males, mean age $74 \pm 9,3$ years (range 53- 92), 19 of whom had not been diagnosed before, mean disease duration $3,4 \pm 4$ years.

Conclusions: In spite PD has been reported to be the third more important disease in Primary Care, still too few patients are referred to specialised clinics. The population of patients of a secondary PD centre appears to be older but with a shorter disease duration as compared to a tertiary centre [1].

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P64

Laryngospasm as initial manifestation of parkinsonism: a case report

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Neurodegenerative parkinsonisms are clinical conditions characterized by tremor, bradykinesia and rigidity, including Parkinson's disease (PD) and Atypical Parkinsonisms, in which extrapyramidal signs and symptoms are combined with pyramidal, autonomic and cerebellar alterations. Inspiratory respiratory dysfunction defined as either diurnal or nocturnal inspiratory stridor is frequent in multisystem atrophy (MSA), whereas it is rare in PD and other atypical parkinsonisms; it is a "red flag", i.e. a potential sign of alternate pathology than PD. IN MSA it appears several years after diagnosis, although cases in which stridor in the initial manifestation are described. A 56 years old woman started to suffer from episodic difficulty of breathing four years ago, diagnosed with laryngospasm with paradoxical adduction of vocal cords, initially once a month and responsive to steroids, then more frequently and scarcely responsive to therapy. Allergy test, pulmonary function test and chest X rays were normal. Several therapies with antidepressant were experimented without substantial benefits. Two years ago her respiratory dysfunction became chronic. The patient was then treated with left posterior cordotomy because of the presence of an adduction vocal cords paralysis. After surgery she developed laryngospasm and a tracheostomy was needed. A neurological assessment revealed intermittent rest tremor of the fifth finger in her left hand and minimal bradykinesia in her left arm. 123I-Ioflupane SPECT was performed, which revealed severe loss of striatal DAT uptake both in caudate and putamen bilaterally. A urinary urgency was also reported by the patient. Unified Parkinson's disease rating scale part III score was 7/108. The diagnosis of parkinsonism was confirmed and therapy with levodopa was started. When the etiology of laryngeal stridor is not evident, a central nervous cause should be investigated. In this case laryngospasm was the first sign of parkinsonism, followed by urinary urgency and after four years by extrapyramidal signs.

P65

Onabotulinumtoxin A intradetrusor injections in the treatment of refractory detrusor overactivity due to Parkinson's disease and Multiple System Atrophy

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Introduction and Objectives: Although anticholinergics are the first-line treatment for overactive bladder (OAB) and detrusor overactivity (DO) in patients with Parkinson's Disease (PD) and Multiple System Atrophy (MSA), the benefit is limited by central adverse effects. We investigated the medium-term efficacy and safety of Onabotulinumtoxin A (Onabot/A) intradetrusor injections in a group of refractory PD and MSA.

Methods: 5 males and 18 females with PD and MSA. At baseline, all patients underwent clinical neurologic (Hoehn & Yahr scale and Unified Parkinson's Disease Rating Score-UPDR) and urologic assessments: 3-day voiding diary, uroflowmetry, the Incontinence-Quality of Life (I-QoL) questionnaire and VAS to score the bother of urinary symptoms on QoL. All patients received Onabot/A (100-200 U) intradetrusor repeat injections. Neurologic and urologic evaluations were repeated at 3 and 6 months after treatment.

Results: Mean±SD disease duration was 12.2±6.8 yrs and mean±SD age at first injection was 67.5±9.7 yrs. The mean±SD Hoehn and Yahr stage and UPDRS at baseline was 2±0.4 and 20.3±2.1 respectively. All patients received at least 2 repeat neurotoxin injections: 24 patients received 2 injections, 2 patients had 3, 1 had 4 and 1 had 5 injections. The mean±SD follow-up was 19.8±6.6 months and the mean±SD interval between 2 consecutive injections was 8.9±1.7 months. At baseline, all patients presented with urgency and 17/24 with urgency incontinence (UI); at the last follow-up, urgency persisted in 5 cases and UI in only one. Day- time and night-time urinary frequencies significantly decreased ($p<0.01$); I-QoL and VAS scores significantly increased ($p<0.01$). No side effects have been observed. 6 patients with PD and 2 with MSA stopped Onabot/A treatments due to a worsening of the neurologic disease.

Conclusions: Onabot/A intradetrusor injections are safe and effective in the medium-term follow-up in patients with DO due to PD or MSA. A rapid progression of the neurologic condition is often possible what precludes the possibility to receive further treatments along time.

P66

Efficacy of intensive multidisciplinary rehabilitation on quality of life of parkinsonian patients: a randomised controlled study

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Introduction: Quality of life (QoL) is the sense of well-being perceived by people. It represents an important index of the quality of health care and it is particularly relevant in chronic diseases, such as Parkinson's disease (PD).

Objective: To evaluate whether a 4-week multidisciplinary, aerobic, motor-cognitive and intensive rehabilitation treatment (MIRT) improves QoL of parkinsonian patients, in the short and long-term period.

Methods: This is a prospective, parallel-group, single centre, single blind, randomized clinical trial. 186 parkinsonian patients, assigned to experimental group, underwent MIRT; conversely, 48 patients, assigned to control group, did not receive rehabilitation. PDQ-39 was assessed 2 (T0), 10 (T1) and 18 (T2, only experimental group) weeks after the enrolment.

We compared T1 versus T0 scores within subjects and delta-scores (T1-T0) between subjects. To investigate the long-term effects, we compared T2 and T0 scores in the experimental group

Results: At T0, no between-group differences in Global Index Score (GBI) were observed (experimental group: 43.6±21.4, controls: 41.6±22.9, p=0.50). At T1, we did not find significant changes in controls (delta score: 1.2±9.9, p=0.23) and we found an improvement of GBI in the experimental group (delta score: -8.3±18.0, p<0.0001), significant also between subjects (p<0.0001). Comparing T2 versus T0 in the experimental group, the GBI maintained a significant improvement (delta score: -4.8±17.5, p<0.0001).

Conclusions: A rehabilitation treatment such as MIRT could improve QoL in PD patients in the short and long-term period. Even though the single-blind design and the possible role of the placebo effect on the conclusive results must be considered as limitations of this study, the improvement in outcome measure, also maintained after a 3-month follow-up period, suggests the effectiveness of MIRT on the QoL.

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“BREMBO” the Brembana Valley Horse way to manage trunk rehabilitation in Parkinson’s disease

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Introduction: Lack of trunk control is often present as Parkinson’s disease sign in many patients and different scientific studies has demonstrated physiotherapy could improve it through different specific programs.

Objective: The aim of our study is finding a new, easy and repeatable technology to improve trunk control in Parkinson’s disease.

Methods: “BREMBO” is a mechanical horse based on springs and levers moved by the patients without any electronic system and the patients’ movements are more flowing. This mechanical horse is also useful to prepare patients to hippotherapy and to rehabilitate the trunk control. We tested 12 patients with Parkinson’s disease with cardiovascular and respiratory stability, without cognitive impairment and Trunk Control Test Score (TCT) from 36 to 61. Each patient was evaluated by physician and then tested with Hunova System™ before riding and after the treatment with our Brembo Horse. The treatment with our mechanical horse is always under clinical control.

Results: We collected 5 women and 7 men and we got an improvement both of Trunk Control Test (TCT) score and Hunova System™. Patients find benefit in improving trunk control, balance and joint rehabilitation, they like the new exercises always trained in safety and under physiotherapist control.

Conclusions: The new technology is cheap because it doesn’t need robot (Trunk Control Test can easily replace Hunova System™) and the maintenance of BREMBO HORSE is very simple. It is an opportunity for patients with these diseases. It is also useful in adults and children as a propedeutic to hippotherapy.

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Suicide after STN-DBS in Parkinson' disease: who, when and how to prevent?

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Introduction: Despite significant motor and quality of life improvement, an unexpected high frequency of suicide has been reported after subthalamic nucleus deep brain stimulation (STN-DBS) in Parkinson's disease (PD) patients.

Objectives: 1) To determine the postoperative attempted and completed suicide rates after STN-DBS in a single center cohort; 2) To determine factors associated with attempted and completed suicide.

Methods: We retrospectively included all PD patients who underwent bilateral STN-DBS surgery at the Grenoble University Hospital between 1993 and 2016. Clinical data were collected from medical records. Detailed preoperative and postoperative neuropsychological evaluations, including frontal and Beck depression inventory (BDI) scores, were gathered. For each patient who committed or attempted suicide, two PD patients with STN-DBS without any suicidal behaviors were matched for age (± 1 years), sex and year of surgery (± 2 years).

Results: A total of 534 PD patients were included (337 males). Completed and attempted suicide percentages were 0.75% (4/534) and 4.11% (22/534), respectively. Observed suicide rate in the first postoperative year (187.20/100000/year, 1/534) was higher than the expected National Observatory on Suicide Risks rate adjusted for age and gender (Standardized Mortality Ratio: SMR=8.1). This rate remained similar over the second and third postoperative year. Comparing the 26 patients completing/attempting suicide with 52 controls, the first group showed: 1) more frequent previous history of suicidal ideation/suicide attempts and psychotic symptoms; 2) higher percentage of familiar psychiatric history (addiction, depression and suicide); 3) higher psychiatric medication use both in the preoperative and postoperative phase; 4) higher preoperative frontal and BDI scores at neuropsychological evaluations.

Conclusions: Suicide and suicide attempts can occur after STN-DBS, especially during the first 3 years, in patients with previous history of psychiatric issues and higher frontal scores. A carefully multidisciplinary assessment and long-term follow-up are recommended to recognize and treat this potentially preventable risk for mortality.

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Dyskinesia-hyperpyrexia syndrome (DHS) after sudden interruption of deep brain stimulation and increase of oral dopaminergic therapy: a case report

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Introduction: DHS is a rare complication of Parkinson’s disease (PD): it represents a movement disorder emergency, characterized by severe dyskinesias, hyperthermia, rhabdomyolysis and alteration of mental status. To date, DHS has been described only in a few case reports. We report the case of a PD patient treated with bilateral deep brain stimulation of subthalamic nucleus (STN-DBS) who developed DHS after the sudden interruption of stimulation.

Case report: A 79-year-old woman with advanced PD, treated with bilateral STN-DBS and achieving a good control of motor fluctuations, was admitted to hospital in May 2017 because of a cutaneous infection at the implantable pulse generator (IPG) site. IPG was surgically removed; cultural examinations were negative. After the IPG explantation, oral dopaminergic therapy was increased to maintain a good control of PD symptoms: the patient immediately presented severe uncontrolled dyskinesias, fever (39°C), confusional state and respiratory failure. Blood tests revealed increase of creatinine kinase (CK) and leucocytes; bacteriological blood and urine cultures were negative. Antiparkinsonian drugs were progressively reduced until the suspension; parenteral fluids, benzodiazepines and antipyretics were administered. After 2 days, dyskinesias disappeared and the patient presented rest tremor, rigidity, normal mental status and no fever. CK levels and leucocytes became normal. After 3 days, dopaminergic therapy was readministered and slowly increased, without side effects.

Conclusion: Pathogenesis of DHS is still not well understood: some characteristics are similar to parkinsonism hyperpyrexia syndrome but, in contrast, DHS is probably the consequence of an excessive dopaminergic replacement in basal ganglia and hypothalamus, influencing the origin of dyskinetic status, confusion and altered body temperature regulation. PD patients treated with STN-DBS can rarely face a sudden interruption of stimulation: an increase of antiparkinsonian drugs is often required to avoid the acute worsening of PD symptoms. We suggest a careful monitoring of these patients for the possible risk of DHS onset.

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Physical therapy as an intervention to mitigate cognitive decline in people with Parkinson's disease

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Introduction: Cognitive impairment is a well-established outcome of people with Parkinson's disease (PD) in the mid-advanced stages of disease, where it represents a major source of eventual treatment-refractory disability and negatively impacts quality of life. Mild cognitive impairment in PD (MCI-PD) is considered a predictor for the development of PD dementia. Physical activity, which has proved effective in improving motor symptom, has also been proposed as a possible non pharmacological intervention for preserving/reverting cognitive impairment in PD.

Objective: The aim of this study is to assess the effect of a 4-week rehabilitation therapy based on physical therapy on the cognitive function of patients with mid- stage MCI-PD.

Methods: 39 PD-MCI patients were randomized between two arms: physical therapy (PT) or no physical therapy (CT). Subjects in PT group (n. 17) attended a rehabilitation program with 6 sessions/week, each lasting 60 minutes, for 4 weeks in addition to their usual pharmacological therapy; while subjects in CT group (n. 22) received only pharmacological therapy. Neuropsychological assessment was performed with a battery of specific tests aimed to investigate executive and attentive functions. Furthermore, we measured motor performances (UPDRS-III, Tinetti Balance Scale and Hauser Index). All indicators were collected at baseline (T0) and at the end of the intervention period (T1).

Results: In PT group, we observed a significant T0 to T1 improvement on MoCA scores and on working memory tests, associated to a parallel improvement in motor performances. Cognitive and motor scores did not change in CT group. At the intergroup analysis, we detected significantly higher scores at MoCA test, Digit-span task, mental flexibility and executive function test (TMT-B) at T1 in PT group when compared to controls.

Conclusions: These results show that PT has positive effects also on cognitive performance and may represent an additional tool to decrease cognitive decline in MCI-PD patients.

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An alternative approach of multidisciplinary, intensive rehabilitation treatment in Parkinson disease

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Introduction: Growing evidences supported rehabilitation as an essential adjuvant treatment to pharmacological and surgical approach in Parkinson Disease (PD). In PD animal model exercise has been demonstrated to increase synaptic strength and influence neurotransmission, mechanisms that may modulate dysfunctional circuitry in PD and promote functional improvement. Multidisciplinary and intensive approach has been demonstrated efficacy on motor and non-motor symptoms and quality of life in PD patients. Nevertheless, interventions applied in different studies are quite heterogeneous and, at moment, there is not consensus on the 'gold standard' approach.

Objectives: The aim of our study was to investigate the effectiveness of our multidisciplinary, intensive program on motor and non-motor symptoms in PD patients through quantitative measures.

Subjects and Methods: 30 PD patients underwent a multidisciplinary, intensive rehabilitation treatment for five weeks. Rehabilitation treatment consisted in: physiotherapy, training on balance platform, treadmill with visual/auditive cues and crossover, occupational therapy, psychotherapy and music therapy. Each patient was evaluated with ad hoc scales before and after rehabilitation treatment.

Results: The results of this study show the improvement, after treatment, on UPDRS, PDSS, FOG, FSS, BERG, BARTHEL, BDI-II and MMPSE. In the sample available the UPDRS decreases for all the patients under observation and overall in a measure of about 40,64%. Concerning UPDRS, PDSS, FSS, BARTHEL the mean difference (i.e. mean difference between PRE and POST), using the t-test is statistically significant (p-value<0,05). Concerning the FOG, BERG, BDI-II and MMPSE on the basis of the data at hand the mean difference is not significant (p-value>0,05).

Conclusions: We proposed a multidisciplinary, intensive rehabilitation program in PD. Preliminary data suggest a potential efficacy on motor and non-motor parkinsonian symptoms; implementation of recruitment and a comparison with a control group (conventional rehabilitation treatment) are in progress.

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Directional deep brain stimulation: what's for?

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Objective: To screen language disorders in patients with Parkinson's disease and atypical parkinsonisms, beyond articulation and phonation alterations.

Methods: Thirty-four patients with Progressive Supranuclear Palsy (PSP), twenty eight with Parkinson's disease (PD) and twenty nine with Multiple System Atrophy (MSA) received a combined cognitive and motor evaluation. The neuropsychological battery included tests evaluating different cognitive functions and a screening language battery (SAND).

