# ABSTRACTS

Società Italiana Parkinson e Disordini del Movimento/LIMPE-DISMOV ETS

# 9° Congresso


**PADOVA**
Padova Congress

**4 • 5 • 6**
**MAGGIO**

SOCIETÀ ITALIANA
PARKINSON
E DISORDINI DEL
MOVIMENTO
LIMPE-DISMOV
ETS

## Presidente del Congresso e del Comitato Scientifico

A. Antonini

## Comitato Scientifico

A. Albanese
G. Arabia
L. Avanzino
P. Barone
L. Bonanni
V. Bonifati
P. Calabresi
G. Calandra Buonaura
R. Ceravolo
C. Colosimo
G. Cossu
G. Defazio
A.B. Di Fonzo
R. Eleopra
G. Fabbrini
A. Fasano
M.C. Malaguti
P. Manganotti
R. Marconi
N. Modugno
F. Morgante
A. Nicoletti
A. Padovani
P. Parchi
L. Parnetti
A. Pisani
A. Priori
A. Quartarone
R. Quatrale
M.C. Romano
M. Sensi
A. Stefani
F. Stocchi
F. Tamma
A. Tessitore
M. Tinazzi
M. Zibetti

SOCIETÀ ITALIANA PARKINSON E DISORDINI DEL MOVIMENTO LIMPE-DISMOV ETS

## Consiglio Direttivo

M. Tinazzi
***Presidente***

G. Fabbrini
***Presidente Eletto***

M. Zappia
***Past-President***

A. Nicoletti
***Segretario***

M. Sensi
***Tesoriere***

***Consiglieri***
L. Avanzino
M. Bologna
M. Carecchio
G. Cossu
R. De Micco
R. Erro
M. Zibetti

# Indice generale



# Comunicazioni Libere

**C1**

## NGS genetic screening and phenotypic characterization of a selected PD population in North-East Italy, a correlation study

*Giulia Bonato*[1], M. Pilleri[2], S. Andretta[1], L. Lerjefors[1], M. Mainardi[1], F. Garrì[1], T. Carrer[1], P. Santurelli[1], D. Ciprietti[1], C. Fogliano[1], F. Baroni[1], F. Pistonesi[1], R. Biundo[1], M. Cassina[3], L. Salviati[3], A. Antonini[1], M. Carecchio[1]

[1]Movement Disorder Unit, Neurology Clinic, Neuroscience Department, University of Padua, Padua, Italy
[2]IRCCS Villa Margherita, Vicenza, Italy
[3]Clinical Genetics Unit, Department of Women and Children's Health, University of Padua, Padua, Italy

*Introduction:* 15% of Parkinson's disease cases are familial, 5-10% are monogenic. Over 30 PD-related loci, risk factors and many uncertain genes have been described since NGS advent.

*Objective:* Screening a PD cohort from North-East Italy by NGS; identifying possible genotype-phenotype correlations and prognostic genetic implications; validating potential selection criteria to optimize diagnostic yield.

*Methods:* 178 PD patients underwent clinical examination and genetic testing (NGS sequencing on Illumina NextSeq550 platform, panel of >80 genes related to movement disorders) between 2017 and 2022 based on either: 1) onset <55 years of age; 2) positive family history; 3) atypical disease course.

*Results:* 86/178 (48%) patients were carriers of at least one variant; 107 variants were found in 31 genes, 48% were pathogenic and 34% were Variants of Unknown Significance (VUS). A diagnosis of monogenic PD was formulated in 35 patients (20%), whereas it remained uncertain in 17% (mainly monoallelic variants in recessive genes and VUS in CSMD1). The most frequent pathogenetic variants were found in GBA (60%), LRRK2 (26%) and PARK2 (8%). The selection criterion "age of onset <55" was a significant predictor of positive test outcome (p 0.034). Monogenic PD patients had earlier onset (mean age 46 vs 52, p 0.03), higher incidence of dyskinesias (71% vs 36%, p 0.0006). GBA patients represent 11.8% of the cohort (mainly N370S); they showed faster disease course and higher complications burden (dyskinesias OR 3.5, sleep disturbances OR 6.55, cognitive disorders OR 4, dysautonomia; p <0.05). Visuospatial and executive domains were more affected.

*Conclusions:* the use of simple selection criteria allows to increase the probability of identifying patients with monogenic PD, with possible future implications for disease-modifying strategies. Our data confirm that GBA mutations are the most frequent genetic risk factor for PD in Italy and lead to a more severe motor and non-motor disease phenotype.

**C2**

## Prediction of falls in Parkinson's disease through machine learning algorithms: evidence from the NeuroArt-P3 project

*Maria Chiara Malaguti*[1]*, C. Longo[1]*, F. Forzanini[2]*, M. Pellegrini[1], R. Bacchin[1], M. Riello[1], B. Giometto[1,4,5], D. Ottaviani[3], R. Di Giacopo[3], P. D'Antonio[3], L. Gios[2], M. Marenco[6], L. Avanzino[6,8], R. Marchese[6], F. Di Biasio[6], F.M. Nobili[6], A. Uccelli[6], M. Piana[7], M. Pardini[6,9], M. Moroni[2], G. Jurman[2], V. Osmani[2]

[*]*These Authors have contributed equally to this work and share first authorship*

[1]Department of Neurology, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[2]Digital Health Centre, Fondazione Bruno Kessler Research Institute, Trento, Italy
[3]Department of Neurology, Santa Maria del Carmine Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Rovereto, Italy
[4]University of Trento, Trento, Italy
[5]University of Trieste, Trieste, Italy
[6]IRCCS San Martino Polyclinic Hospital, Genoa, Italy
[7]LISCOMPlab, University of Genoa, Genoa, Italy
[8]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[9]Department of Neuroscience (DINOGMI), University of Genoa, Genoa, Italy

*Introduction:* The NeuroArtP3 (NET-2018-12366666) is a multicenter project co-funded by the Italian Ministry of Health, involving clinical and computational centres to identify variables as predictors of the disease trajectories in neurodegenerative diseases, including Parkinson's disease (PD). The course of PD is influenced by many variables, among which falls have a great impact [1]. Therefore, understanding which variables could predict the risk of falls could have a significant impact.

*Objectives:* To identify patterns of clinical variables as predictors of fall risk in PD patients through Machine Learning (ML) algorithms.