Results: Naming, word and sentence comprehension, semantic association, unpredictable sentences repetition and non-word reading tasks were more impaired in PSP than MSA and PD ($p < 0.05$), without differences between the last two groups. PSP patients had significantly worse performance than PD, but not MSA in word and predictable sentences repetition and reading tasks. Dividing patients according to impaired/normal score on the Montreal Cognitive Assessment, we found a significant difference in the reading tests in PSP, in the naming task and word comprehension of living things in PD, and in word and sentence comprehension, word repetition and reading in patients with MSA. We found significant correlations between language tests and executive functions, in particular in tests assessing planning and divided attention.

Conclusions: We found that PSP patients have a significantly worse performance than MSA and PD patients in a large number of language tests, whereas MSA patients have a worse performance than PD patients only in selected tests. The global cognitive status of patients significantly influences language scores in MSA patients. Language performance is significantly related to executive functions, particularly in MSA and PD patients.

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Looking for the optimal dose in outpatient rehabilitation of people with Parkinson's disease. A retrospective cohort study

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Introduction: Rehabilitation has been shown effective at improving functional abilities of people with Parkinson's disease (pwPD), through task-oriented and aerobic training, though the exact role of exercise intensity has not yet been determined.

Objective: The study purpose is to evaluate the impact of different intensity rehabilitation protocols on the short and medium term progression of disability in pwPD.

Methods: Using a retrospective cohort study design, the medical records of pwPD who consecutively underwent task-oriented outpatient rehabilitation from 2008 to 2016 at a University Hospital were retrieved. Subjects were considered eligible if they: a) had undergone a single cycle/year of gait and balance training, b) had stable drug therapy during the whole study period, and c) the UPDRS II subscore was available both at the baseline, at the end of treatment and 4 + 2 months after. The UPDRS part-III, TUG test, 6MWT, FOG-Q, Falls Efficacy Scale (FES) and PDQ-39 were also looked for as secondary outcome measures.

Results: Eighty out of 420 records met the eligibility criteria. A Low-Intensity (LIT) (39 cases) and a High-Intensity Training (HIT) (41 cases) group were defined according to a total training duration of less or more than 1000 minutes, respectively. HIT group included a greater rate of responders than LIT (65% cases with a meaningful gain in the UPDRS II, vs 35%; $\chi^2:3.8;p=.04$). At variance with the LIT group, HIT subjects also showed a persistent improvement in UPDRS scores ($F:14.5;p<.0001$) and in FES ($F:6.7;p=.002$) at the 4-month follow-up. No significant between-group differences were found comparing TUG, 6MWT and PDQ-39 changes.

Conclusions: A total training duration of at least 90 minute/session per 20 sessions of task-oriented and aerobic training is recommended in pwPD, in order to ensure a clinically meaningful and persistent reduction of their disease-related disability.

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Memory benefit of computer-based cognitive rehabilitation in patient's with Parkinson's disease

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Introduction: Cognitive rehabilitation represents a therapeutic approach designed to improve memory complication of Parkinson's disease (PD). Computer-based cognitive rehabilitation uses multimedia and informatics resources to optimize cognitive compromised performances.

Objective: The objective of this study was to examine the effect of computer-based cognitive rehabilitation on cognitive function in patients with PD.

Methods: 5 patients diagnosed as having idiopathic PD were recruited (aged 58–83 years; education 8-13 years). Patients received computerized cognitive rehabilitation program using The MediaHospital® platform 60 minutes/day, 1 time/week for 8 weeks. The platform provides multimedia laboratories for cognitive functions training to promote the rehabilitation process using exercises specifically designed for treating patient pathological condition. A comparative analysis on all subjects was conducted before (T0) and after (T1) the treatment through a global and cognitive memory assessment (Montreal Cognitive Assessment, Rey Auditory Verbal Learning Test, Forward Digit Span, Backward Digit Span and Rey-Osterrieth figures).

Results: After 8 weeks of therapy, patients presented statistically significant improvement only in Rey Auditory Verbal Learning Test-Immediate Recall [(mean±SE) T0: 21.80±3.7 vs T1: 27.80±4.5, p= 0.04]. No changes were found in the other tests (p=>0.05).

Conclusions: Despite the small sample size, our study revealed that a cycle of computer-based cognitive rehabilitation with the MediaHospital® improves verbal learning and memory in PD patients. Computerized cognitive rehabilitation therapy is an easy, safe and always available program that can be used as a treatment tool beneficial not only in cognitive functions but also in other potentially disease-connected issues that may have a strong impact on patient's life.

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Education therapy in Parkinson's disease: non-pharmacological interventional, multicentric, randomized controlled trial

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Introduction: Parkinson's disease (PD) is a chronic-progressive illness that significantly affects the quality of life of patients and their caregivers, especially in the advanced and complicated phases of the disease. Patient education in PD appears to have potential as a useful and feasible intervention, complementing medical treatment in PD but it is still unclear whether can also lead to an improvement of motor function of the patients.

Objective: The aim of this multicentric, prospective, randomized study was to evaluate the overall capabilities of self-management of PD patient and his/her caregiver, before and after the intervention of educational therapy. For PD patients, the primary outcome was to measure the decrease of OFF time of the patient during the 24 hours with ON-OFF diary. At the same time, we expected an improvement of the burden of care on the part of the caregiver to coping with stressful situation.

Methods: Three PD centers evaluated 40 patients each affected by complicated PD (stage HY \geq 2,5 in ON) and their related caregiver, dividing them in an intervention and in a control group. The intervention consisted of six weekly sessions of 180 minute duration for 3 months. At baseline and at follow up, all patients and caregivers were measured with appropriate clinical scales.

Results: Preliminary results from one out of the three centers (69 patients) showed a statistically significant difference in the intervention group in terms of reduction of OFF time (Wilcoxon Signed Rank test, $p=0.0023$) with a mean reduction of 1.23 hours, whilst control group showed no differences.

Conclusions: This program may contribute essentially to improve, achieve, or maintain, the greatest autonomy reducing the OFF time without any complex management of the medications. Complete results should confirm this trend and further studies shall explore the efficacy of this non-pharmacological intervention in time.

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Parkinson patients' choice to undergo deep brain stimulation

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Introduction: Deep brain stimulation (DBS) is currently the treatment of choice for advanced Parkinson's disease (PD). DBS has been shown to decrease the motor symptoms with a significant effect on patients' quality of life. In addition, dopaminergic medication may be reduced by an average of 50.0%. Despite the overall effectiveness of DBS, only a few percentage of eligible patients undergo the procedure.

Aim: The aim of this study was to find the reasons for the low acceptance of this treatment and to clarify to what extent a lack of knowledge about this therapeutic option plays a role.

Method: A multiple-choice questionnaire was specifically created to explore parkinsonian patients' knowledge and opinion about DBS. The questionnaire was composed of 33 items, 15 about medical history and 18 concerning DBS. We used both web-based and paper questionnaires sent to several Italian PD Associations.

Results: 61 PD patients answered our questionnaire (39 males; aged 61-70 years). A general knowledge of DBS emerged in 86% patients; 44,3% underwent DBS surgery. Information about DBS were received from the neurologist (44,3%), internet (14,9%), other patients (13,1%), patients association (13,1%) and general practitioner (1,6%). The main benefits obtained were drugs reduction (37,7%), improvement of motor symptoms (32,8%) and quality of life (24,6%), whereas side effects were language (19,7%), balance (18%) and mood or cognitive (27,9%) problems. Fear (8,2%) and lack of information (8,2%) are the most important reasons why patients do not undergo surgery. DBS has never been proposed at 45.9% of patients.

Conclusions: Our study shows that DBS is generally known but not all patients undergo it because they do not receive specific information or DBS is not proposed, this might explain why referral rates are below what would be expected. This data needs further specification to clarify if the lack of information is also present in healthcare professionals.

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Proprioceptive focal stimulation may improve quality of gait in middle- advanced Parkinson's disease patients. Double-blind, double-dummy, randomized, crossover, Italian multicentric study

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Objective: Object of the study was to evaluate the efficacy of proprioceptive focal stimulation on Gait in middle–advanced Parkinson (PD) patients by a crossover, randomized, double blind double dummy study using Equistasi[®], nanotechnological device of the dimension of a plaster which generates high frequency segmental vibration.

Background: The efficacy of Gait Analysis (GA) on evaluating gait modification on Parkinson's Disease (PD) Patients [1] is already well known. On the other hand, several studies have shown that proprioceptive focal stimulation seems to be useful in symptoms amelioration in several neurological disease. Therefore, GA was recorded in a group of PD patients in randomized blind double dummy study using Equistasi[®] device and its placebo (inactive plaque).

Methods: Forty-eight PD patients (age 68,7 years, Duration disease 8.34 years, duration therapy 37,3 years; H&Y 2.52) at their best on therapy, were enrolled in the study. They were randomized. Four GA were performed always at the morning. Three plaques devices were put on the skin: one at C7, one at the right and the left leg, on soleus muscle [2] Equistasi[®] is a nanotechnological device of the dimension of a plaster which generates high frequency segmental vibration. Clinical state was monitored by MDUPDRS part III. Parametric (One-way ANOVA and paired t-Student) and not – parametric statistic (Freidman ANOVA and Wilcoxon test) were used.

Results: The analysis of the spatial–temporal variables showed a significant improvement of Mean Velocity (MV) (p=0.03) and Stride Length (SL) (p=0.005). Moreover Stance (STA), Swing (SWI) and Double Support Stance (DSS) both in left and right stride, in active evaluation, were significant modified mostly in the more compromised PD. MDUPDRS Part III was statistically reduced both in active and inactive device evaluation (Active: p=0.000; Inactive: p=0.003), but items 3.10 and 3.12 were statistically reduced only in the active treatment.

Conclusions: The results, in this group of patients, encourage to investigate the mechanical focal vibration as stimulation of proprioceptive system in PD. The effect of the device on more severe patients may open a new possibility to the management of this stage of PD. Over the influence on postural stability previously reported, the present study indicates as the device ameliorates also gait performance, and confirms the support that GA gives to underlight the modifications of gait in PD patients.

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Segue P77

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Symptomatic delayed-onset edema following deep brain stimulation for Parkinson's disease: occurrence, symptoms, management and outcomes. Experience of a single center

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Background: Symptomatic delayed-onset edema (SDE) is an unexpected complication of deep brain stimulation (DBS) surgery in subjects with Parkinson's disease (PD). The clinical presentation of SDE can be severe and no data are currently available on its clinical course and long term follow-up.

Aim: To report on occurrence, symptoms, management and outcomes of SDE following DBS of either the subthalamic nucleus (STN) or Globus pallidum interna nucleus (GPi) DBS.

Methods: We evaluated the patients with PD and STN- or GPi-DBS that developed SDE from June 2015 to 2017. The same neurosurgeon performed all surgeries utilizing single pass microelectrode recordings (MER). We implanted directional and conventional leads. Each patient underwent clinical evaluations, neuropsychological assessment and brain imaging follow-up until one year after SDE resolution.

Results: Out of the 55 implanted patients, seven developed SDE (12%). The patients who developed SDE did not differ to the others in terms of age, education, neuropsychological profile, disease duration, medication dosage and disease severity. Also of note, they didn't show any particular cardiovascular risk factors. In all SDE cases, the brain MRI performed immediately after surgery were negative for hemorrhage or edema. Clinically, SDE onsets after an average of 5 days and confusional state, emotional lability and behaviour disorders were the most frequent symptoms. No motor deficit was reported. SDE was perielectrode (more 5 cm), bilateral, deep and extended to the frontal lobe. All seven patients were treated with dexamethasone and SDE improved over 4-6 weeks, till complete clinical remission. Still, the neuropsychological follow-up at one year showed a worsening in two patients (30%).

Conclusion: SDE can complicate DBS procedures and its etiology remains unclear, as no clear correlation with surgical aspects or patient-related factors was found SDE transient nature suggests a conservative approach, but patients and caregivers must be alerted to this possible delay complication.

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Usefulness of safinamide in the management of patients with Parkinson's disease with motor fluctuations

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Background: Parkinson's Disease (PD) is a neurodegenerative disorder characterized by motor symptoms (resting tremor, rigidity, bradykinesia and postural instability) and non-motor symptoms (NMS). In the advanced phase of the disease, motor fluctuations usually affect seriously patients' quality of life. Safinamide is a reversible monoamine oxidase-B inhibitor with dopaminergic and non-dopaminergic properties approved in Europe for the treatment of PD with motor fluctuations.

Aim of Study: The aim of this study was to evaluate motor functions and fluctuations, non-motor symptoms and quality of life, before and after the start of the treatment with safinamide in a cohort of patients with PD.

Methods: This was a cohort study where we compared two groups of parkinsonian patients, one treated with standard dopaminergic therapy and the other with standard dopaminergic therapy and safinamide. We evaluated motor status and fluctuations with UPDRS, non-motor symptoms with NMSS, cognitive skills with MoCA and quality of life with PDQ-39 questionnaire, at the baseline and after 6 months of treatment.

Results: We included 35 consecutive patients with a diagnosis of PD with motor fluctuations in the study. 25 of these patients were treated with standard dopaminergic therapy and safinamide, while 10 patients were treated with standard dopaminergic therapy alone. The mean age of the population was 72,37 years old and mean UPDRS score at the baseline was 58,07. After 6 months of treatment, there was a significant reduction in UPDRS total score in the safinamide group (-2.6 points; p=0.05). The improvement was significant also in UPDRS III (-3.19 points; p=0,025). There was also a slight improvement of quality of life and a reduction of complications.

Conclusion: The results of this study confirmed the efficacy of add-on therapy with safinamide over standard dopaminergic therapy on motor symptoms in a cohort of PD patients with motor fluctuations.

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Levodopa/carbidopa intestinal gel in advanced Parkinson's disease: a two-year experience in the Neurology Unit of L'Aquila Hospital

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Background: Continuous duodenal infusion of levodopa/carbidopa intestinal gel (LCIG) is an established treatment to control motor fluctuations in Parkinson's Disease (PD). Oral treatment with levodopa and dopamine agonists is the main treatment in the initial phase of PD, but over time, the duration of the response to treatment becomes shorter and the patients experience motor fluctuations that affect seriously the quality of life. Duodenal infusion allows a steady absorption of levodopa directly in the small bowel, bypassing the stomach and reducing motor fluctuations.

Aim of the Study: The aim of this study was to evaluate motor functions and fluctuations and the independence in activities of daily living before and after LCIG and to assess the frequency of complications related to the treatment.

Methods: We evaluated motor status and complications with MDS-UPDRS at the baseline and after the start of the treatment. The patients with residual fluctuations were treated with safinamide. The functional independence of the patients was assessed with ADL and IADL. We reported all the complications occurring during the treatment.

Results: We treated 12 patients with LCIG from December 2015 to December 2017. 6 patients were treated with safinamide. The mean Hoehn and Yahr stage was 3.75 ± 0.87 . The mean treatment period was 12 months. There was a significant reduction in UPDRS III score (-2.94 points; $p=0.03$) and in UPDRS IV score (-2.83 points; $p=0.05$). There was also an improvement of functional independence ($p=0.07$). Complications occurred in 75% of patients. Most of these were minor complications (83.3%).

Discussion: LCIG is a valid therapeutic option in patients with advanced PD, with a reduction of motor complications and an improvement of motor status. Treatment related complications are quite common, but most of these are minor and reversible.

P81

Efficacy of safinamide on Parkinson's Disease motor complications and non-motor symptoms

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Safinamide (Zambon SpA Italy) is not just another MAO-B inhibitor, but has a unique dopaminergic and non-dopaminergic mode of action. The effects of safinamide on motor complications and on non-motor symptoms were investigated using the data from three pivotal studies. Safinamide significantly improved motor fluctuations, dyskinesia and pain in PD patients, irrespective of whether or not other drugs were added to the baseline levodopa treatment, thus suggesting that could be an appropriate choice as a first adjunct medication in PD patients not sufficiently controlled on levodopa. These favourable effects may be explained by its modulation of glutamatergic hyperactivity.

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Effects of safinamide on dysexecutive symptoms during wearing-off in Parkinson's disease

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Introduction: Wearing-off (WO) refers to the predictable worsening of motor and/or non-motor symptoms of Parkinson's disease (PD) at the end of levodopa (LD) dose that improves with the next drug dose. Safinamide is a reversible MAO-inhibitor recently approved for treatment of WO. In addition to its dopamine-enhancing properties, the drug blocks sodium calcium channels thus modulating glutamate release. Here we investigated the therapeutic potentials of safinamide on cognitive symptoms during WO in PD.

Methods: Thirteen patients affected by PD and reporting symptoms of WO were consecutively enrolled. WO was verified by means of the WO-19 questionnaire and by a $\geq 25\%$ difference of UPDRS-III score between a first (30 min before the second daily dose of LD) and the second (45 minutes after the second daily dose of LD). At enrollment (T0), patients were submitted to the Stroop's test (SWCT) and the Frontal Assessment Battery (FAB) 30 min before the second daily dose of LD. Safinamide was initiated the day next to enrollment. Treatment was carried out at 50 mg/day for the first 2 weeks, and 100 mg/day for further 10 weeks. At the end of observation period, patients underwent a final visit (T1), including the SWCT, FAB and UPDRS-III scale with the same daily time schedule as T0. Paired t-test was applied to analyze differences between T0 and T1.

Results: Safinamide produced significant improvement of UPDRS-III, SWCT and FAB subscores.

Conclusions: These preliminary findings suggest that safinamide may improve dysexecutive symptoms of WO in PD patients.

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Bisphenol A glucuronidation in patients with Parkinson's disease

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Introduction: The widespread endocrine disruptor Bisphenol A (BPA), an estrogen-mimetic molecule, has got documented effects on the dopamine system. It can be found in canned food, dental sealants, thermal paper etc. It undergoes liver conjugation with glucuronic acid and urine excretion.

Objectives: In the present study we dosed the amount of free and conjugated blood Bisphenol A in patients affected by Parkinson Disease (PD) and their spouses as controls.

Methods: Subjects were interviewed in order to look for possible confounders in BPA exposure. Free and conjugate BPA were analyzed by gas chromatography coupled to mass spectrometry.

Results: Patients had a statistically significant lower amount of conjugated Bisphenol A compared to controls, while total BPA concentrations were comparable in the two classes. No differences were found between the two studied populations in terms of exposure to possible Bisphenol A sources, apart from exposure to canned tuna and canned tomatoes, since PD patients consumed significantly more of both ($p < 0.05$). Moreover, no differences in Bisphenol A glucuronidation were found after patient stratification according to the class(es) of anti-Parkinson's drug taken and after conversion to the Levodopa Equivalent Daily Dose.

Conclusions: Parkinson disease patients showed a lower percentage of blood conjugate BPA. The possible mechanisms involved in Bisphenol A metabolism in PD patients need further elucidation. Moreover, further study may explain a possible role of this molecule in the pathogenesis of the disease, due to its dopaminergic toxicity.

P84

A naturalistic observation on 20 consecutive Parkinson's disease patients under LCIG at the University of Rome "Tor Vergata"; psychological counseling and/or other alternative strategies for avoiding LCIG discontinuation?

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Introduction: Levodopa/carbidopa intestinal gel (LCIG) allows providing stable levodopa plasmatic levels, contributing at restoring "continuous dopaminergic stimulation" in advanced Parkinson disease (PD) patients [1]. However, exact levodopa concentration onto the synaptic clefts is not always as expected in severe PD stages, when levodopa pharmacodynamics is elusive. Interestingly, a recent Italian survey showed the LCIG discontinuation rate as high as 25.7% [2].

Objectives: To examine our recent 3-year experience with LCIG focused on patients' dropout rate due to patient dissatisfaction.

Methods: 20 advanced PD patients underwent LCIG-treatment with standard approach including special care in neuro-psychological assessment. In order to evaluate the tolerance to treatment, all PD patients underwent a NJ test period before PEG-J placement.

Results: At 36-month follow-up, 10 patients were still good responders in terms of motor disability reduction and QoL improvement. We observed the optimal clinical response to LCIG in female patients, who had experienced > 2 hours/daily troublesome OFF-time under oral levodopa. On the remaining 13 patients, 3 deceased for co-morbidities; 4 discontinued LCIG within the first 18 months because dissatisfied by the clinical improvement achieved. In the last 3 patients, LCIG discontinuation was discouraged by proposing a 24/h drug delivery, by using low drug flow at nighttime (1,2 ml/h). These patients were predominantly males (6/7) and all of them had manifested some degree of dopamine dysregulation syndrome or ICD under oral therapy.

Conclusions: We observed that the compliance to long-lasting LCIG might be biased by gender or individual vulnerability to dopaminergic therapy side-effects. Our preliminary data, although obtained in a small-size cohort, support the possibility to use a non-conventional 24/h LCIG regimen in specific PD patients. We emphasize the importance of an appropriate counseling during and after LCIG procedure, in order to minimize delusion of patient expectations and avoid the risk of LCIG withdrawal not device-related.

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P85

Continuous dopaminergic stimulation in Parkinson's disease patients treated with daytime levodopa-carbidopa intestinal gel and overnight rotigotine patch: our experience

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Introduction: Physiologically, dopamine neurons have relatively constant rates of tonic activity, exposing striatal dopamine receptors to constant levels of dopamine [1]. In Parkinson's disease (PD), degenerative process leads to the progressive loss of remaining striatal dopamine terminals and consequently decreased capacity to buffer fluctuations in dopamine levels. PD patients receiving long-term L-Dopa oral therapy develop motor complications with "on-off" phenomena and involuntary movements, leading to disability [2, 3], linked to intermittent stimulation of dopamine receptors and consequent alterations in neuronal firing patterns [4].

Objectives: To achieve continuous dopaminergic stimulation (CDS) in advanced PD patients to improve motor and non-motor symptoms and reduce long-term complications.

Methods: Twelve advanced PD patients, suffering from motor fluctuations with wearing-off phenomena, unpredictable and sudden off periods and morning akinesia, underwent LCIG-treatment with standard approach. To obtain CDS we set treatment with daytime LCIG and overnight rotigotine patch. At baseline and follow-up visits we assessed: Unified Parkinson's Disease Rating Scale (UPDRS), Hauser Diaries (HD) ("on" without dyskinesia, "on" with dyskinesia, and "off"), PDQ-39 Questionnaire, PD Sleep Scale-2 (PDSS-2) and Epworth Sleepiness Scale (ESS).

Results: LCIG administered from 7:00 a.m. to 10:00 p.m. significantly reduced motor fluctuations and akinesia. The administration of overnight (from 10:00 p.m. to 7:00 a.m.) rotigotine patch induced the improvement of night's sleep, with better movement fluency and disappearance of morning akinesia as assessed by HD, PDSS-2. ESS showed reduced diurnal hypersomnolence. PDQ-39 showed the improved global quality of life.

Conclusions: Both LCIG and rotigotine transdermal patch have the potential to ensure CDS, which conceptually more closely mimics physiologic striatal dopamine receptor function, clarifying the efficacy of both treatments respectively on motor fluctuations and sleep quality.

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P86

Clinical pharmacokinetics of pramipexole, ropinirole and rotigotine in patients with Parkinson's disease

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Introduction: Pramipexole (PRA), ropinirole (ROP) (oral formulations) and rotigotine (ROT) (transdermal patch) are non-ergoline dopaminergic agonists (DAs) used as first line drugs to treat Parkinson's disease (PD) and restless legs syndrome. Clinical experience has disclosed a series of central and peripheral possibly dose-related DAs adverse effects (AEs), including impulse control disorders and risk of heart failure. Clinical pharmacokinetics of these compounds is poorly characterized in PD patients.

Objectives: We aimed to evaluate the possible relationship between steady-state plasma concentrations (C_{ss}) of DAs and a series of clinical variables (age, sex, presence of AEs) in a population of PD patients on chronic DA therapy.

Methods: Blood samples were prospectively collected in the morning, at a median 17-hour distance from last dose administration from patients with PD on stable (>3 months) treatment. DAs plasma concentrations were measured by ultra high pressure liquid chromatography-tandem mass spectrometry.

Results: Ninety-one patients on PRA (group A), 50 on ROP (group B) and 37 on ROT (group C) were enrolled in the study. A significant ($p < 0.001$) linear correlation between DAs C_{ss} and daily dose (mg/kg/day) was found in groups A and B, not in C. Plasma drug concentration-to-weight-adjusted dose ratio (C/D) significantly ($p < 0.001$) increased with age in group A, while was unaltered in groups B and C. No sex-mediated differences in C/D ratios were observed in any group. Median DAs C/D ratios were similar in patients with or without evidence of DAs-related AEs within each group.

Conclusions: Overall, at a given daily dose a remarkable interpatient variability was observed in matched plasma drug concentrations within each patients' group. These observations are the first ones obtained in real PD patients. Monitoring of plasma DAs concentrations may be helpful in the pharmacokinetic optimization of the drug dosage schedule in selected patients.

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Slow release levodopa at bed time as treatment for nicturia in Parkinson's disease patients

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Background: Bladder function of patients with Parkinson's disease (PD) alters significantly: the majority of patients have overactive bladder as urinary urgency/frequency, and nocturia is the most complained one. This seems to be the result of an altered brain–bladder relationship, as in PD, the frontal-basal ganglia D1 dopaminergic circuit that normally suppresses the micturition reflex is altered. Previous studies demonstrated a beneficial effect supported by a combined chronic stimulation of D1 and D2 receptors on detrusor overactivity in PD population and other authors demonstrated an amelioration of nicturia in patients treated with rotigotine and apomorfine, drugs sharing a combined balanced stimulation of both dopaminergic receptor subfamilies. Aim of our study was to evaluate the possible beneficial effect of slow release l-dopa administered at bed time on nocturia and on nocturia related quality of life (NqoL).

Methods: 86 PD patients (H and Y >1 and > 4 , mean age 68 yrs , 49 females and 37 males) were consecutively enrolled by seven different Movement Disorders specialized out-patients clinics. Patients were submitted to IPSS (International Prostatic Symptoms Scale) that comprises one item that specifically test Nicturia, and to NqoL questionnaire at baseline during their chronical therapy. Sequentely, subjects received as add on treatment 125mg of l-dopa/carbidopa slow release (Madopar 125 slow release) at bed time (10 p.m.) and after two months, the two scales were administered again mantaining stable other medications.

Results: statistical analysis demonstrated a significant amelioration of Item 7 of IPSS focused on nicturia and of NqoL when patients were assuming L-dopa slow release treatment at bed time. Moreover an invers correlation of the reported amelioration was observed with disease severity and duration.

Conclusions: our results demonstrated a clear positive effect of the combined D1 and D2 agonism supported by slow release l-dopa, supporting previous evidence of a pathofisiological role of dopaminergic circuit on urologic disfunction in PD patients.

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Safinamide in our experience: efficacy and tolerability

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Introduction: Safinamide is a third-generation Monoamine Oxidase B Inhibitor (MAOB-I) drug with an adjunctive mechanism of action of glutamate release modulation, indicated for treatment of motor fluctuations in Parkinson's Disease (PD) as add-on therapy.

Objective: To prospectively evaluate the clinical effect and tolerability profile of safinamide as adjunct therapy in a cohort of 162 patients with idiopathic PD and motor fluctuations.

Methods: Patients were evaluated by neurologists experienced in movement disorders, using clinical scales prior and after initiation of therapy with safinamide. We used Unified Parkinson's Disease part IV (UPDRS IV, for motor fluctuations items 36+37+38+39 and for dyskinesias items 32+33) and Hoehn & Yahr scale.

Results: 162 patients started therapy with safinamide 50 mg. 66 patients still need to be re-evaluated after initiation of treatment and were not included in this study. 96 patients (38 female, 58 male, age 69.0 ± 8.2 years, disease duration 10.2 ± 6.4 years) completed the period of observation. Among them, 24 patients (25.0%) discontinued treatment: 15 for ineffectiveness or motor symptom worsening and only 8 for non-motor adverse effects; no-one showed severe adverse reactions. At baseline evaluation, Hoehn & Yahr stage was 2.0 ± 0.7 , UPDRS score for motor fluctuations was 2.1 ± 1.1 , UPDRS score for dyskinesias was 1.4 ± 1.5 . At the dosage of 50 mg, 45.6% of patients reported subjective improvement, UPDRS score for motor fluctuations was 1.6 ± 1.4 , UPDRS score for dyskinesias was 1.4 ± 1.4 . At the dosage of 100 mg, 50% of patients reported subjective improvement, UPDRS score for motor fluctuations was 1.6 ± 1.2 , UPDRS score for dyskinesias was 1.6 ± 1.4 .

Conclusions: In our experience, safinamide has demonstrated moderate efficacy in improving motor fluctuations, with an objective decrease of UPDRS scores; dyskinesias did not significantly worsen, particularly at the dosage of 50 mg; we reported a good drug tolerability profile, without severe adverse reactions. Follow-up is ongoing.

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Efficacy of safinamide on non-motor symptoms in a cohort of patients affected by Idiopathic Parkinson's disease

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Introduction: Non-motor symptoms (NMS) are poorly recognized and inadequately treated; they may be intrinsic to disease pathology or consequences of treatments. They can even precede motor symptoms. A dysfunction of dopaminergic and non-dopaminergic systems may contribute to their development. Safinamide provides highly selective and reversible inhibition of MAO-B, it blocks voltage-dependent sodium channels and modulates calcium channels, with inhibition of dopamine reuptake and modulation of glutamate release. A possible effect on NMS has been suggested.

Objectives: To evaluate the effect of safinamide on NMS.

Methods: 20 PD patients, 10 women, 75±6,3 years, disease duration 14,5±6,8 years, with motor fluctuations, in treatment with l-dopa alone or in combination with DA. At T0 we assessed SCM; NMS assessment scale for PD, MMSE, Cognitive assessment, H&Y scale, CISI-PD, HADS, Mental Fatigue, PDSS, PDQ-8 and EQ-5D. These scales were assessed at least after 3 months from the introduction of safinamide (4.4±1.05 months) in a period of stable management of the disease (T1). Continuous variables were treated with descriptive statistics, using mean and standard deviations. A one-way analysis of the variance (ANOVA) was carried out, using Microsoft Excel Data Analysis Toolpack with Two-tailed p values <0,05.

Results: We found a statistically significant reduction of SCM, CISI-PD, NMS, HADS and PDQ scores. MMSE, cognitive score and H&Y stage did not reveal statistically significant variations. We observed a general decrease in the vast majority of NMS items, with the exception of NMS11, NMS7, NMS13 and NMS19.

Conclusions: We found an improvement of NMS scores, in particular regarding cardiovascular involvement and sleep, and a worsening of the items describing mood, hallucinations and sialorrhea. Safinamide may represent a valid therapeutic option for NMS, even in early stages. Trials on de novo patients with safinamide as monotherapy may be helpful in the understanding of the pathophysiology and management of NMS.