*Methods:* Demographic, motor, clinical, and pharmacological data of 265 PD patients followed at Movement Disorder Clinic in Trento, Rovereto and Genoa were retrospectively collected at four intervals: baseline, after 12, 24, and 36 months. Outcome variable was the incidence of falls after the baseline, in the next 3 years. We externally evaluated two models based on Logistic Regression (LR) and Random Forest (RF). 175 patients were used to derive the machine learning model, while the other 90 patients were used to evaluate the predictive performance of the model, using the Area Under the Receiver Operating Characteristic (AUC) curve.

*Results:* External evaluation of the model yielded AUC of 0.81 for the RF model and AUC of 0.76 for the LR model in prediction falls in the following three years. Variable saliency analysis of the RF model showed that the top five most predictive variables were the falls at the baseline, H&Y scale, cognitive status, depression and disease duration. Freezing of gait was the sixth most predictive variable.

*Conclusions:* Our work has shown that ML can be used to predict the risk of falls of PD patients in the next three years. Consistently with the objectives of the NeuroArt-P3, these results may allow the clinician to personalize the treatment for the prevention of falls.

**References:**

[1] Fasano A., Canning C.G., Hausdorff J.M., Lord S., Rochester L. (2017). Falls in Parkinson's disease: A complex and evolving picture. Mov. Disord. 32:1524–1536. DOI: 10.1002/mds.27195.

**C3**

## The course of orthostatic hypotension after deep brain stimulation in Parkinson's disease

*Ilaria Cani*[1], G. Giannini[1,2], P. Guaraldi[2], G. Barletta[2], P. Cortelli[1,2], G.C. Buonaura[1,2]

[1]Department of Biomedical and NeuroMotor Sciences (DIBINEM), Alma Mater Studiorum - University of Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

*Introduction:* Orthostatic hypotension (OH) is a crucial feature of advanced Parkinson's disease (PD), possibly related to autonomic failure and levodopa treatment (LD). The course of OH after deep brain stimulation (DBS) and variations in LD dosage is overlooked.

*Objective:* Clinical and instrumental evaluation of OH before and after subthalamic nucleus DBS surgery.

*Methods:* Autonomic functions were evaluated before and 6-months after surgery, through self-reported questionnaires (SCOPA-AUT, COMPASS 31) and cardiovascular reflex tests (RCV). Head-up tilt test (HUTT) was carried out before and 60 minutes after the administration of the first morning dose of levodopa.

*Results:* Fifty-two patients underwent COMPASS 31 and SCOPA-AUT questionnaires before and after DBS surgery (age=61[54-66] years, disease duration=10.5[8-15] years). Score at post-DBS evaluation did not differ compared to pre-DBS(COMPASS 31: 16[8-23] vs 17[11-30], SCOPA-AUT: 17[11-21] vs 14[11-18]).
Ten patients underwent RCV before and after DBS in pre-LD and post-LD conditions.
At pre-DBS, OH was detected in 1 out 10 patients during pre-LD HUTT and 4 out 10 patients at post-LD HUTT. The drop of systolic blood pressure (SBP) during post-LD HUTT was significantly greater compared to pre-LD HUTT (-3[-15-7]mmHg vs -15[-27- -6]mmHg, p=0.038).
After DBS surgery, OH was present in 1 patient at pre-LD HUTT and 2 patients at post-LD HUTT. Similarly to pre-DBS study, SBP drop during post-LD HUTT was greater than pre-LD (-6[-11-10]mmHg vs -12[-19- -8]mmHg, p=0.019). BP and HR changes at pre-LD HUTT and post-LD HUTT did not differ between pre-DBS and post-DBS evaluation.
Occurrence of OH did not correlate with the LD dose or variation in LD dosage after DBS.
OH is associated to an absent overshoot at Valsalva Maneuver.

*Conclusion:* Incidence of OH is similar before and after DBS surgery resulting from multiple factors. The role of levodopa is unclear but it seems to induce OH in patients with underlying autonomic disfunction both before and after DBS.

## C4

### Relations between sex hormones and high-density EEG functional connectivity in Parkinson's disease

*Matteo Conti*[1], R. Bovenzi[1], C. Simonetta[1], V. Ferrari[1], R. Cerroni[1], N.B. Mercuri[2], M. Pierantozzi[1], T. Schirinzi[1], A. Stefani[1]

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

*Introduction:* Sex-specific differences in epidemiology and clinical manifestations of Parkinson's disease (PD) has suggested that hormones might contribute to the clinical-pathological spectrum of the disease [1]. The study of functional connectivity (FC) through different techniques allowed us improving the understanding of the PD pathophysiology. While some sex-related differences in brain connectivity has been already observed with functional neuroimaging, [2] there are no data based on EEG. Likewise, the association between sex hormones and brain FC has never been evaluated in PD patients.

*Objective:* To investigate the association between sex and sex hormones on cortical FC alterations in PD, by means of high-density EEG.

*Methods:* 34 early-stage PD patients (18/16 male/female) and 19 age-matched healthy controls (HC) (10/9 male/female) were included in the study. Sex hormone levels (total-testosterone, estradiol, follicle-stimulating hormone (FSH) and luteinizing hormone (LH)) were quantified in PD patients blood. Data were recorded with a 64-channels EEG system. Source reconstruction method was used to identify brain regions activity. We analysed cortico-cortical FC, based on weighted phase-lag index (wPLI) [3], in three bands (θ-α-β). Network-based statistic (NBS) was used to compare FC between HC, PD males and female, and to study relationship between FC and sex hormones.

*Results:* PD exhibited a significantly disrupted network at α band ($t=2.8$, $p=0.002$). PD males compared to PD females showed an impaired FC network at α-band ($t=2.5$, $p=0.036$), mainly composed by frontal and sensorimotor regions. Regarding the hormonal pattern, in PD males the estradiol directly correlated with mean connectivity at α-band ($r=0.90$, $p=0.0002$), while in PD females FSH negatively correlated with mean FC at α-band ($r=-0.78$, $p=0.021$).

*Conclusion:* Our results revealed the presence of direct relationships between brain FC and sex hormones in both male and females PD, supporting their influence on PD pathophysiology and the subsequent potential role as therapeutic targets.