P90

Affective impairment and emotional tone of early Richardson's syndrome and Progressive Supranuclear Palsy with predominant parkinsonism: the role of alexithymia and anhedonia

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Introduction: Progressive Supranuclear Palsy (PSP) and its variants, in particular Richardson's syndrome (PSP-RS) and PSP with predominant parkinsonism (PSP-P), are characterized, since the early stage of illness, from several neuropsychiatric and neuropsychological symptoms. Among them, alexithymia and anhedonia have not been yet investigated.

Objective: To define qualitative and quantitative differences of alexithymia and anhedonia among PSP-P, PSP-RS and PD patients recruited within 24 months after the onset of motor symptoms.

Methods: One hundred fifty five PD, 11 PSP-P and 14 PSP-RS patients were identified. All patients were submitted to a complete assessment of psychiatric, cognitive, and motor symptoms. In particular, all patients were submitted to the Toronto Alexithymia Scale-20 item (TAS-20) for evaluation of alexithymia and the Snaith Hamilton Pleasure (SHAPS) for assessment of hedonic tone.

Results: The comprehensive neuropsychological battery indicated significantly worse performances of PSP-P and PSP-RS patients at several neuropsychological domains as compared to PD patients. PD patients scored better than other two groups at the Apathy Rating Scale score. PSP-RS had increased diagnosis of depression than the other two groups and the diagnosis of apathy were more frequent in both PSP subtypes with respect to PD patients. Interestingly, the three groups differed significantly at the TAS-20 scores. In particular, PSP-P and PSP-RS scored worse in the TAS-20 total in comparison to PD. Moreover, PSP-RS showed worse scores in F2 subscale than PD patients. Finally, in PSP-P and PSP-RS groups the frequency of alexithymia diagnosis was higher with respect to PD group.

Conclusions: Alexithymic symptoms are identifiable very early in PSP-P, and PSP-RS patients. These symptoms seem to differentiate PSP group from PD group but not the two subtypes of PSP. Altered emotional capability could be related to specific neurophysiological dysfunction occurring precociously in PSP, therefore its identification could orient the diagnosis toward PSP cases.

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A new method for continuous monitoring of movement disorders

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Introduction: The clinical assessment of Parkinson’s disease (PD) symptoms is typically performed with neurological examinations and motor tests. However, this may only consider the severity of motor symptoms during the length of the recording and may fail to capture variations in a patient’s motor state, which change continuously during the day. Various current methods for continuous monitoring of movement disorders are based on using wearable devices that evaluate the frequential content of signals in the typical range of movement disorders. However, the typical daily motor activities performed by patients may have a power spectrum into the same range of motor symptoms and habitual activity may be indistinguishable from that due to movement disorders.

Objectives: In this work, we propose a new device and method for the continuous and long-term monitoring of movement disorders to reduce the probability of mistaking the discrimination between movement disorders and normal daily activity.

Methods: Data were acquired by means of a wrist-worn device (i.e. “Parkinson’s disease-watch”, PD-Watch) for 24 hours and then processed; the proposed processing method is based on the evaluation of frequential data content from multi-axial sensors and on the identification of specific movement patterns that movement disorders are typically associated with.

Results: A preliminary evaluation of the proposed method was performed (sensitivity of 0.993 and accuracy of 0.989). In this study, 14 patients with PD were recruited. As example, for a patient, a 64 percent reduction of the proposed tremor index was detected from the first monitoring (untreated patient) to the second monitoring (patient treated with dopaminergic drug).

Conclusions: While results need to be extended with further clinical trials, the proposed device appears promising and suitable for the use as part of clinical trials and routine clinical practice for supporting the evaluation of motor symptoms, disease progression, and quantification of therapeutic effects.

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Abnormal striatal plasticity in a DYT11/SGCE myoclonus dystonia mouse is reversed by adenosine A2A receptor inhibition

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Introduction: Basal ganglia dysfunction is implicated in many movement disorders, including dystonia [1][2]. However the precise nature of defects often remains uncharacterized, which hinders therapy development. Different dystonia-causing mutations differentially affect the striatum [3] and could converge onto a common underlying mechanism of altered striatal plasticity with, as a consequence, abnormal striatal output [4].

Objective: To examine striatal function in a mouse model of a rare form of genetic dystonia: DYT11/SGCE myoclonus dystonia [5].

Methods: We generated a mouse line (Sgce^{+/-}) that lacks exon 5 of mouse SGCE to model a pathogenic splice site deletion to prevent translation of full-length ϵ -sarcoglycan protein. SGCE- Δ exon5 allele, paternally inherited, mimics a myoclonus dystonia-causing SGCE loss of function mutation. All experiments were also performed on littermate controls (Sgce^{+/+}). RNA libraries were prepared to compare the striatal Transcriptomes of littermate Sgce^{+/+} and Sgce^{+/-} animals. Library preparation, sequencing and statistical analysis were performed by VIB Nucleomics Core. Electrophysiological recordings of striatal medium spiny neurons (MSNs) and cholinergic interneurons (ChIs) were performed through conventional sharp and patch-clamp techniques.

Results: Comparison of the striatal transcriptomes of Sgce^{+/+} and Sgce^{+/-} animals did not show significant differences in the expression of dystonia genes and genes encoding proteins of striatal neurochemistry, which suggests that striatal microcircuitry is spared by the disease insult. Electrophysiological recordings showed normal intrinsic electrophysiological properties and normal basic responses to excitatory and inhibitory neurotransmission. Nevertheless, high frequency stimulation in Sgce^{+/-} failed to induce a physiological long-term depression (LTD) at corticostriatal glutamatergic synapses. Pharmacological inhibition of adenosine 2A receptors (A2ARs) restored LTD [6][7].

Conclusions: SGCE loss causes the impairment of corticostriatal LTD. This observation emphasizes that neurophysiological changes can occur in the absence of broad striatal dysfunction. The ameliorating effect of A2AR antagonists indicates that this drug class could be tested for DYT11/SGCE dystonia pharmacological therapy.

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Segue P92

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P93

A prospective study of movement disorders emergencies

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Introduction: Acute movement disorders are etiologically heterogeneous and puzzling entities. Studies on the relative frequency of different clinical phenomenology and their underlying diseases are, however, limited.

Objective: To describe nature, spectrum and outcomes of acute movement disorders in a prospective cohort study.

Methods: We describe acute movement disorders in 96 consecutive patients, admitted in emergency ward from 2013 to 2017, from 16 years old. Time of disease onset, type of movement disorder according to published diagnostic criteria, diagnostic workout and outcome during a follow up period of 3 years were prospectively collected.

Results: 73% of patients had hyperkinetic movement disorders and tremor was the most common movement disorders seen in 20,8%, followed by myoclonus in 17,7%, dystonia in 14,5% and chorea in 11,4%; other hyperkinetic movement disorders included were: gait disorders 3%, dyskinesia 2%, akathisia 2%, hemiballism 1%, oculogyric crisis 1%. Hypokinetic movement disorders included acute parkinsonism in 14% of patients followed by off-state 4%, akinesia 3%, rigidity 3%, and 19,7% of all patients had mixed movement disorder, with co-occurrence of more than 1 kind of movement disorders. The duration from the onset of movement disorders to the neurological consultation was considered between <24 hours and 28 days. In descending order of frequency, 8 etiological groups were recognized: drug induced 28%, functional 19%, neurodegenerative diseases 15%, structural damage 11%, others 23% (metabolic, immunological/inflammatory, infective, undetermined). Outcome was better for neuro degenerative disease, particularly for adjustment of medications, and for movement disorder due to medication. Functional movement disorders showed less favourable outcome, mainly because of relapses during follow-up.

Conclusions: Acute movement disorders represent an important clinical entity in emerging settings. Movement disorder is an important side effect of medications, and a leading cause of emergency room admission. Uncertain course is seen in functional movement disorders, and supposed in structural brain lesions and in acute symptoms onset.

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Longitudinal study of a cohort of MSA-C patients in South Italy: survival and clinical features

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Introduction: Multiple system atrophy is a progressive fatal neurodegenerative disorder causing parkinsonism, cerebellar ataxia, autonomic and pyramidal dysfunction in various combinations. Two major forms of the disease are recognized, the parkinsonian (MSA-P) and the cerebellar (MSA-C) [1]. MSA typically shows onset in the middle age (from 52.5 to 60 years). Factors predicting survival are not fully established. A recent meta-analysis identified as unfavorable predictors of survival severe dysautonomia and early development of combined autonomic and motor features but not MSA phenotype, early falls but not sex [2]. There was conflicting evidence regarding the prognostic effect of aging, age at onset and stridor.

Aim: To evaluate clinical features, disease progression and survival and to identify variables that may modify the rate of disease progression in an ethnically homogeneous sample of Italian Multiple System Atrophy (MSA-C) patients.

Patients and Methods: We investigated a cohort of 60 patients (31 F, 29 M), 51 with diagnosis of probable, 9 of possible MSA-C. Cerebellar impairment was estimated using the Inherited Ataxia Clinical Rating Scale, non-cerebellar features using UMSARS and MMSE. MRI, PET, [123I]FP-CIT, NCV were performed when required.

Results: Mean age at onset was 56.4 years (± 7.8), mean age at examination was 61.9 (± 7.1). The most frequent features were: ataxia (98.3%), dysarthria (88.3%), urinary incontinence (86%), sexual dysfunction in males (85%), RBD (78.6%), increased tendon reflexes (76.7%), dysphagia (72.7%), tremor (73.3%). MRI scan detected hot cross bun sign (HBS) in 58.2% patients and pontine atrophy in 75%, putamen rim hyperintensity in 14.3%. 35 patients lost independent gait, median time was 5 years, at 61.2 years. 25 patients were confined to wheelchair, median time 10 years, at 63.1 years; 17 patients died, median time 10 years, at 64.5. Increased tendon reflexes, RBD, parkinsonism, nystagmus, and HBS at MRI were associated with a shorter survival.

Conclusions: Mean survival (10 years) in our patient was in agreement with previous studies and some clinical features predicted faster progression to death. The last finding should be replicated on a large population.

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Gait impairment and cognitive functions in SCA2 patients

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Introduction: Dominant clinical manifestations of Spinocerebellar Ataxia type 2 (SCA2) are ataxic gait [1], impaired balance and speech, dysmetria, slow eye movements. Recent studies, however, also raised the possibility that abnormal cognition contribute to the clinical spectrum [2,3]. Interestingly, studies conducted in older adults and in patients with Mild Cognitive Impairment, Alzheimer's Disease and Parkinson's Disease showed that cognitive domains may contribute to gait regulation.

Objective: To test cognitive domains and their correlation with severity of cerebellar signs, evaluated by the Scale for the Assessment and Rating of Ataxia (SARA) and an automated computerized analysis of gait, in patients with SCA2.

Methods: Twenty SCA2 outpatients and 20 healthy subjects participated into the study. A battery of neuropsychological tests was administered to both patients and controls. SARA was used to measure the severity of ataxia in patients: SARA total score and two subscores, SARA gait-stance subscore (SARA-GS) and SARA upper limb subscore (SARA-UL), were analysed. Spatio-temporal gait parameters were recorded by a stereo-photogrammetric system (SMART-E, BTS, Milan, Italy).

Results: On univariable linear regression analysis, higher SARA-TOT, SARA-GS and SARA-UL were significantly associated with poorer performance on Winesconsin Card Sorting Test, while SARA-TOT and SARA-GS were negatively correlated with Wechsler Memory Scale, Logical Memory and Visual Reproduction subscores.

Univariable linear regression between gait analysis parameters and cognitive tests showed that greater stance phase duration, double support sub-phase duration and step width and lower step length were associated with poorer cognitive performance on WCST. Stance phase duration and double support sub-phase duration inversely correlated to MMSE.

Conclusions: The findings from the present study may be helpful in identifying new targets for rehabilitation in ataxic patients and provide strong support to the observation that gait is not a mere automatic motor activity but a more complex task requiring cognitive abilities.

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P96

Cognitive profile and its evolution in a cohort of Multiple System Atrophy patients

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Introduction: Multiple System Atrophy (MSA) is a neurodegenerative disease characterized by parkinsonian and/or cerebellar features and autonomic failure. Dementia is an exclusion criterion in current diagnostic criteria. Previous studies observed the occurrence of cognitive dysfunctions and dementia in MSA, but the features and the progression of these dysfunctions have not been defined in details.

Objective: To describe the cognitive profile and its progression in a cohort of MSA patients.

Methods: We retrospectively selected from all patients diagnosed with MSA in our department, 60 patients that underwent at least one neuropsychological evaluation (mean disease duration 5±3 SD).

Results: Forty out of 60 patients performed only one evaluation (T0). The remaining 20 underwent also a follow-up evaluation (T1) within 18 months. At T0 37 out of 60 patients (61%) were cognitively impaired: 17 showed impairment in attention and executive functions, 14 in memory or visuo-spatial functions and 6 were classified as demented. Eight (40%) out of 20 patients performing two evaluations, were cognitively normal both at T0 and T1. Seven out of the remaining 12 patients presented a stable degree of cognitive impairment at T1, while 5 progressed. The progressor patients were severely impaired in attention and executive functions and mildly impaired in memory and visuospatial functions. In 3 patients the impairment evolved to a subcortical dementia. We detect no differences in demographic and clinical features between patients with and without cognitive impairment both at baseline and at follow-up.

Conclusions: Our study describes the cognitive characteristics of 60 MSA patients. In this cohort we observed 3 different cognitive profiles: normal cognition, stable attentive and executive deficits, progressive cognitive deficits evolving to subcortical dementia. The detection of cognitive impairment in a patient with a suspected MSA does not exclude the diagnosis but suggests the need of comprehensive and longitudinal neuropsychological evaluations.

P97

McLeod syndrome: should we trust acanthocytes?

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Background and aim: McLeod syndrome (MLS) is a recessive X-linked disease usually manifesting in middle age with chorea, polyneuropathy, cardiomyopathy and acanthocytosis. Acanthocytes (acantha=thorn) define the neuroacanthocytosis spectrum, which includes MLS, chorea-acanthocytosis and abeta-lipoproteinemia [1]. MLS is due to the mutation of the XK gene, associated with Kell antigen expression on erythrocytes. Here we report a case of MLS due to R133X mutation, reviewing all 5 reported cases, highlighting the variability of acanthocytes detection.

Results: A 71 year old Italian male developed chorea at age 55. Personal anamnesis revealed generalized epilepsy of unknown origin from age 55 and restless leg syndrome from age 56. Familial history revealed a cousin diagnosed with undefined chorea, died at age 57 for myocardial infarction. At examination diffuse choreo-athetosis, absent reflexes and scapular hypotrophy were noted. Brain MRI revealed bilateral severe caudate atrophy. Blood tests confirmed hyperCK (x2-x10). A first blood smear turned out negative for acanthocytes. Kell antigens were weakly positive; blood smear was repeated, revealing sparse (<8%) acanthocytes. DNA analysis was positive for R133X mutation in exon 2 of XK gene, leading to MLS diagnosis.

Conclusions: Only five cases of MLS due to R133X mutation have been reported. MLS is characterized by generalized chorea associated with areflexia, axonal neuropathy and increased CK. from thorough revision, generalized idiopathic epilepsy emerged being frequent (2/5). However, 2 out of 5 patients showed none or scarce (<8%) acanthocytes in blood smear. Hence, we recommend to perform Kell antigen group and DNA analysis to avoid misdiagnosis.

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P98

Apathy, but not depression, is associated with dysfunctional general cognitive status in focal dystonias

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Introduction: Some studies revealed the presence of psychiatric disorders (i.e. depression, apathy, obsessive-compulsive disturbances) in patients suffering from focal dystonias. Moreover, few studies showed impairment in several cognitive domains. To our knowledge, until now, no study has explored the relationship between behavioral disturbances and cognitive dysfunctions in this type of movement disorder.

Objectives: To explore the relationship between apathy, depression and cognitive dysfunctions in focal dystonias.

Methods: A sample of fifty-one non-demented consecutive patients with focal dystonia was enrolled. They underwent the Montreal Cognitive Assessment (MoCA) assessing global functioning and several questionnaires to assess subjective memory complaints (by the Multifactorial Memory Questionnaire, MMQ), depression (by the Beck Depression Inventory-II, BDI-II) and apathy (by the Dimensional Apathy Scale, DAS).

Results: Correlational analyses showed moderate correlations of the total DAS score with the MMQ total score ($\rho=-0.489$; $p<0.001$), the contentment subscale of the MMQ ($\rho=-0.400$; $p=0.004$) and the MoCA total score ($\rho=-0.347$; $p=0.013$). Executive subscale of the DAS strongly correlated with the MMQ total score ($\rho=-0.556$; $p<0.001$) and with the contentment subscale of the MMQ ($\rho=-0.604$; $p<0.001$), and moderately correlated with the ability subscale of the MMQ ($\rho=-0.401$; $p=0.004$). Cognitive/Behavioral Initiation subscale of the DAS strongly correlated with the MMQ total score ($\rho=-0.496$; $p<0.001$) and moderately correlated with the contentment subscale of the MMQ ($\rho=-0.378$; $p=0.006$), with the MoCA total score ($\rho=-0.389$; $p=0.005$) and with the memory subscale of the MoCA ($\rho=-0.350$; $p=0.012$). The BDI- score did not correlate with any cognitive scores.

Conclusions: The present study evidenced that a higher level of apathy rather than depression is related to reduced objective and subjective global cognitive dysfunction in focal dystonia. The present evidence suggested that apathy and cognitive dysfunction in dystonias may be two epiphenomena of a damage of a shared neural correlate.

P99

The predictive power of transcranial sonography in movement disorders: a longitudinal cohort study

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Introduction: Transcranial sonography (TCS) is a non-invasive, easily performed and commonly available neuroimaging technique useful for the study of brain parenchyma in Movement Disorders. This important tool has been increasingly used in the diagnosis of Parkinson disease and atypical parkinsonisms.

Objective: The aim of the study was to evaluate the applicability of this technique as supportive tool in the early diagnosis of movement disorders.

Methods: We performed TCS on 315 individuals which were diagnosed as healthy controls or affected by idiopathic parkinson’s disease, monogenetic subtypes of parkinson’s disease, atypical parkinsonism, and dementia with lewy bodies. Five TCS diagnostic patterns were defined on the basis of substantia nigra’s and lenticular nuclei’s echogenicity. TCS evaluations were performed by two blinded neuro-sonographers. Clinical diagnosis on all individuals was performed at baseline and at 4-years follow-up. The concordance rate between TCS patterns and clinical diagnosis and the specificity of TCS pattern to discriminate each group of individuals was compared at baseline and at follow-up.

Results: The concordance rate between TCS patterns and clinical diagnosis of all individuals was 84% at baseline and increased at follow-up (91%) significantly ($p=0.01$). The specificity of TCS pattern in the comparison between patients diagnosed as affected by idiopathic parkinson’s disease and atypical parkinsonism showed a significant increase at follow-up ($p=0.03$).

Conclusions: Our study strongly confirms the role of TCS as a non-invasive and cost-effective tool in early diagnosis of movement disorders.

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Subclinical gait impairment in patients with focal dystonia

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Background: Isolated adult onset focal dystonia (FD) is a movement disorder that affects limited body parts. A previous study of our group showed that cervical dystonia (CD) patients present subclinical walking impairment consistent with a parkinsonian gait [1]. A basal ganglia dysfunction could be a relevant element in the pathophysiology of gait alteration in CD and therefore it is reasonable to speculate whether those alterations could be present also in other FD.

Aim of the study: To investigate gait motor pattern in patients with different types of focal dystonia.

Method: Gait motor pattern in patients with FD was studied with computerized gait analysis (CGA) using Davis protocol. Only spatiotemporal parameters were analysed. Patients enrolled in the study presented laryngeal, oromandibular and hand dystonia. Other dystonia types that can limit walking abilities (such as blepharospasm, foot and trunk dystonia) were excluded. Data of FD subjects were compared with measures obtained in healthy controls (HC) matched for age and sex.

Results: This study included 13 patients with idiopathic FD (6 Females, 7 Males) with mean age of 60.3±7.9 years and mean disease duration of 5.9±5.7 years. FD Patients showed a statistically significant reduction of stride and step length and an increased step asymmetry compared to HC ($p < 0.05$, Mann Whitney test). Cadence was also reduced in FD patients showing a trend for a statistical significance ($p = 0.08$, Mann Whitney test). Remaining parameters were comparable between groups.

Discussion: Patients with idiopathic and isolated FD present mild walking abnormalities detected by CGA possibly consistent with hypokinetic gait. These findings seem to be similar to those found in CD. These results may support the idea that a walking impairment could be a subclinical feature of FD, possibly caused by a basal ganglia dysfunction.

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P101

ABBV-8E12, a humanized anti-tau monoclonal antibody for the treatment of Progressive Supranuclear Palsy and Early Alzheimer's Disease: multiple dose, randomized, double-blind, placebo-controlled phase 2 studies

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Background and Aims: ABBV-8E12 is a humanized anti-tau monoclonal antibody being developed for treatment of Early Alzheimer's Disease (AD) and Progressive Supranuclear palsy (PSP). Results of a phase 1 study in PSP patients (NCT02494024) showed that when administered as a single dose up to 50 mg/kg, ABBV-8E12 exhibited an acceptable safety/tolerability profile to support repeat-dose testing in patients with tauopathies. Here we present the designs of ongoing phase 2 studies in Early AD and PSP patients.

Methods: One phase 2, double-blind, placebo-controlled study assesses the 96-week efficacy and safety of ABBV-8E12 in Early AD patients (NCT02880956). A total of 400 male and female subjects, aged 55 to 85 years, will be enrolled at approximately 65 global study sites. A second phase 2, double-blind, placebo-controlled study assesses the 52-week efficacy and safety of ABBV-8E12 in PSP subjects (NCT02985879).

Results: Primary efficacy outcome in the Early AD study is the change in CDR – Sum of Boxes (CDR-SB) from baseline to Week 96. Primary efficacy outcome in the PSP study is the change in the PSP Rating Scale total score from baseline to Week 52. Adverse events will be monitored.

Conclusions: A significant unmet medical need exists for the development of disease-modifying drugs for AD and PSP which directly impact the biology of the diseases and reduce the associated burdens. ABBV-8E12 has shown an acceptable safety and tolerability profile in patients with PSP during phase 1 testing. The current studies are designed to evaluate the efficacy and safety of ABBV-8E12 in patients with Early AD and PSP.

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Proprioceptive control of the head is impaired in patients with cervical dystonia and tremor

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Background: In focal dystonia, there is evidence pointing to abnormalities in proprioceptive processing at a cerebellum-cortical level for defective sensorimotor integration processes. Recently it has been suggested that cerebellum may play a role in the expression of tremor in CD, by showing that some cerebellar functions (eyeblink conditioning and motor adaptation) are exclusively impaired in CD patients with tremor [1,2].

Aim: We investigated proprioceptive function in the affected body segment in patients with cervical dystonia (CD) with and without tremor.

Material and methods: Twenty-one patients with CD, with (CDT+) and without (CDT-) tremor, and 20 healthy controls (HC) were enrolled. Cervical proprioceptive ability was assessed by means of a position-matching task. While participants were blindfolded, an operator executed a passive mobilization of the head for bending and rotation on both sides to the 50% and 75% of the maximal individual active ROM. After the passive mobilization, subject's head was taken to the neutral position and participants had to reproduce actively the same movement. Each movement were reproduced 3 times for each condition (50% and 75% of the maximal ROM) in a random order. Head movements were recorded by means of an optoelectronic system (Qualysis).

Results: Mean position errors were larger in CD patients with tremor respect to CD patients without tremor and controls. Particularly, RM-ANOVA showed a main effect of GROUP ($p=0.001$) and post hoc analysis showed that for both bending and rotation mean error was larger in CDT+ than CDT- and HC ($p=0.010$ and $p<0.0001$ respectively) with no difference between CDT- and HC ($p=0.45$).

Conclusions: Patients with cervical dystonia and tremor display abnormal proprioceptive function. Our findings point to a possible role of a network comprising the cerebellum and sensory cortex in the expression of a clinical phenotype in dystonia.

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P103

Pain in focal dystonias – A focused review to address an important component of the disease

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Introduction: Focal dystonia is characterized by involuntary muscle contractions that cause abnormal postures and/or twisting movements in a segment of the body. Motor symptoms have a major impact on disability in this condition, but the presence of pain represents an additional source of impairment and poor quality of life. Pain indeed occurs in up to 70% of patients with cervical dystonia (CD) and in a relevant proportion of subjects with focal dystonia of the limbs. Despite these conspicuous epidemiological figures, pain has received little attention from researchers and controlled trials are scant.

Objective: We undertook this review to summarize the current knowledge on the clinical assessment and management of pain in focal dystonias.

Methods: We searched the literature published in Pubmed, EMBASE, and the Cochrane Library using the following keywords: “cervical dystonia” OR “hand dystonia” OR “limb dystonia” OR “focal dystonia” AND “pain” AND “pathogenesis” OR “scale” OR “measurement” OR “pharmacologic treatment” OR “non-pharmacological treatment” OR “physical therapy” OR “rehabilitation”.

Results: No specific criteria exist for pain classification in CD and in focal dystonias of the limb. Only in the case of CD could we identify two scales that, though not specifically devised for pain detection, include a section for pain assessment: the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and CDIP-58. Botulinum toxin emerges as the only treatment with evidence-based efficacy in relieving painful symptoms of focal dystonia. Physical therapy may be considered as a useful tool in pain relief of patients with focal dystonia and should be used in association with botulinum toxin to synergize effectiveness.

Conclusions: The collated data will hopefully improve the clinical management of focal dystonia and, more importantly, stimulate future research on dystonia-associated pain. Optimization of the outcome indeed requires the identification and the management of all the factors that determine disability.

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Hypertrophic Olivary Degeneration: the spectrum of aetiology

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Background: Hypertrophic Olivary Degeneration (HOD) appears as an increased T2/FLAIR signal intensity of the inferior olive on MRI and is observed in patients developing palatal tremor (PT) or oculopalatal tremor (OPT). HOD may result from a brainstem or cerebellar lesion interrupting the dentato-rubro-olivary pathway (unilateral or bilateral HOD), or could be part of the syndrome of progressive ataxia and palatal tremor (PAPT), in the latter case HOD appears bilaterally. PAPT could be sporadic or familial; Alexander disease is one of the most reported known etiologies of familial PAPT.

Aim: To describe two cases of HOD, with different onset and etiology.

Case Description: Patient A, a 65 years-old woman, with hypothyroidism and hypertension, was admitted for new onset oscillopsia and instability. 4 months before she had a pontine haemorrhage caused by a bleeding cavernoma treated with microsurgical resection. On admission she also presented mild ataxic gait, cranial inspection revealed a continuous ocular bobbing consisting in rhythmic vertical oscillations of both eyes, and a palatal tremor synchronous with the ocular vertical movement. Brain MRI showed right HOD, secondary to the surgical lesion in the pons. Patient was treated with clonazepam and gabapentin with improvement of oscillopsia. Patient B was a 76 years-old man with ten-year history of progressive dysarthria and instability. His past medical and familial history was unremarkable. Neurological examination revealed gait ataxia, brisk tendon reflexes with bilateral extensor planter response, and continuous tremor of the soft palate. Brain MRI showed bilateral HOD. Cervical MRI revealed no cervical cord atrophy. FDG PET scan showed hypometabolism in the cerebellar cortex. Alexander disease was ruled out.

Conclusions: A brainstem lesion involving the specific connections of the Guillain–Mollaret triangle could lead to the appearance of HOD on MRI and to the development of PT/OPT regardless of aetiology.

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A clinical improvement on a transdermal rotigotine treated patient with idiopathic cervical dystonia: a case-report

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Introduction: Cervical dystonia is a subtype of Primary Focal Dystonia due to the phasic and/or tonic involuntary contractions of different combinations of neck muscles. The etiology of cervical dystonia is still unknown. The dopamine agonist-response dystonia has been described in patients with an autosomal recessive L-amino acid decarboxylase deficiency. [1] Rotigotine is a high-affinity agonist at several dopamine receptors, notably D1, D2 and D3. [2]

Case-report: We report a case of 67 old woman with a forced involuntary and painful contraction of right neck muscles combined with dystonic tremor. Patient complained also an anxiety depression with insomnia (Beck's Depression Inventory=19). Both brain, neck and shoulder muscles MRI, showed no abnormalities. The needle EMG argued a typical pattern of co-contraction of agonists and antagonists right neck muscles. The first-line treatment was transdermal rotigotine slowly increased until 8mg/24h. After 3 weeks of treatment with transdermal rotigotine (6mg/24h), already both painful sensation at the rightneck and depression symptoms were improved. After 5 weeks of treatment with transdermal rotigotine (8mg/24h), we observed a reduction of involuntary contraction on the right sternocleidomastoid muscle and the BDI score was 12. The second-line treatment was injections of botulinum toxin in the involved muscles associated with transdermal rotigotine 8mg/24h with almost complete resolution of the symptoms. After 6 months follow-up, patient no longer needed of other botulinum injections.

Conclusion: Cervical dystonia is a common movement disorder with unknown etiology. The dopamine agonist-response dystonia is an inherited autosomal dominant disease caused by L-amino acid decarboxylase deficiency. Since rotigotine acts as a high-potency agonist at human dopamine D1, D2, D3 receptors and as a lower-potency agonist at D4 and D5 human dopamine receptors, we suggest a more wide clinical application of this innovative agonist receptors drug. In our patient, we showed both a mild clinical improvement in cervical dystonia and an antidepressant effect. Moreover, we observed a delay in the subsequent botulinum injections in a patient that underwent the transdermal rotigotine. Further studies will be required to validate this hypothesis for a wider application of rotigotine in movement disorders.

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P106

Reversible symptomatic dystonic tremor: a unique case description

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We would show and discuss clinical features (videos available at poster presentation), brain imaging, and physiopathology of a peculiar and tightly unilateral dystonic tremor due to a rare lesion of the left middle cerebral artery, widening the spectrum of conditions causing symptomatic tremor. A 40-year-old man came to our attention with a 6-months history of tremor limited to his right arm. The tremor (about 4 Hz of middle amplitude) was always present during writing and at certain angles when shaving or drinking. It was also present at rest during emotional activation. Clinical examination revealed impairment of fine movements in patient's right hand due to mild focal dystonia and tremor, a slight increase of muscular tone in his right arm was present too. Swing of his right arm was slightly reduced during walking. Neurological examination was otherwise normal. MRI and angio-MRI disclosed a left middle cerebral artery bifurcation giant aneurysm with almost complete thrombosis. The lesion resembled a space occupying process, determining a marked compression on the left mesencephalon, thalamus, and basal ganglia. The patient underwent surgery with a complete removal of the aneurysm and a significant improvement of tremor and motor impairment. Currently (10 years after aneurysm excision), the patient has an almost normal neurological examination with neither tremor nor dystonia. This is a case of pure juvenile and strictly unilateral extrapyramidal syndrome, characterized by dystonic tremor almost limited to the right arm. A tightly localized disorder may suggest a focal lesion in basal ganglia rather than an idiopathic disease. A giant aneurysm has been previously reported as an exceptionally rare cause of symptomatic hemiparkinsonism [1] but this is a case of focal dystonic tremor, maybe due to the involvement of Vim thalamic nucleus or to impairment of cerebello-thalamic pathways as reported in dystonic tremor and Holmes' tremor [2,3].