**References:**

[1] J. C. Jurado-Coronel, R. Cabezas, M. F. Ávila Rodríguez, V. Echeverria, L. M. García-Segura, and G. E. Barreto, "Sex differences in Parkinson's disease: Features on clinical symptoms, treatment outcome, sexual hormones and genetics," Frontiers in Neuroendocrinology. 2018, doi: 10.1016/j.yfrne.2017.09.002.
[2] R. De Micco et al., "Sex-related pattern of intrinsic brain connectivity in drug-naïve Parkinson's disease patients," Mov. Disord., vol. 34, no. 7, 2019, doi: 10.1002/mds.27725.
[3] T. M. Lau, J. T. Gwin, K. G. McDowell, and D. P. Ferris, "Weighted phase lag index stability as an artifact resistant measure to detect cognitive EEG activity during locomotion," J. Neuroeng. Rehabil., vol. 9, no. 1, 2012, doi: 10.1186/1743-0003-9-47.

## C5

### Oligomeric α-synuclein and tau aggregates in NDEVs differentiate Parkinson's disease from atypical parkinsonisms

*Mario Meloni*[1], C. Agliardi[1], F.R. Guerini[1], M. Zanzottera[1], E. Bolognesi[1], S. Picciolini[1], M. Marano[2], A. Magliozzi[2], A.B. Di Fonzo[3], A. Arighi[3], C. Fenoglio[4], G. Franco[3], F. Arienti[3], F.L. Saibene[1], J.S. Navarro[1], M. Clerici[1,4]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Via Capecelatro, 66, 20148, Milan, Italy
[2]Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine, Fondazione Policlinico Campus Bio-Medico, Rome, Italy
[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[4]Department of Pathophysiology and Transplantation, University of Milan, 20122 Milan, Italy

*Introduction:* The early differential diagnosis of Parkinson's disease (PD) and atypical Parkinsonian syndromes (APS), including corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP), is challenging because of an overlap of clinical features and the lack of reliable biomarkers. Neural-derived extracellular vesicles (NDEVs) isolated from blood provide a window into the brain's biochemistry [1-2].

*Objective:* To determine whether the NDEVs oligomeric α-Synuclein and aggregated Tau content can discriminate between PD and APS.

*Methods:* Blood sampling and clinical data, including disease duration, motor severity, global cognition, and levodopa equivalent daily dose (LEDD) were collected from patients with a diagnosis of either PD (n = 70), PSP (n = 21), or CBD (n = 19). NDEVs were isolated from serum by immunocapture using an antibody against the neuronal surface marker L1CAM; oligomeric α-Synuclein and aggregated Tau were measured by ELISA.

*Results:* NDEVs analyses showed that oligomeric α-Synuclein is significantly augmented in PD compared to APS, whereas Tau aggregates are significantly increased in APS compared to PD ($p < 0.0001$). ROC analyses showed that these two biomarkers have a "good" power of classification ($p < 0.0001$ for both proteins), with high sensitivity and specificity, with NDEVs concentration of Tau aggregates and oligomeric α-Synuclein being respectively the best biomarker for PD/PSP and PD/CBD diagnostic differentiation.
Logistic and multiple regression analysis confirmed that NDEVs-derived oligomeric α-Synuclein and Tau ag- gregates differentiate PD from CBD and PSP ($p < 0.001$). Notably, a positive correlation between NDEVs oligomeric α-Synuclein and disease severity (disease duration, $p = 0.023$; Modified H&Y, $p = 0.015$; UPDRS motor scores, $p = 0.004$) was found in PD patients.

*Conclusions:* A minimally invasive blood test measuring the concentration of α-synuclein and Tau aggregates in NDEVs can represent a promising tool to distinguish with high sensitivity and specificity PD from CBD or PSP patients.

**References:**

[1] Agliardi, C., Meloni, M., Guerini, F.R., Zanzottera, M., Bolognesi, E., Baglio, F., Clerici, M., 2021. Oligomeric α-Syn and SNARE complex proteins in peripheral extracellular vesicles of neural origin are biomarkers for Parkinson's disease. Neurobiol. Dis. 148, 105185.
[2] Shi, M., Liu, C., Cook, T.J., Bullock, K.M., Zhao, Y., Ginghina, C., Li, Y., Aro, P., Dator, R., He, C., Hipp, M.J., Zabetian, C.P., Peskind, E.R., Hu, S.C., Quinn, J.F., Galasko, D.R., Banks, W.A., Zhang, J., 2014. Plasma exosomal α-synuclein is likely CNS-derived and increased in Parkinson's disease. Acta Neuropathol. 128 (5), 639–650.

## C6

### Impact of cardiovascular risk factors on clinical features of idiopathic adult-onset dystonia

*Marcello Mario Mascia*[1], A.F. Gigante[2], R. Erro[3], D. Belvisi[4,5], M. Esposito[6], A. Trinchillo[7], G. De Joanna[6], R. Ceravolo[8,9], S. Mazzucchi[8,9], E. Unti[8,9], P. Barone[3], S. Scannapieco[3], M.S. Cotelli[10], M. Turla[10], M. Bianchi[10], L. Bertolasi[11], A. Pisani[12,13], F. Valentino[13], M.C. Altavista[14], V. Moschella[14], P. Girlanda[15], C. Terranova[15], F. Bono[16], G. Spano[16], G. Fabbrini[4,5], G. Ferrazzano[5], A. Albanese[17], A. Castagna[18], D. Cassano[19], M. Coletti Moja[20], R. Pellicciari[21], A.R. Bentivoglio[22,23], R. Eleopra[24], G. Cossu[25], T. Ercoli[1], F. Di Biasio[26], S. Misceo[2], L. Magistrelli[27], M.C. Romano[28], C.L. Scaglione[29], M. Tinazzi[30], L. Maderna[31], M. Zibetti[32,33], A. Berardelli[4,5], G. Defazio[21]