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P107

Are there two different forms of functional dystonia? A multimodal brain structural MRI study

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Introduction: Whether underlying neurobiology of functional (psychogenic) dystonia (FD) is common regardless of the distinct phenotypes or unique neurobiological mechanisms are responsible for different clinical presentations is still unknown.

Objective: This study assessed brain structural alterations in two diverse clinical FD forms – the typical phenotype fixed dystonia (FixFD) and the recently recognized new phenotype “mobile” dystonia (MobFD).

Methods: Forty-three FD patients (13 FixFD, 40 MobFD) and 42 healthy controls were recruited. All subjects underwent 3D T1-weighted and diffusion tensor (DT) magnetic resonance imaging (MRI). Cortical thickness, volumes of grey matter (GM) structures, and white matter (WM) tract integrity were assessed.

Results: Normal cortical thickness in both FD patient groups compared to age-matched healthy controls were found. When compared with FixFD, MobFD patients showed cortical thinning of the left orbitofrontal cortex, and medial and lateral parietal and cingulate regions bilaterally. Additionally, compared to controls, MobFD patients showed reduced volumes of the left nucleus accumbens, putamen, thalamus, and bilateral caudate nuclei, while MobFD patients compared to FixFD demonstrated atrophy of the right hippocampus and globus pallidus. Compared with both controls and MobFD cases, FixFD patients showed a severe disruption of WM architecture along the corpus callosum, corticospinal tract, anterior thalamic radiations, and major long-range tracts bilaterally.

Conclusions: This study showed different MRI patterns in two variants of FD. MobFD had alterations in GM structures crucial for sensorimotor processing, emotional, and cognitive control. On the other hand, FixFD patients were characterized by a global WM disconnection affecting main sensorimotor and emotional control circuits. These findings may have important implications in understanding the neural substrates underlying different phenotypic FD expressions.

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P108

Sensory symptoms are associated with tremor in patients with cervical dystonia: data from the Italian Dystonia Registry

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Segue P108

Background: Cervical dystonia (CD), the most common type of dystonia, is characterized by intermittent or constant abnormal postures and sometime by involuntary repetitive movements of the head, often described as tremors, reported in 30-70% of patients. Pathophysiology of tremor in CD has not been elucidated, although an interesting hypothesis indicates the involvement of the cerebellar circuits. Cerebellum is crucial for motor control, but also for sensory and sensorimotor functions. The features that better highlights the involvement of sensory and sensorimotor processes in dystonia are the “sensory trick” and the presence of pain.

Aim: Our aim is to better characterize the clinical phenotype of CD population with and without head tremor. Our hypothesis is that patients with head tremor present a higher correlation with sensory trick and pain.

Methods: Clinical and demographic data from 717 patients with CD were extracted from the Italian Dystonia Registry. The patients were divided according to the presence of head tremor in dystonic patients with (CD T+) and without (CD T-) tremor. The association between head tremor and sensory trick or pain was assessed by means of Chi-square tests. A logistic regression model was run to test for the effect of age, gender and disease duration.

Results: Chi-square tests showed that there was a significant association between head tremor and pain ($p=0.013$) and between head tremor and sensory trick ($p=0.027$) in our population. The percentage of patients who experienced pain was 58.5% in the CD T+ group and 41% in the CD T- group. For sensory trick, 33.9% of patients reported sensory trick in the CD T+ group, while only 21% reported sensory trick in the CD T- group. Association between head tremor, sensory trick or pain remained significant after adjusting for age, gender and disease duration.

Discussion: Our results show an association between head tremor and sensory symptoms in patients affected by CD.

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Language screening in patients with movement disorders: a comparative study

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Objective: To screen language disorders in patients with Parkinson's disease and atypical parkinsonisms, beyond articulation and phonation alterations.

Methods: Thirty-four patients with Progressive Supranuclear Palsy (PSP), twenty-eight with Parkinson's disease (PD) and twenty nine with Multiple System Atrophy (MSA) received a combined cognitive and motor evaluation. The neuropsychological battery included tests evaluating different cognitive functions and a screening language battery (SAND).

Results: Naming, word and sentence comprehension, semantic association, unpredictable sentences repetition and non-word reading tasks were more impaired in PSP than MSA and PD ($p < 0.05$), without differences between the last two groups. PSP patients had significantly worse performance than PD, but not MSA in word and predictable sentences repetition and reading tasks. Dividing patients according to impaired/normal score on the Montreal Cognitive Assessment, we found a significant difference in the reading tests in PSP, in the naming task and word comprehension of living things in PD, and in word and sentence comprehension, word repetition and reading in patients with MSA. We found significant correlations between language tests and executive functions, in particular in tests assessing planning and divided attention.

Conclusions: We found that PSP patients have a significantly worse performance than MSA and PD patients in a large number of language tests, whereas MSA patients have a worse performance than PD patients only in selected tests. The global cognitive status of patients significantly influences language scores in MSA patients. Language performance is significantly related to executive functions, particularly in MSA and PD patients.

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Progressive spastic paraparesis with cerebellar ataxia: a case of hereditary spastic paraplegia caused by mutation in the SPG7 gene

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Introduction: Hereditary spastic paraplegias (HSP) are a group of heterogeneous neurodegenerative diseases, characterized by lower limb weakness and spasticity with subtle onset and slowly progressive course, that could be associated with additional neurological and systemic features.

Case Report: A 50 years old man started complaining about gait disturbance, leg stiffness and urinary urgency. He was admitted to a Neurology Unit at another Hospital where a spastic paraparesis with hyperreflexia in lower limbs were revealed; blood tests, with autoantibodies and serological investigations, MRI of the brain, lumbar puncture and electromyography didn't show any abnormalities. He also underwent motor evoked potentials and sensory evoked potentials, which were altered in lower limbs. A MRI of the cervical and thoracic spine showed a cervical disc herniation (C5-C6) with slight compression of the dural sac, that was treated with neurosurgery without clinical benefits. During the following years, the patient worsened and, seven years after the appearance of signs and symptoms, he was admitted to the center for Rare Neurological Diseases at the Neurology Department, Careggi University Hospital, Florence. At neurological examination the patient had a paraparetic-ataxic gait, clonus, Babinsky sign bilaterally, spasticity, hyperreflexia and dysmetria in the lower limbs. Bilateral pes cavus was observed. He underwent a new MRI of the brain that showed marked cerebellar atrophy. In the suspicion of a hereditary spastic paraplegia, genetic tests for SPG4 and SPG7 were performed, although he had not familiar history for neurological diseases. Test for SPG4 was negative, while a compound heterozygous mutation in SPG7 was identified.

Conclusions and Discussion: Hereditary spastic paraplegias should be considered in patients with spastic paraparesis with or without other neurological features, after the exclusion of other causes of spastic paraparesis. SPG7 mutation leads to a complicated HSP characterized by adult onset spastic paraparesis, ataxia, pes cavus and sphincter disturbances.

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Hemidystonia due to midbrain hemorrhage: an unusual complication of Deep Brain Stimulation

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Introduction: Intraoperative bleeding is a possibile complication of deep brain stimulation (DBS), sometimes leading to chronic disability. In this case report, we describe the development of hemidystonia due to hemorrhagic complication after subthalamic (STN)-DBS in a patient with Parkinson’s disease (PD).

Case report: A 59-year-old woman with PD developed a left hemiparesis immediately after STN-DBS, due to right midbrain hemorrhage. In addition to pyramidal signs, we observed a complete resolution of left limbs rigidity due to a lesional effect, while the right parkinsonian signs improved with unilateral left STN-DBS. After a 2-months intensive rehabilitation, left hemiparesis greatly improved, without the recurrence of parkinsonian signs. Unfortunately, the patient progressively developed a left hemidystonia, not responsive either to right STN-DBS and to oral therapy. Therefore, hemidystonia was treated with botulinum toxin injections, with a complete resolution on upper limb and partial responsiveness on lower limb.

Discussion: Hemorrhage is probably the most severe complication of DBS, with an incidence of about 5%. The most frequent sequelae are changes in consciousness, hemiparesis and visual loss. Secondary dystonia has been described in a few cases after midbrain hemorrhage but, to our knowledge, it has never been reported as STN-DBS complication. In our case, the combination of unilateral STN-DBS and botulinum toxin treatment lead to a quite good control of either parkinsonian and dystonic features.

P112

Two novel mutations in RAB39B gene cause X-linked parkinsonism with intellectual disability

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Introduction: RAB39B pathogenic variants were first identified in patients affected by X-linked Intellectual Disability (XLID) in comorbidity with autism spectrum disorder, macrocephaly and epilepsy. More recent evidence showed that RAB39B mutations also have a causative role of in the pathogenesis of early onset Parkinsonism associated to XLID (Waisman syndrome-WSMN, OMIM 311510). Since few RAB39B mutations have been identified so far, the genotype-phenotype correlation is still unclear.

Methods: Three patients characterized by early onset Parkinsonism associated to XLID from two different kindreds received neurological evaluation and underwent RAB39B sequencing. GBA, LRRK2 exons 29-30-31-35-41, PRKN, PINK1, DJ-1, ATP13A2, FBXO7, PLA2G6, DNAJC6 or SYNJ1 were also analysed by Sanger sequencing. Deletion/duplications in PRKN were analysed by quantitative PCR.

Results: Two novel RAB39B frameshift variants were identified (family 1:c.137dupT; family 2:c.371delA). These mutations resulted in the absence of RAB39B protein. Patients showed unilateral rest tremor and bradykinesia; one of them also displayed an early-onset postural tremor. One patient presented early sensorineural hearing loss. Paramagnetic substance deposition in the substantia nigra, globus pallidi, red nucleus, putamen and pulvinar was assessed by brain imaging. Two patients also showed moderate calcification of globus pallidi. [123I]-FP CIT SPECT imaging showed a severe reduction of the radioligand uptake at the level of left putaminal nucleus.

Conclusions: This study describe the pattern of clinical and neuroimaging features attributable to RAB39B pathogenic variants in two different Italian families. Levodopa responsiveness and [1123I]-FP CIT SPECT suggest that these RAB39B mutations cause SNc degeneration.

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Tremor in motor neuron disease may be central rather than peripheral in origin

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Background: Motor neuron disease (MND) refers to a spectrum of degenerative diseases affecting motor neurons. Recent clinical and postmortem observations have revealed considerable variability in the phenotype [1]. Rhythmic involuntary oscillations of the hands during action, resembling tremor, can occur in MND, but its pathophysiology has not yet been investigated.

Methods: 120 consecutive MND patients were screened for tremor. Twelve patients with action tremor and no other movement disorders were found. Ten took part in the study. Tremor was recorded bilaterally using surface electromyography and triaxial accelerometer, with and without a variable weight load. Power spectra of rectified electromyography and accelerometric signal were calculated. To investigate a possible cerebellar involvement, eye blink classic conditioning (EBCC) was performed in five patients [2].

Results: Action tremor was present in about 10% of our population. All patients showed distal postural tremor of low amplitude and constant frequency, bilateral with a small degree of asymmetry. Two of them showed also simple kinetic tremor. A peak at the electromyography and accelerometric recordings ranging from 4 Hz to 12 Hz was found in all patients. Loading did not change peak frequency in either the electromyographic or accelerometric power spectra. Compared with healthy volunteers, patients had a smaller number of conditioned responses during EBCC.

Conclusions: our data suggest that MND patients can present with action tremor of a central origin, possibly due to a cerebellar dysfunction. This evidence supports the novel idea of MND as a multisystem neurodegenerative disease and that action tremor can be part of this condition.

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P114

KinesioTaping improves pain and modulates somatosensory processing in Cervical Dystonia

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Introduction: Pain is a prominent and disabling symptom of cervical dystonia (CD). First-line treatment is botulinum toxin (BoNT) that ensures an overall duration of benefit of about 12 weeks; yet, individual response is variable with some patients experiencing an earlier wearing off of BoNT benefit with pain relapse. Ancillary treatments to prolong the effect of BoNT are an unmet need.

Objective: To investigate the effects of KinesioTaping (KT) on pain and abnormal posture in CD patients with wearing-off of BoNT effects.

Methods: We enrolled 10 patients with idiopathic CD and pain and applied KT at least 3 months after BoNT injection. KT was applied according to inhibition technique over the hyper-contracted muscles (mono-or bilaterally) and kept for 5 days. Clinical evaluation included Toronto Western Spasmodic Torticollis Rating Scales (TWTSRS) (severity, disability and pain scales) and patient's Clinical Global Impression (PCGI). Somatosensory processing was evaluated by tactile temporal discrimination threshold (TDT). Each subject was assessed before and at 5 days of KT.

Results: At 5 days of KT, there was a significant improvement of TWSTRS severity scale ($p=0.008$) and pain scores (severity: $p=0.028$, duration: $p=0.043$). Moreover, TDT significantly decreased in the most affected side ($p=0.012$), as patients improved their ability to process tactile somatosensory stimuli. CD patients with tremor had more severe dystonia and showed a greater improvement after KT in term of severity (TWTSRS total score $p=0.03$), global disability ($p=0.03$) and pain disability ($p=0.025$).

Conclusions: This pilot study demonstrates that KT can reduce pain and disability in patients with CD, especially if presenting with tremor, through enhancing the effect of BoNT toxin in the interval between consecutive injections.

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Voice cepstral analysis in adductor-type spasmodic dysphonia

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Objective: To investigate differences in voice parameters between patients affected by adductor-type spasmodic dysphonia (ASD) and Healthy subjects (HS).

Background: ASD is a task-specific focal dystonia manifesting with involuntary laryngeal muscle spasms [1]. ASD is often poorly recognized, because of the lack of diagnostic criteria. In the present study, we performed voice analysis in ASD patients by using cepstral analysis. Cepstral analysis is the Fourier transform of the logarithm power spectrum of an acoustic signal and reflects the dominant harmonic in the voice sample [2].

Methods: We investigate 20 ASD patients and 20 age and sex-matched HS. Symptoms were scored using the Voice Handicap Index scale and a dysphonia clinical scale. The crucial variable in the voice cepstral analysis is the normalized cepstral peak prominence (CPP). We collected voice samples using a high-definition audio recorder (H4n Zoom Corporation, Japan) and a Shure WH20 Dynamic Headset Microphone. Voice samples were digitized and analysed using the Matlab software. CPP together with other cepstral and spectral features, such as CPPS (smoothed CPP), Hi/Low frequencies rate, harmonics-to-noise ratio, shimmer and jitter were extracted. Finally, we performed a classification with both neural networks and Support Vector Machine (SVM), using Weka software.

Results: Voice analysis discriminates HS from ASD, with a sensitivity of 82% by using neural networks and 87% by applying SVM; and a specificity of 90% by using neural networks and 97% by applying SVM. Positive predictive value is 87% by using neural networks and 88% by applying SVM. Negative predictive value is 85% by using neural networks and 84% by applying SVM.

Conclusions: Cepstral analysis discriminates ASD patients from HS. These results suggest the idea that voice features extraction and classification are important instruments to support clinicians in the correct diagnosis of ASD, among different voice disorders.

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Sensory trick phenomenon in cervical dystonia: a functional MRI study

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Introduction: Previous studies using positron emission tomography and transcranial magnetic stimulation suggested the possible role of sensory trick (ST) in modulating the sensorimotor cortex excitability in dystonia (DYT) patients. However, the mechanisms underlying the ST effect in DYT subjects remain to be fully understood.

Objective: This study investigates the patterns of brain functional MRI (fMRI) during resting-state (RS) with and without ST and during the ST imagination in subjects with cervical DYT.

Methods: We recruited 17 patients with cervical DYT, treated with botulinum toxin at least three months before, and 15 healthy controls (HC). In 9 patients (DYT-trick), ST almost reversed head rotation to primary position, while 8 patients (DYT-notrick) did not show any trick effect. All groups underwent RS fMRI, and DYT groups repeated RS fMRI performing ST. DYT patients also performed a functional MRI task in which they were asked to imagine an ipsilateral ST (i.e., slight touch on the cheek/chin).

Results: DYT-notrick subjects showed an increased connectivity of the sensorimotor network relative to HC during RS fMRI without ST. During RS fMRI with ST, DYT trick patients showed a reduced connectivity of the sensorimotor network relative to RS fMRI without ST, while DYT-notrick did not show any ST effect. During the imagination of ST, DYT-trick cases had an increased recruitment of the cerebellum bilaterally compared to DYT-notrick subjects.

Conclusions: This study suggests an hyperconnectivity of the sensorimotor areas during RS in cervical DYT-notrick subjects. In DYT-trick patients, the ST was associated with a “normalization” of such a phenomenon. The increased activation of the cerebellum in DYT-trick patients during the ST imagination suggests a possible role of this area in modulating cortical activity. These findings call for novel therapies for cervical DYT such as electrical stimulation of cerebellum and modulation of proprioception using vibration or electrocutaneous stimulation devices.

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“Ultra-late” onset painful limb dystonia secondary to vascular injury

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Introduction: A 51-year-old man came to our attention complaining of severe pain involving his left arm, with marked limitation of elbow and hand movements. The onset was sub-acute. Basal CT scan was negative for acute lesions, electrophysiological assessment was negative. After diagnosis of brachial tenosynovitis, physical treatment was recommended. In his history ischemic transient attacks 8 years earlier, with MRI evidence of right caudate and putamen restricted diffusion on DWI. For a dilated cardiomyopathy secondary to viral myocarditis he underwent heart transplantation. Immunosuppressive therapy with cyclosporine and micofenolate-mofetil was started. After the first months of treatment occurred a seizure, related to unstable drug blood levels. Brain MRI demonstrated restricted diffusion on the right temporal lobe and confirmed a widespread microvascular encephalopathy with a small right basal ganglia injury.

Methods: Neurological examination showed dystonic posture of the left arm with sustained flexion of elbow and fingers and associated athetotic movements. He reported severe pain not responsive to NSAIDs, with poor benefit after Clonazepam. Blood tests, iron and copper metabolism, cyclosporine blood levels were normal. Brain MRI confirmed previous reports, cervical MRI was normal. FDG-PET showed severe hypometabolism of right putamen and caudate tail. He was treated with botulinum toxin injection with dramatic improvement of dystonia and remission of associated pain after two weeks; functional recovery was almost complete.

Conclusions: Dystonia can occur after cerebrovascular lesions affecting the basal ganglia, with a mean delay of 9.5 months, up to a maximum of 6 years. Limb dystonia was reported during cyclosporine treatment; onset is in the first months of treatment, associated to posterior reversible encephalopathy syndrome. Clinical and radiological findings in our case support vascular hypothesis with atypical very late onset, as a result of a re-modulation of basal ganglia circuits, which follows even minor strokes. Botulinum toxin represents an efficacious and long-lasting therapeutical strategy.

P118

Isolated freezing of gait: a case report

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Background: Idiopathic normal-pressure hydrocephalus (iNPH) is a clinical syndrome characterized by gait dysfunction accompanied by frontal and subcortical cognitive deficits and bladder detrusor overactivity, with the radiological evidence of ventriculomegaly and a clinical response to Cerebrospinal fluid (CSF) shunt. Generally, gait disturbance plus one additional feature is required to consider the diagnosis of probable iNPH.

Case presentation: A 73-years-old man was admitted to our Neurology Department with a three years history of gait disorder with difficulty in gait initiation. Neurological examination showed a broad-based gait with short steps, start hesitation and turning difficulty. The remaining exam was normal (MMSE was 28/30, no urinary disturbances, no extrapyramidal signs). Medical history was significant for diabetes mellitus type II and dyslipidemia. A brain-CT and a EMG/ENG of the inferior limbs were normal. After admission, a brain-MRI showed ventricular enlargement, periventricular signal hyperintensity in T2-weighted sequences and enlarged sylvian fissures. The patient underwent a lumbar puncture with 40 mL CSF removal and showed a marked improvement in motor performance, especially in freezing of gait.

Discussion: Isolated freezing of gait evolving in the absence of other neurologic abnormalities for at least three years is rarely seen alone in iNHP and it is the clinical hallmark of Primary Progressive Freezing of Gait (PPFG), which is considered a clinical variant of Progressive Supranuclear Palsy (PSP). In our case, the MRI-findings, the brilliant response to the tap-test and the lack of extrapyramidal signs clearly support the diagnosis of iNPH. However, we cannot rule out the development of a neurodegenerative disease, as suggested by recent studies in which PSP was found to be an important underlying pathology of iNPH in post-mortem analysis of patients diagnosed with iNHP ante-mortem, thus challenging the dignity of iNPH as a separate entity. Clinical and instrumental follow-up is ongoing.

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Dopaminergic involvement in a drummer with focal dystonia: a case study

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Introduction: Focal task specific dystonia (FTSD) affects an isolated body part and is triggered by specific actions in individuals repeating stereotyped movements. Musician's dystonia (MD) is a form of FTSD affecting muscles involved in playing a musical instrument. A dopaminergic dysfunction occurs in many movement disorders, including some FTSD such as writer's cramp but it has not been reported for MD yet.

Objectives: To describe a case of MD presenting with dopaminergic deficiency at the iodine-123 ioflupane SPECT.

Methods: Retrospective review of clinical and neuroimaging data of a patient affected by MD.

Results: The patient is a 49 years old man, professional drummer, playing since the childhood. Medical history encompassed a Tourette syndrome and an obsessive-compulsive disorder with depression treated with neuroleptics, benzodiazepines and serotonin's reuptake inhibitors. At 46 years, he experienced, during drumming, the loss of dexterity in the left hand that later progressed into a sensation of pulling associated with the internal torsion of the entire arm and finally became an involuntary movement occurring even at rest. Brain MRI, blood tests, EEG and physical examination were unremarkable. Iodine-123 ioflupane SPECT showed about 25% lower tracer uptake into the right striatum than left striatum. An acute submaximal and a chronic administration of levodopa were ineffective. Instead, a stable amelioration was achieved with trihexyphenidyl and botulinum toxin injections.

Conclusions: MD has been occasionally described as an onset symptom of PD but, here, a number of features, seems to exclude PD suggesting a "primary" MD. Improbable that dopaminergic dysfunction originated by Tourette syndrome; more likely it was due to previous neuroleptics exposure or idiopathic nigrostriatal degeneration. Our case represents the first report of upper limb dystonia in a professional drummer. Moreover, presynaptic dopaminergic deficiency seems to play a role in pathophysiology of focal dystonia and this case provides similar insights for MD.

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Freezing of gait is still a mystery: a case report

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Background: Freezing of Gait (FOG) is a mysterious phenomenon: it is a motor manifestation related to cognitive dysfunction, is typical of parkinsonian syndromes but is also present in various diseases, can be related to heterogeneous brain lesions and shows different response to treatments.

Aims: Here we describe a case of FOG, worsened by levodopa and improved by amantadine, in a man with previous legionella's encephalopathy.

Methods and Results: A 66-years old man came to our attention referring gait disorder, insidiously appeared six months before and rapidly worsened. Twenty-three years before he had been affected by legionella's pneumonia, complicated by encephalopathy, followed by recovery. At the time of our examination, severe FOG was present, characterized for start, turn and destination hesitation, with minimal impairment in fine movements. Tremor and rigidity were absent, voice and ocular movements were normal and no cerebellar, sensitive or pyramidal signs were present. Clinical assessment was suggestive of Primary Progressive Freezing of Gait (PPFG). Brain MRI showed diffuse brain atrophy, without mesencephalic or focal cortical involvement nor hydrocephalus. ¹²³I-FPCIT SPECT showed decreased uptake in both striatum. Patient started treatment with low dose of levodopa but FOG rapidly worsened. Drug was discontinued and FOG slightly ameliorated. Then, amantadine was administrated, until 100 mg twice daily. After few days, FOG drastically improved and this effect lasted until now.

Conclusions: This case has several elements of interest: levodopa-induced worsening resembles the so-called "on fog" described in PD; improvement induced by amantadine is not always predictable and very few data exist for PPFG; this kind of FOG could be related to either the involvement of non-dopaminergic pathways or, similar to some DBS-induced motor complications, to a dystonic strand; finally, previous legionella's encephalitis, known to produce brainstem involvement, stimulates the hypothesis of a possible relationship, as an atypical case of post-encephalitis parkinsonism.

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May cognitive tasks improve increased blinking and dystonic spasms in patients with blepharospasm?

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Introduction: Blepharospasm (BSP) is characterized by involuntary, bilateral and symmetrical spasms of the orbicularis oculi (OO) muscles. Increased spontaneous blinking may also be present in BSP and it may be influenced by several factors including cognitive tasks. Whether cognitive tasks also modulate OO spasms is still unknown. Having more information about this issue could contribute to better understand the pathophysiological mechanisms underlying increased blink rate (BR) and OO spasms in BSP.

Objective: To assess the effect of various cognitive tasks including writing, speaking and reading on BR and OO spasms in BSP patients compared to those obtained in healthy subjects (HS) and in patients with hemifacial spasm (HFS). To see whether changes in head position per se during writing may influence BR and spasms, as a control experiment, we examined BR and OO spasms during writing on a blackboard while keeping the head in a straight position.

Methods: We enrolled 30 patients with idiopathic BSP, 20 with idiopathic HFS, and 20 age-matched HS. All participants were videotaped according to a standardized procedure. Two independent movement disorders specialists reviewed the videotapes and measured the number of blinks and OO spasms at rest and during the various cognitive tasks.

Results: BR at rest significantly differed across the three groups ($F=8.8$; $p=0.0003$), being higher in BSP patients than in HSF and in HS, and significantly changed during the cognitive tasks ($F=64.2$; $p=0.000004$). Post hoc analysis showed that in BSP reading and writing significantly reduced BR ($p=0.005$, $p=0.012$), whereas speaking left BR unchanged ($p=0.13$). In BSP OO spasms significantly decreased during writing ($p=0.0000002$) and reading ($p=0.003$), but not during conversation ($p=0.72$). In HSF patients cognitive tasks did not influence OO spasms ($p=0.43$).

Conclusions: Cognitive tasks, particularly reading and writing, improve OO spasms in BSP and might be considered as possible cognitive tricks.

P122

Botulinum toxin for treating Pisa syndrome

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Introduction: Pisa syndrome (PS) is a term used to define a mobile dystonic flexion of the trunk on the lateral axis, frequently associated with Parkinson disease (PD) and characterized by low-back pain and postural instability.

Objective: We sought to assess the clinical efficacy of ultrasound (US) and electromyography (EMG)-guided botulinum toxin (BoNT) injections for the symptomatic treatment of PD-associated PS.

Materials and Methods: Thirteen consecutively selected patients were enrolled in a 3-month prospective observational study. Inclusion criteria consisted of idiopathic PD and newly diagnosed PS. Exclusion criteria were severe spine orthopedic diseases; enrollment in programs of physical therapy specifically targeting trunk postural abnormalities; and relevant changes in pharmacological treatments with a possible effect on trunk posture. EMG and US-assisted BoNT injections were delivered in muscles with asymmetric pattern of EMG activation when standing. As primary endpoint, we measured the angle of trunk flexion on the lateral axis. As secondary endpoint, we measured pain or discomfort associated with PS, as per a patient self-rated visual-analog scale (VAS) of 0 to 10. Data collected at baseline (T0) were compared to those collected after 3 months since the injection of BoNT (T1).

Results: There was a 52.3% improvement in the lateral trunk flexion ($p < 0.001$), with 84.6% of patients ($n=11/13$) reporting a clinically relevant amelioration of trunk posture abnormalities between T0 and T1. The VAS score improved in all patients, by an average of 50.3% ($p < 0.001$). Age, PS severity at baseline, PS duration, levodopa equivalent dose, and PD motor symptoms severity, as measured by the MDS-UPDRS-III, did not correlate with the final outcome ($p > 0.094$).

Conclusions and Discussion: Our findings support the utility of EMG- and US-guided BoNT injections for the symptomatic management of PD-associated PS. A randomized clinical trial is warranted to confirm these promising results.

P123

SCAs genes as disease modifiers in Huntington's disease

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Introduction: Huntington's disease (HD) is an autosomal dominant neurodegenerative disease, clinically characterized by movement disorders, cognitive deficits, and psychiatric problems. HD is caused by the expansion of a CAG repeat within exon 1 of IT15 gene. HD exhibits the typical phenomenon of genetic anticipation and the symptoms of the disease appear earlier and more severe in subsequent generations due to meiotic instability. The CAG repeat accounts only for approximately 56%- 70% of the variation in age at onset in HD. It is likely that modifying genetic variations, which segregate independently from the primary mutation, could influence the age at onset.

Aims of the Study: Genetic, pathological, and clinical similarities exist between HD and spino-cerebellar ataxias (SCAs). In this study, seven SCAs genes have been studied as modifiers of age at onset in a cohort of HD patients.

Materials and Methods: We enrolled 50 HD patients. For every HD subject, CAG repeats have been measured on the larger allele of ATXN1, ATXN2, ATXN3, CACNA1A, ATXN7, PPP2R2B, and TBP genes. Regression analysis was used to evaluate the effects of CAG repeats in SCAs genes on age at motor, cognitive and psychiatric onset in HD patients.

Results: We did not find extensive correlations between CAG repeats in SCA genes and age at onset of HD. The only exceptions were represented by ATXN2 and CACNA1 genes for age at motor onset, and ATXN2 for age at psychiatric onset. When a multiple regression model was tested, a small additional effect on age at motor onset was identified only for CACNA1A. CAG repeats in expanded IT15 and larger CACNA1A alleles account for 64% of age at motor onset in HD patients.

Conclusions: CACNA1A gene could represent a mild genetic modifier of age at onset in HD patients. Further studies, conducted on larger HD patients' cohorts, are needed to confirm our data.

P124

The association of primary dystonia with tics - chance or new syndrome?

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Introduction: Primary cranio-cervical dystonia (PCCD) is an idiopathic condition, which typically occurs in late adulthood and in women more than men. Primary tics (PT) generally start during childhood/adolescence, and a later age of onset or other associated movement disorders are “red flags” to suspect secondary causes. Primary dystonia and PT are distinct entities, but nevertheless, a clinical syndrome with these two features has been described. We report a series of patients presenting both PCCD and PT.

Objective: This study aimed to evaluate the association between dystonia and tics as a primary clinical entity.

Methods: 248 patients with PCCD attending our Botulinum toxin clinic at the National Hospital of Neurology and Neurosurgery were examined for PT over 4 months.