[1] University Hospital of Cagliari, Cagliari, Italy
[2] Section of Neurology, San Paolo Hospital, Bari, Italy
[3] Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[4] IRCCS Neuromed, Pozzilli, Italy
[5] Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[6] Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[7] Department of Neurosciences, Reproductive Sciences and Odontostomatology, “Federico II” University, Naples, Italy
[8] Parkinson and Movement Disorders Centre, Neurology Unit Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[9] Clinical and Experimental Medicine University of Pisa, Pisa, Italy
[10] Neurology Unit, ASST Valcamonica, Esine, Italy
[11] Neurology Unit, University Hospital, Verona, Italy
[12] Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[13] IRCCS Mondino Foundation, Pavia, Italy
[14] Neurology Unit, San Filippo Neri Hospital, ASL Roma 1, Rome, Italy
[15] Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[16] Center for Botulinum Toxin Therapy, Neurology Unit, A.O.U. Mater domini, Catanzaro, Italy
[17] Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[18] IRCCS Fondazione Don Carlo Gnocchi Onlus, Milan, Italy
[19] Unit of Neurology, Ospedale Maria Vittoria, Turin, Italy
[20] Departmentt of Neurology, Ospedale degli Infermi, Ponderano, Biella, Italy
[21] Department of Translational Biomedicine and Neuroscience (DiBraiN), University of Bari 'Aldo Moro', Bari, Italy
[22] Agostino Gemelli IRCCS University Hospital Foundation, Rome, Italy
[23] Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[24] Neurology Unit 1, Fondazione IRCSS, Istituto Neurologico "Carlo Besta", Milan, Italy
[25] Neurology Service and Stroke Unit, Department of Neuroscience, AO Brotzu, Cagliari, Italy
[26] Ospedale Policlinico San Martino IRCCS, Genoa, Italy
[27] Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[28] Neurology Unit, Villa Sofia Hospital, Palermo, Italy
[29] IRCCS Institute of Neurological Sciences, Ospedale Bellaria, Bologna, Italy
[30] Neurology Unit, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy
[31] Department of Neuroscience, U.O. of Neurophysiology, IRCCS Istituto Auxologico Italiano, Milan, Italy
[32] Department of Neuroscience “Rita Levi Montalcini”, University of Torino, Torino, Italy
[33] Neurology 2 Unit, A.O.U. Città Della Salute e Della Scienza di Torino, Torino, Italy

*Introduction:* Acquired dystonia may occur secondary to brain insults of different pathologies including ischaemic and haemorrhagic stroke [1]. However, if brain damage secondary to cerebrovascular disease may affect clinical features and evolution of idiopathic dystonia is still undefined.

*Objective:* To investigate the impact of cardiovascular risk factors (CVRFs) on clinical features of adult-onset idiopathic dystonia (AOID).

*Methods:* Data were obtained from the Italian Dystonia Registry (IDR). Patients with a diagnosis of AOID were stratified into two group according to the presence/absence of CVRFs and compared for the following clinical and demographic variables: age, disease duration, family history for dystonia, dystonia distribution, dystonia phenotypes, and dystonia associated features [sensory trick, ocular symptoms associated with blepharospasm (BSP), pain associated with cervical dystonia (CD) and tremor].The spread of dystonia to an additional body site was also estimated.

*Results:* A total of 1108 patients were included in the study. Since there were no CVRFs reported in the IDR in patients aged less than 40, comparison between groups was performed only in those aged 40 or more (1076 patients). Patients with CVRFs (555 patients) had a higher age (74.7 ± 9.8 vs 64.3 ± 12.2) and a longer disease duration (17.5 ± 10.6 vs 16.1 ± 9.5). BSP and sensory trick were significantly more frequent (54,1% vs 28,4%; 42,3 vs 35,7 respectively) while CD, task-specific upper limb dystonia and lower limb dystonia less frequent (45,4% vs 60,7%; 3,2% vs 11,1%; 1,8 vs 3,6% respectively) in patients with CVRFs. The two groups were similar for the other variables examined.

*Conclusions:* Results of the present study showed that CVRFs may impact clinical features of dystonia in patients with AOID. The association between CVRFs and cerebrovascular lesions [2,3] may suggest that cerebrovascular disease may play a role in the clinical expression of idiopathic dystonia.

**References:**

[1] Albanese A, Bhatia K, Bressman SB, Delong MR, Fahn S, Fung VS, Hallett M, Jankovic J, Jinnah HA, Klein C, Lang AE, Mink JW, Teller JK. Phenomenology and classification of dystonia: a consensus update. Mov Disord. 2013 Jun 15;28(7):863-73. doi: 10.1002/mds.25475. Epub 2013 May 6.

[2] Vermeer SE, Tom Den Heijer, Peter J Koudstaal, Matthijs Oudkerk, Albert Hofman, Monique M B Breteler, Rotterdam Scan Study. Incidence and risk factors of silent brain infarcts in the population-based Rotterdam Scan Study. 2003 Feb;34(2):392-6. doi:10.1161/01.str.0000052631.98405.15.

[3] Anand SS, Jack V Tu, Dipika Desai, Phillip Awadalla, Paula Robson, Sébastien Jacquemont , Trevor Dummer, Nhu Le, Louise Parker, Paul Poirier, Koon Teo, Scott A Lear, Salim Yusuf, Jean-Claude Tardif, Francois Marcotte, David Busseuil, Jean-Pierre Després, Sandra E Black, Anish Kirpalani, Grace Parraga, Michael D Noseworthy, Alexander Dick, Jonathan Leipsic, David Kelton, Jennifer Vena, Melissa Thomas, Karleen M Schulze, Eric Larose, Alan R Moody, Eric E Smith, Matthias G Friedrich. Cardiovascular risk scoring and magnetic resonance imaging detected subclinical cerebrovascular disease. Eur Heart J Cardiovasc Imaging 2020 Jun 1;21(6):692-700. doi: 10.1093/ehjci/jez226.

**C7**

## Pervasive and diffuse muscle activity during REM and NREM sleep differentiates multiple system atrophy and Parkinson's disease

*Luca Baldelli*[1], A. Silvani[1], G. Giannini[1,2], P. Guaraldi[2], L. Sambati[2], A. Cecere[2], F. Mignani[2], P. Cortelli[1,2], G. Calandra Buonaura[1,2], F. Provini[1,2]

[1]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

*Introduction:* Multiple system atrophy (MSA) and Parkinson's disease (PD) may share overlapping features particularly at early disease stage, including sleep alteration, but have profoundly different prognoses. Certain sleep phenomena and disorders of motor control are more prevalent in MSA, such as prominent motor dyscontrol during sleep and REM sleep behavior disorder (RBD). Tonic electromyographic (EMG) activity of submentalis and tibialis anterior muscles has been reported as common in subjects with MSA compared to those with obstructive sleep apneas, although without quantitative confirmation [1]. We applied a novel automatic EMG analysis technique [2] (DNE: PMID 28329117) to investigate whether pervasive muscle activity during non-REM sleep and REM sleep occurred in different muscles in subjects with MSA vs. PD.

*Methods:* Laboratory polysomnographic studies were performed in 50 consecutive subjects with PD and 26 age- and gender-matched subjects with MSA at <5 years from disease onset. The DNE analysis focused on submentalis and on bilateral wrist extensor and tibialis anterior muscles in different wake-sleep states during the night.

*Results:* Subjects with MSA had significantly higher activity of submentalis, wrist extensor, and tibialis anterior muscles than subjects with PD during non-REM sleep, including separately in stages N1, N2, and N3, and during REM sleep, but not during nocturnal wakefulness. DNE indexes of EMG activity of wrist extensor and tibialis anterior muscles during non-REM sleep were significantly higher in subjects with MSA and RBD than in those with PD with RBD.

*Conclusions:* With respect to PD, MSA is characterized by a pervasive and diffuse muscle overactivity that involves axial and limb muscles and occurs not only during REM sleep, but also during non-REM sleep and between patients with comorbid RBD. In perspective, targeted studies with test and validation cohorts are needed to test whether submentalis and/or limb muscle activity during non-REM sleep and REM sleep is a useful prognostic or diagnostic biomarker for MSA.

**References:**

[1] Vetrugno R, et al. Sleep disorders in multiple system atrophy: A correlative video-polysomnographic study. Sleep Med 2004;5:21–30.
[2] Silvani A, et al. Muscle activity during sleep in human subjects, rats, and mice: Towards translational models of REM sleep without atonia. Sleep 2017;40: zsx029.

**C8**

## Deep brain stimulation treating dystonia: data from Italian Dystonia Registry

*Denise Cerne*[1], F. Di Biasio[2], R. Eleopra[3], M. Golfrè Andreasi[3], A.R. Bentivoglio[4], M. Petracca[4], M. Esposito[5], A. Castagna[6], R. Erro[7], M. Zibetti[8], F. Bono[9], M. Tinazzi[10], N. Modugno[11], R. Pellicciari[12], L. Bertolasi[13], G. Fabbrini [4,11], M.C. Romano[15], L. Magistrelli[16], A. Albanese[17], P. Girlanda[18], F. Morgante [18,19], R. Marchese[2], L. Avanzino[2,20], G. Defazio[21]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[2]IRCCS, Ospedale Policlinico San Martino, Genoa, Italy
[3]SC Neurologia 1, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Movement Disorders Unit, Center for Parkinson's Disease and Extrapyramidal Disorders, Institute of Neurology, Catholic University, Rome, Italy
[5]Department of Neurosciences, Reproductive Science and Dentistry, Federico II University of Naples, Naples, Italy
[6]IRCCS, Fondazione Don Carlo Gnocchi, Milan, Italy
[7]Center for Neurodegenerative Diseases (CEMAND), Neuroscience Section, University of Salerno, Salerno, Italy
[8]Department of Neuroscience 'Rita Levi Montalcini', University of Turin, Turin, Italy
[9]Center for Botulin Toxin Therapy, Neurologic Unit A.O.U. Mater Domini, Catanzaro, Italy
[10]Neurologic Unit, Department of Neuroscience, University Hospital, University of Verona, Verona, Italy
[11]IRCSS Neuromed, Pozzilli, (IS), Italy
[12]Department of Basic Science, Neuroscience and Sense Organs, Aldo Moro University of Bari, Bari, Italy
[13]Department of Neurological, Neuropsychological, Morphological and Movement Sciences, University of Verona, Italy
[14]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[15]Neurology Unit AOOR Villa Sofia Cervello, Palermo, Italy
[16]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[17]Department of Neurology, IRCCS Istituto Clinico Humanitas, Rozzano, Milano, Italy
[18]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[19]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[20]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy
[21]Dipartimento di Biomedicina Traslazionale e Neuroscienze, Univesità degli Studi di Bari "Aldo Moro", Bari, Italy

*Introduction:* Mounting evidence indicates that deep brain stimulation (DBS) is an effective treatment in dystonic patients [1]. More controversial is the best target in relation to the phenotype and the influence of genetic etiology in DBS outcome [2-3].

*Objective:* To evaluate the clinical features of the dystonic patients with DBS recruited in the Italian Dystonia Registry (IDR) [4], with particular attention to the target and genetic test.

*Methods:* We retrospectively analyzed data from the IDR, selecting demographic data, year of onset, associated features, etiology coded according to the revised classification of dystonia [5].

*Results:* We identified 77/2324 (3%) with DBS (43 females, 34 males). Mean age at onset was 31.73 y ± 22.94. 29/77 (38%) had generalized dystonia; 31/77 (40%) had multifocal/segmental dystonia; 15/77 (19%) had focal dystonia, and 2/77 (3%) had emidystonia. 47/77 (61%) patients had idiopathic dystonia, 9/77 (12%) had positive genetic test, 2/77 (3%) had iatrogenic dystonia, 6/77 (8%) had symptoms of parkinsonism, 3/77 (4%) head trauma and 9/77 (12%) other neurological conditions. Mean age at surgery was 43.29y. Mere years of waiting before DBS was 14.84y. DBS target was GPi in 69/77 (90%), STN in 4/77 (5%) and Vim in 4/77 (5%). Genetic testing was performed in 31/77 (40%). Only 9/31 (29%) of them had positive genetic test. Tremor was present in 21/77 (27%) patients. Related to Vim, 4/4 (100%) had tremor. Pain was present in 40/77 (52%).

*Conclusions:* A small percentage of patients from the IDR underwent DBS. Genetic testing was performed in 40% of patients. The most selected target was GPi (90%), while only 5% of patients underwent Vim DBS. These results support the hypothesis that more methodical genetic testing should be done prior to DBS. Furthermore, a more accurate selection of the DBS target in relation to phenotype is needed.

**References:**

[1] Kim HJ, Jeon B. Arching deep brain stimulation in dystonia types. J Neural Transm (Vienna). 2021 Apr;128(4):539-547.

[2] Paoli D, Mills R, Brechany U, Pavese N, Nicholson C. DBS in tremor with dystonia: VIM, GPi or both? A review of the literature and considerations from a single-center experience. J Neurol. 2023 Jan 21.