Results: We have found 16 patients (6,5%) also presenting PT. Thirteen patients are male and in fourteen dystonia started below the age of 40. Eleven had a focal involvement, while 5 a segmental. Dystonia was found to affect neck (13), vocal cords (4), jaw (1) eyes (1) and arms (4). Six patients displayed a sensory trick. The association with tics can be stratified as follows: 3/16 patients presented tics before 21 years old, fitting Tourette’s syndrome (GTS) criteria (also presenting >1 motor tic and ≥1 vocal tic); for the other patients, we were not able to recall the onset, which was therefore more likely to fall into the Adult Primary Tics (APT) category. Most of our patients also showed psychiatric issues (hyperactivity, anxiety, depression or obsessive-compulsive features), which were generally mild.

Conclusions: We described a primary clinical entity of PCCD associated with PT. This syndrome differs from pure cranio-cervical dystonia by a higher prevalence in males and a lower age of onset. It presents a tic disorder, which, in a minority of cases resembles GTS, whereas more frequently falls into APT category.

P125

Decision-making and impulsivity in patients with functional neurological disorders and with obsessive compulsive disorders

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Introduction: Patients with functional neurological disorders (FND) are more impulsive, have higher rates of alexithymia, and show a significantly higher prominence of obsessive-compulsive personality disorder compared to healthy subjects (HS).

Objective: We aimed to compare FND patients to patients with Obsessive-Compulsive-Disorders (OCD) and to HS in performing a test assessing decision-making under risk.

Methods: Ten FND patients, 18 OCD patients, 25 HS performed the IGT. Participants were also assessed by means of: Hamilton depression rating scale; Hamilton anxiety rating scale; The 20-item Toronto Alexithymia Scale (TAS-20); Barratt Impulsiveness Scale, Version 11 (BIS-11); Sensitivity to Reward/Punishment Questionnaire (SPSRQ).

Results: There was a significant difference across groups in depression ($F(2, 50)=8.4$; $p=0.001$), anxiety ($F(2,50)=7.02$; $p=0.002$), alexythymia ($F(2,50)=5.7$, $p=0.0079$), impulsivity ($F(2,50)=4.2$, $p=0.01$) and sensitivity to reward ($F(2,53)=3.0$, $p=0.05$). Indeed, OCD were more depressed ($p=0.001$), more anxious ($p=0.002$), more alexithymic ($p=0.006$) and had a higher sensitivity to reward ($p=0.05$) than HS but there was no difference between OCD and FND and between FND and HS in these variables. FND were more impulsive than HS ($p=0.02$). Total netscore was significantly different across groups ($F(2,40)3.6$; $p=0.03$) where FND had a lower score than HS ($p=0.04$). Netscore Block 1 was different among groups ($F(2,50)3.9$; $p=0.03$), again FND had lower score than HS ($p=0.02$). Mixed ANOVA with netscores in the 5 blocks as within-subjects factor and group (OCD vs FND vs HS) as between-subject variable showed that there was significant difference in netscore across blocks ($F=8.3$; $p=0.006$) and a difference in performance across groups ($F=3.6$; $p=0.03$) but no group by block interaction. There was significant correlation between reward sensitivity and impulsivity, depression, anxiety and alexithymia ($p<0.05$). Impulsivity was correlated with anxiety ($p=0.001$).

Conclusions: Patients with FND were more impulsive and showed a more risky choice pattern compared to healthy subjects but they did not differ from OCD patients.

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Effects of propranolol on head tremor in patients with essential tremor and dystonia

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Background: Head tremor often occurs in the context of essential tremor (ET). Head tremor can also be a feature of dystonia. A few clinical observations suggested that propranolol can be used in ET as well as for the management of tremor in dystonia. However, it is still unclear whether propranolol has a beneficial effect on head tremor. Moreover, no studies have investigated whether propranolol has a differential effect on head and upper limb tremor in ET and dystonia.

Aim: To assess the therapeutic effects of propranolol on head tremor in patients with ET and dystonia. We also evaluated how clinical and demographic features correlate with the response to propranolol.

Methods: Twenty-eight patients with head tremor were enrolled in the study. Fourteen had ET and 14 had dystonia. All patients had head and upper limb tremor of variable severity. Patients underwent tremor assessment using clinical scales (Fahn Tolosa Tremor Rating Scale-FTMRS) and kinematic analysis. Patients were assessed in two sessions, 'without' (baseline) and 'during' treatment with propranolol (mean dose \pm DS: 70.0 \pm 24.0 mg).

Results: At baseline, head tremor was more severe in patients with dystonia than in ET (mean clinical score ET/dystonia: 2.2/4.4). ET patients had higher FTMRS total score in comparison to dystonia patients (mean FTMRS ET/dystonia: 27/17.1), due to the more severe involvement of the upper limbs. Clinical and kinematic assessment showed that propranolol had no effects on head tremor (all $P_s > 0.05$) although it reduced tremor of the upper limbs in both groups (both $P_s < 0.05$). Clinical and demographic features did not significantly correlate with the therapeutic response to propranolol.

Conclusions: The results indicate that propranolol is not effective on head tremor in patients with ET and dystonia, while its effect is evident on upper limbs tremor. Propranolol effects do not differentiate ET from dystonic tremor.

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Quantitative evaluation of functional limitation of upper limb movements in subjects affected by Dementia with Lewy Body

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Introduction: Dementia with Lewy Body (DLB) is a neurodegenerative disease characterized by the combination of a peculiar cognitive impairment and parkinsonian motor signs. Therefore, rigidity and bradykinesia are thought to significantly contribute to movement impairment. Recent neuropathological findings indicating the presence of Lewy body in the cerebellum have raised the possibility that a cerebellar dysfunction contributes to DLB motor impairment.

Objectives: To quantitatively characterize functional changes in upper limb movements in DLB patients, using an optoelectronic system for objective measurements.

Methods: Ten DLB patients and 10 age- and sex-matched healthy controls (HC) were recruited. Subjects were tested by a motion capture system while performing a hand-to-mouth task, one of the most studied functional movements in current literature on the biomechanical analysis of the upper limb. Kinematic parameters, including total and subphases duration, velocity and adjusting sway (AS) were computed.

Results: DLB needed a longer time to complete the task (2.52 +1.01 vs. 1.26+0.31 sec, $p<0.001$) and to precisely locate the mouth (19.15+8.89 vs 5.59+5.22 sec, $p<0.001$). Moreover, they exhibit a less smooth movement with increased frequency in the direction changes and increased AS (17.23+15.52 vs. 2.21+1.96 mm, $p<0.001$) compared to HC.

Conclusion: Quantitative assessment of UL movement during the hand-to-mouth task revealed that DLB patients perform less smooth and more segmented movements when approaching the target than HC. A similar picture has been observed in ataxic patients, thus supporting a cerebellar contribution to movement impairment in DLB.

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Conversion disorder from psychology to biology: increased limbic glutamate + glutamine in patients with functional motor symptoms

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Introduction: Conversion disorder impacts on all the fields of clinical medicine and clinicians in their practice have to cope with its diagnosis. Among the most frequent forms of conversion disorder there are psychogenic movement disorders or functional motor symptoms (FMS). Despite the high prevalence of FMS, their pathophysiology is still unknown. Brain magnetic resonance techniques provides the opportunity to study the neural mechanisms underlying FMS and to understand how they are linked to psychological risk factors.

Aim: This study assessed by magnetic resonance spectroscopy (MRS) N-Acetyl- aspartate (NAA), myo-inositol (MI), choline (Cho), glutamate + glutamine (Glx) and creatine (Cr) in the anterior cingulate cortex (ACC)/medial prefrontal cortex (mPFC) and in the occipital cortex (OCC) (control region), in patients affected by FMS and in healthy controls.

Methods: Ten patients affected by FMS and 10 healthy volunteers were included. Subjects underwent brain MRS and were tested by Mini Mental State Examination (MMSE), Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), 20-Item Toronto Alexithymia Scale (TAS-20) and EuroQol 5D (EQ5D). The assessment of functional motor symptoms was performed by the Psychogenic Movement Disorders scale (PMD scale).

Results: Glx/Cr was significantly increased in the ACC/mPFC but normal in the OCC of patients with FMS. All the other metabolites were normal in both regions. Glx/Cr increase in the ACC/mPFC correlated with TAS-20, HAM-A and PMD score, therefore demonstrating that Glx levels in these brain regions correlated with alexithymia, anxiety and severity of symptoms.

Conclusions: The abnormal increase of Glx in the limbic system underlies the pathophysiology of conversion disorder FMS type, possibly by altering limbic-motor interactions, ultimately leading to abnormal movements. Drugs modulating glutamatergic activity could be therefore a novel and alternative strategy in the management in this disabling disorder.

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Efficacy and safety of incobotulinum toxinA treatment in professional musicians affected by upper limb focal dystonia (ULFD)

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Introduction: Musician's dystonia is a task specific movement disorder which presents as loss of voluntary motor control and often causes careers end. Botulinum toxin (BoNT) injected in dystonic muscles is considered an efficacious treatment [1]; US guide has recently been recognize to be very important in the muscle targeting [2].

Aim: To demonstrate the efficacy and safety of incobotulinumtoxinA injected with US-EMG guide in dystonic muscles in musician.

Methods: Professional musicians diagnosed to be affected by ULFD, afferent in the last 3 years to the "Sol Diesis" out patients clinic were clinically analyzed and video recorded by a multidisciplinary skilled team during musical performance and then treated with EMG-US guided incobotulinum toxinA injected in the dystonic muscles. Patients were asked to estimate their average playing ability before and after each toxin treatment using a VAS Performance Scale. Data were statistically analyzed using Student t test.

Results: 21 treatment sessions were performed in 14 musicians (mean age $43,9 \pm 14,54$; 13 males and 1 female, 11 professional player (3 violin, 6 guitar, 1 conductor, 1 accordion) and 3 professional teachers (3 guitars). No major side effect were reported (only one case of overshoot weakness after 1 session); inter-injection intervals were variable. Significant statistically improvement of the VAS performance scale after each session (21) was recorded ($p < .05$) with a mean value of VAS 5 ± 1.5 pre and 8 ± 1.9 post. 9 patients received one treatment, the others repeated sessions. 35 muscles were injected. Median efficacious dosage on single finger flexor muscle was 15.6 ± 7.2 U (dilution 1 ml saline).

Conclusions: Incobotulinum toxinA can be considered a safe and efficacious treatment in ULFD in particular involving finger flexors muscles, also at low dosage. EMG/US guide is very important for the muscle targeting and to limit side effects (i.e. weakness) with low interference with musicians's performace.

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Effectiveness of a combined treatment of cervical dystonia through a new rehabilitation approach in association with botulinum toxin

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Introduction: Cervical dystonia (CD) is a movement disorder, characterized by involuntary twisting movements or abnormal posture. Although botulinum toxin (BoNT) injections represent the gold standard treatment for CD, the efficacy can't be fully satisfactory. There are in the literature some data about the benefit of association of rehabilitation programs.

Aim: To evaluate the effectiveness on severity and quality of life of a multimodal treatment combining BoNT with SPRInt (Sensorimotor Perceptive Rehabilitation Integrated, Clinical trial.gov NCT03247868) approach based on motor learning techniques (bio-feedbacks) and spatial rehabilitation, compared to standard BoNT treatment.

Methods: 11 CD patients (48,6±8,4 yo) underwent a longitudinal 2 phases, 5 points clinical study, 6 months long. At T0 they received BoNT and then reviewed at 6/12 weeks later (T1 and T2). After the second injection at T2, SPRInt programme started (18 45-minutes sessions, three times a week) and patients were evaluated after 6/12 weeks (T3 and T4-follow up). At each time point a kinematic analysis of the cervical region (optoelectronic system BTS) and clinical scales (Toronto Western Spasmodic Torticollis Rating Scale TWSTRS, EuroQol 5D-5L) were performed. Statistics: Friedman ANOVA test ($p < 0.05$) and post hoc ($p > 1.89$) with Bonferroni.

Results: Longitudinal improvements were recorded in disability, severity and kinematics at rest, especially at T3, after SPRInt ($p < 0.02$) and partially maintained at follow up. Post hoc analysis revealed that the major gains were obtained at T3 in disability score ($p > 2.70$), severity ($p > 2.31$), and cervical deviation ($p > 2.27$), while pain scores changed at T1 and T3 ($p > 1.90$). Disability score improvement between T2 and T3 was maintained at follow up ($p > 2.22$).

Conclusions: SPRInt approach was effective in improving disability, severity and cervical deviation. At the contrary, BoNT alone was more efficacious on reducing pain. Further studies are necessary to gain more evidences of the rehabilitation role in CD treatment.

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Effective geste antagoniste in writer's cramp

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Introduction: Geste Antagoniste (GA) is a highly specific feature of dystonia [1], but its frequency depends upon the affected body district. In crania-cervical dystonia the prevalence of GA varies from 44% in OMD, 87% in blepharospasm and 89.6% in cervical dystonia. On the contrary, in arm dystonia the frequency is reported to be around 20% [2]. It has been suggested that variability in the frequency of GA might reflect pathophysiological differences among the various forms of focal dystonias.

Objective: To assess the prevalence of effective GA in a cohort of 29 patients with idiopathic adult onset Writer's Cramp (WC)

Methods: Twenty-nine right handed patients, affected by WC participated into the study. Each patient was asked to write a standard sentence twice, before and after GA (the patient was asked to gently grab his right wrist with his left hand). Overall legibility of the two sentences was compared by one blinded observer. Graphologic elements were also measured, including the length of the sentence and the height of the letter d [3].

Results: GA yielded a better comprehension of the written sentence in 13/29 patients (45%). Effective GA was also characterized by sentence shortening and reduction in letter height. There was no correlation between years of disease and the effectiveness of GA.

Conclusions: Our study shows that an effective GA may be present in about the 45% of patients with arm dystonia, (more than double than what observed in previous studies). GA also affected the assessed writing features (sentence length and letter height), therefore suggesting that the typical disgraphism in WC is probably a macrographia.

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Low expanded allele SCA17 mimics MSA-C imaging features: a case report and literature survey

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Introduction: Spinocerebellar ataxia 17 (SCA17) is a genetic cause of adult-onset ataxia caused by the expansion of CAG/CAA sequence in TBP gene. Subjects with range between 41 and 48 expansions may or may not develop symptoms, whereas a number of repeats higher than 49 is certainly pathological with full penetrance. Furthermore, clinical picture and MRI findings can vary greatly in SCA17. Although a specific correlation between number of repeats and phenotypic features has not yet been identified, literature suggests that low expanded alleles correlate clinically with parkinsonism.

Objectives: To evaluate a possible relationship between genotypic characteristics and phenotypic features in SCA17.

Methods: We report a case of SCA17 with low number of repeats and we review all reported cases with small expansions, highlighting brain MRI findings.

Results: A 53-year old woman presented with a two-years history of progressive postural and gait unsteadiness. Her neurological examination revealed gait ataxia, dysarthria, dysmetria and light multiple-domain cognitive deficits. On T2-weighted imaging, the “hot cross bun” sign, typically associated to Multisystem Atrophy-Cerebellar type (MSA-C), was evidenced. [123I]-FP-CIT-SPECT showed dopamine depletion, more pronounced in the putamen bilaterally. Molecular analysis of SCA genes detected 44 repeats in SCA 17-related gene. So far, three reported SCA17 patients, including ours, presented the “hot cross bun” sign [1,2]. All of them had low range of repeats. Finally, among patients with low expanded alleles, two of them showed dopaminergic deficit on [123I]-FP-CIT-SPECT [3].

Conclusions: First, our findings indicate that not only cerebellar pathways but even nigrostriatal system can be involved in SCA17. Secondly, SCA17 can mimic not only clinical features but also imaging characteristics of parkinsonism, especially MSA-C, when expansions are in a low range. We recommend to screen patients with cerebellar ataxia for SCA, even when neuro-imaging findings are suggestive of other neurodegenerative diseases, such as atypical parkinsonisms.

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