[3] Jinnah HA, Alterman R, Klein C, Krauss JK, Moro E, Vidailhet M, Raike R. Deep brain stimulation for dystonia: a novel perspective on the value of genetic testing. J Neural Transm (Vienna). 2017 Apr;124(4):417-430.

[4] Defazio, G. and Berardelli, A. (2021), Is Adult-Onset Dystonia a Rare Disease? Time for Population-Based Studies. Mov Disord, 36: 1119-1124.

[5] Albanese A, Bhatia K, Bressman SB, Delong MR, Fahn S, Fung VS, Hallett M, Jankovic J, Jinnah HA, Klein C, Lang AE, Mink JW, Teller JK. Phenomenology and classification of dystonia: a consensus update. Mov Disord. 2013 Jun 15;28(7):863-73.

**C9**

## Assessing smell performance in essential tremor plus patients

*Maria Russo*, C. Sorrentino, M. Picillo, A. Landolfi, M.T. Pellecchia, P. Barone, R. Erro

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

*Introduction:* Essential tremor (ET) plus is a heterogeneous syndrome of bilateral upper limb action tremor with either rest tremor or soft signs, which has been suggested to represent a prodromal stage of Parkinson disease (PD) in some cases. Hyposmia is a prodromal symptom of PD, which can be detected with the University of Pennsylvania Smell Identification Test (UPSIT).

*Objective:* To evaluate smell performance in ET plus with rest tremor.

*Methods:* ET plus patients with rest tremor were evaluated with an 8-item Italian version of the UPSIT. Results were compared with both PD patients and healthy subjects (HS). Analysis of Variance (ANOVA) was performed to compare the 8-item UPSIT scores between the three groups using SPSS software, version 26.0.

*Results:* The study sample consisted of 25 ET plus patients, 68 PD patients and 61 HS. The three groups were homogeneous in terms of age (71.0 ± 10.0 vs. 61.9 ± 8.9 vs. 59.6 ± 8.6, ET plus, PD and HS, respectively, $p = 0.20$) and sex distribution (men/women: 68%/32% vs. 60.3%/39.7% vs. 44.3%/55.7%, ET plus, PD and HS, respectively, $p = 0.07$). Twenty ET plus patients exceeded the proposed cut-off (i.e., $\leq 6$) for pathological smell performance. The mean UPSIT score was significantly different between the groups [$F(2, 153) = 65.12$; $p < 0.05$]. Post-hoc analyses demonstrated the mean UPSIT score in ET plus patients was significantly different from both PD (4.9 ± 1.5 vs 3.4 ± 1.8, $p<0.05$) and HS (4.9 ± 1.5 vs 6.7 ± 1.5, $p<0.05$).

*Conclusions:* Hyposmia appears to be common in ET plus with rest tremor, although it is milder than PD; its presence might hint at the possibility of neurodegenerative process underlying some cases of ET plus.

**C10**

## Muscle synergies during gait in Parkinson's disease

*Alessandro Zampogna*[1], M. Patera[1], F. Castelli Gattinara Di Zubiena[2], G. Cusolito[3], V. Laudanna[2], M. Paoloni[3], E. Palermo[2], A. Suppa[1,4]

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

*Introduction:* Gait disorders are a major cause of morbidity and mortality in Parkinson's disease (PD), involving continuous and episodic disturbances associated with abnormal activation of individual muscles. Still, it is unclear whether also muscle synergies (i.e., groups of synchronously-activated muscles, variably combined to produce complex movements) are impaired during gait [1-3].

*Objective:* To investigate muscle synergies during gait and their relationship with L-Dopa in PD.

*Methods:* Fifteen PD patients (OFF and ON therapy) and 10 healthy subjects (HS) were monitored through inertial and electromyography (EMG) wearable systems while walking on a 20-m straight path. Eight IMUs were used to reconstruct joint angles and the gait cycle. Muscle synergies were extracted from the surface EMG of 11 muscles of the dominant lower limb by a non-negative matrix factorization method. The "Variance Accounted For" (VAF) (i.e., the correlation coefficient between measured and reconstructed EMG signals) was analysed to examine the variability amount of recorded data explained by extracted synergies.

*Results:* Patients showed a similar number and composition of muscle synergies to HS, irrespective of the state of therapy. Four synergies were associated with a VAF >90% in both patients and HS. L-Dopa did not change the number and composition of muscle synergies in PD but increased the VAF, in line with improved gait in patients ON compared to OFF therapy. Despite similar composition of synergies, the amplitude peaks of involved muscles were different in patients and HS and only partially responsive to L-Dopa.

*Conclusions:* The number and internal structure of muscle synergies during gait are normal in PD, suggesting preserved lower-level central generators. Dysfunctional higher-level centres, including basal ganglia and cortical motor areas, may be responsible for abnormal modulation of muscle synergies. The limited effects of L-Dopa on muscle synergies support the contribution of non-dopaminergic pathways in the pathophysiology of gait disorders in PD.

**References:**

[1] D'Avella et al., 2003. Nat. Neurosci. 6, 300–308.
[2] Bizzi et al., 2008. Brain Res Rev. 57:125-33.
[3] Mileti et al., 2020. Sensors (Basel) 20(11):3209.

## C11

### RFC1 pathological expansion screening in late onset ataxia patients

*Nunzia Cuomo*[1], M. Barghigiani[2], G. De Michele[1], A. Tessa[2], T. Fico[1], G. Natale[2], F. Saccà[1], C. Pane[1], A. De Rosa[1], S. Pappatà[3], G. De Michele[1], F.M. Santorelli[2], A. Filla[1]

[1]Department of Neurosciences Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2]Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Fondazione Stella Maris, Pisa, Italy
[3]Institute of Biostructure and Bioimaging (IBB), Consiglio Nazionale delle Ricerche (CNR), Naples, Italy

*Introduction:* CANVAS (Cerebellar Ataxia, Neuropathy Vestibular Areflexia Syndrome) or RFC1-ataxia is a rare, adult onset disorder, due to a biallelic intronic AAGGG expansion in the Replication Factor C subunit 1 (RFC1) gene [1]. The first description reported an AAGGG pathogenic expansion ranging from 400 to more than 2000 repeats (AAGGG400-2000), but later smaller expansions (AAGGG100-160) have also been described [2].

*Objective:* We tested a cohort of late onset ataxia patients to define the prevalence of RFC1 pathogenic expansion.

*Methods:* Sixty-two Italian patients with late-onset ataxia (34 M; mean age at onset ± SD 56.8 ± 8.8 years; range 38–80), observed at the Neurological Unit of the Federico II University, were screened for AAGGG pentanucleotide expansion in RFC1 gene. The clinical diagnoses at first visit were MSA-C in 44 patients and Sporadic Adult Onset Ataxia in 18 patients. Genomic DNA from peripheral blood leukocytes (150 ng/µl) were tested by standard PCR and repeat-primed PCR (RP-PCR) to identify patients with the biallelic AAGGG expansion associated with CANVAS.

*Results:* Among the 62 investigated patients, we found nine (14,5%) of them – six in the SAOA group and three in the MSA-C group - harboring a homozygous AAGGG expansion in RFC1.

*Conclusions:* Genetic testing for RFC1 expansions associated with CANVAS is highly recommended in Late Onset Ataxia patients.

**References:**

[1] Cortese A, Simone R, Sullivan R, Vandrovcova J, Tariq H, Yau WY, Humphrey J, Jaunmuktane Z, Sivakumar P, Polke J, Ilyas M, Tribollet E, Tomaselli PJ, Devigili G, Callegari I, Versino M, Salpietro V, Efthymiou S, Kaski D, Wood NW, Andrade NS, Buglo E, Rebelo A, Rossor AM, Bronstein A, Fratta P, Marques WJ, Züchner S, Reilly MM, Houlden H (2019) Biallelic expansion of an intronic repeat in RFC1 is a common cause of late onset ataxia. Nat Genet 51:649–658.
[2] Cortese A, Reilly MM, Houlden H (2021) RFC1 CANVAS/spectrum disorder. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Mirzaa G, Amemiya A (eds) GeneReviews ® [Internet].University of Washington, Seattle

## C12

**Identification of pre-frailty in the elderly through serum metabolomics and its impact on Parkinson's disease phenotype**

*Alberto Imarisio*[1], M. Avenali[2,3], G. Buongarzone[2], M. Picascia[3], T. Nuzzo[4], C. Gasparri[5], F. Errico[4,6], C. Marino[7], M. Grimaldi[7], M.C. Monti[8], A. Filosa[8], M. Rondanelli[3,9], C. Pacchetti[3], A.M. D'Ursi[7], A. Usiello[4], E.M. Valente[1,3]

[1]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]IRCCS Mondino Foundation, Pavia, Italy
[4]Laboratory of Translational Neuroscience, Ceinge Biotecnologie Avanzate, Naples, Italy
[5]Endocrinology and Nutrition Unit, Azienda di Servizi alla Persona "Istituto Santa Margherita", University of Pavia, Pavia, Italy
[6]Department of Agricultural Sciences, University of Naples "Federico II", Portici, Naples, Italy
[7]Department of Pharmacy, University of Salerno, Fisciano, Salerno, Italy
[8]Unit of Biostatistics and Clinical Epidemiology, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy
[9]Unit of Human and Clinical Nutrition, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy

*Introduction:* Pre-frailty is a potentially reversible condition increasingly common with aging. However, whether it represents a continuum between healthy and frail status or a well-defined clinical entity is still unclear.

*Objective:* We attempted to better characterize pre-frailty using serum metabolomics in a large cohort of elderly subjects without neurodegenerative diseases. Next, we sought to investigate the impact of concurrent pre-frailty on elderly subjects with Parkinson's disease (PD).

*Methods:* We recruited 96 elderly non-PD subjects and classified them as non-frail, pre-frail, and frail based on Fried criteria. Untargeted metabolomics was carried out using Nuclear Magnetic Resonance (1H-NMR) on serum samples. Partial least-squares discriminant analysis and Pathway enrichment analysis were used to identify metabolites and biochemical pathways discriminating the three groups. Next, 83 mild-stage PD patients underwent Fried classification and assessment of motor and non-motor domains, ADL and QoL.

*Results:* Serum metabolomics identified three distinct clusters for non-frail (n=39), pre-frail (n=20), and frail (n=37) non-PD, with pre-frails showing the most evident separation from other groups. Multivariate analyses revealed L-Serine, Betaine, and Histidine as the most discriminating molecules. Pathway analysis pointed to dysregulation of amino acid metabolism, first of all, Serine-Glycine ($p<0.001$). In PD, pre-frail (n=25) patients showed intermediate levels of motor, ADL, QoL, and psychiatric impairment compared to both non-frail (n=45) and frail (n=13) subgroups (all FWER-adjusted $p<0.05$).

*Conclusions:* We identify L-Serine pathway dysregulation as a distinctive signature of pre-frailty in the elderly. In PD, pre-frailty status significantly affects both clinical phenotype and QoL, representing a potentially modifiable factor to be targeted with specific interventions.

## C13

### The contribution of small vessel disease to clinical phenotype in progressive supranuclear palsy

*Maria Francesca Tepedino*[1], F. Diana[2], F. Abate[1], A.R. Avallone[1], M. Caterino[1], R. Erro[1], M.T. Pellecchia[1], P. Barone[1], R. Manara[3], M. Picillo[1]

[1]Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Salerno, Italy
[2]Department of Neuroradiology, Azienda Ospedaliera Universitaria San Giovanni di Dio e Ruggi d'Aragona, University of Salerno, Salerno, Italy
[3]Neuroradiology Unit, Department of Neurosciences, University of Padua, Padua, Italy

*Introduction:* Severe leukoencephalopathy represents an exclusion criterion for the diagnosis of idiopathic Progressive Supranuclear Palsy (PSP). However, it is not surprising to detect different degrees of white matter hyperintensities (WMH) in PSP patients. The contribution of small vessel disease (SVD) to the clinical phenotype and severity in PSP has not been explored yet.

*Objectives:* Aims of the study were to investigate the contribute of SVD detected with brain MRI on clinical motor, cognitive and behavioral aspects of PSP.

*Methods:* Sixty-seven subjects with idiopathic PSP were enrolled between May 2016 and July 2022 at the University of Salerno. Demographic, clinical, motor, cognitive, behavioral performances and brain MRI were collected. Age-related white matter change (ARWMC) of each lobe and total score were computed according to published methods [1]. Comparisons between groups were performed with t-test or $\chi 2$ as needed and correlation analysis with Spearman's rho.

*Results:* Sixty patients were included in the analysis. Twenty presented no ARWMC (-), while forty presented any ARWMC score>0 (+). ARWMC were more prevalent in frontal (90% right and 95% left) and parietal (52,5% bilaterally) lobes. No clinical and demographic differences were found between abovementioned group, except for greater duration of disease in ARWMC (p=0. 045). There was a positive correlation between ARWMC total score and PSP rating scale (PSP-rs) (p=0.002) and MDS-UPDRS-III total score (p=0.008). PSP-rs total score was also related with frontal right (p=0.003) and left (p=0.001), parietal right (p=0.008) and temporal right (p=0.014) ARWMC scores. MDS-UPDRS-III total score was also related with frontal right (p=0.014) and left (p=0.024), parietal right (p=0.031) and temporal right (p=0.001) ARWMC scores. No correlations were found between ARWMC scores and cognitive or behavioral performances.

*Conclusions:* We suggest SVD may contribute to the severity of motor symptoms but not to cognitive or behavioral disturbances in PSP patients.

**References:**

[1] LO Wahlund, F Barkhof, F Fazekas, L Bronge, M Augustin, M Sjögren, A Wallin, H Ader, D Leys, L Pantoni, F Pasquier, T Erkinjuntti, P Scheltens. A new rating scale for age-related white matter changes applicable to MRI and CT (2001). Stroke. 32(6):1318–1322.

**C14**

## Long-term motor symptoms improvement in advanced Parkinson's disease by switching DBS polarity in case of off-targeting

*Giulia Saccardin*[1,2], G. Di Rauso[1,2], S. Coniglio[1,2], G. Argenziano[1,2], F. Cavallieri[3], A. Puzzolante[4], R. Stanzani[4], A. Feletti[5], F. Antonelli[2], V. Fioravanti[3], G. Pavesi[4], S. Meletti[1,2], F. Valzania[3], V. Rispoli[2]

[1]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[4]Neurosurgery, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[5]Institute of Neurosurgery, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona - AOUI Verona, Verona, Italy

*Background:* Off-targeting in deep brain stimulation (DBS) dramatically narrowed the therapeutic window, due to the recruitment of surrounding structures.

*Objectives:* To describe the long-term benefit on motor symptoms of switching DBS polarity in a case of lead off-targeting in Parkinson's disease.

*Methods:* A 56 y.o. man, affected by young-onset Parkinson's disease with troublesome dyskinesias and severe fluctuations, underwent bilateral STN-DBS with directional leads. The monopolar review disclosed a very restricted therapeutic window (TW) for the left lead, because of facio-brachial tonic spam occurrence. Indeed, conventional stimulation setting, namely monopolar (even directional) and bipolar stimulation, did not avoid these side effects. So, a patient-specific post-operative neuroimaging processing was performed together with setting of advanced programming options.

*Results:* The post-operative reconstruction of the left lead demonstrated that it laid within the corticospinal tract laterally to the subthalamic nucleus. Advanced programming with low frequency, low pulse width, current steering longitudinally or perpendicularly to the lead did not allow significant TW enlargement. By contrast, the switch to anodic stimulation significantly reduced the corticospinal tract engagement compared to cathodic stimulation. After more than 24 months of follow-up, an extremely meaningful difference between OFF-medication/ON-DBS and OFF-medication/OFF-DBS persists.

*Conclusions:* This report may foster further investigations in anodic stimulation as an additional programming option in the neurologist's armamentarium, especially in case of non-optimal lead placement.

## C15

### Predictors of speech worsening after subthalamic stimulation in Parkinson disease

*Francesco Cavallieri*[1], F. Bove[2], A. Zampogna[3], A. Castrioto[4], S. Meoni[4], A. Gessani[5], E. Schmitt[4], A. Bichon[4], E. Lhommée[4], P. Pélissier[4], A. Kistner[4], E. Chevrier[4], F. Valzania[1], E. Seigneuret[6], S. Pinto[7], S. Chabardès[6], V. Fraix[4], E. Moro[4]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[4]Grenoble Alpes University, Division of Neurology, Centre Hospitalier Universitaire of Grenoble, Grenoble Institute of Neuroscience, Grenoble, France
[5]Neurology Unit, Department of Neuroscience, S. Agostino Estense Hospital, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[6]Division of Neurosurgery, Centre Hospitalier Universitaire (CHU) Grenoble Alpes, Grenoble, France
[7]Aix-Marseille Univ, CRNS, LPL, Aix-en-Provence, France

*Introduction:* In patients with advanced Parkinson disease (PD), deep brain stimulation of the subthalamic nucleus (STN-DBS) is a well- recognized effective treatment in both short- and long-term follow-up. However, the impact of STN-DBS on speech can vary, and possible worsening of speech intelligibility can counterbalance the benefits of STN-DBS.

*Objective:* To identify preoperative predictive factors of postoperative speech worsening in a large cohort of consecutive PD patients with bilateral STN-DBS.

*Methods:* All consecutive PD patients who underwent bilateral STN-DBS at the Grenoble University Hospital (France) from 1993 to 2015 were evaluated before surgery and at 1-year follow-up after surgery. Demographic variables, neuroimaging data and clinical characteristics were retrospectively collected. Predictors of postoperative speech worsening were assessed with univariate and multivariate logistic regression analyses. Speech poor outcome was defined as a worsening of speech subscore (UPDRS item 18; MDS-UPDRS item 3.1) in the postoperative on-stimulation/off-medication condition compared with the preoperative defined-off condition.

*Results:* 324 PD patients (males: 196; disease duration at surgery: 11.10 [±4.13] years; age at surgery: 56.25 [±8.52] years) were included in the analysis. From this cohort, 22.50% of the patients (73/324) presented a worsening of speech one year after surgery. A lower preoperative speech subscore in the off-medication condition and a lower degree of motor improvement after surgery predicted the postoperative worsening of speech.

*Conclusions:* The severity of speech impairment in the preoperative off-medication condition and the degree of motor improvement after surgery represented the main preoperative predictors of speech worsening after STN-DBS in our cohort. These results may give a better understanding of PD features associated with postoperative speech worsening after surgery, also allowing to implement, in necessary, early speech interventions after surgery in patients at higher risk of speech deterioration.

## C16

### Identification of candidate Parkinson's disease predisposition genes in high-risk pedigrees

*Paolo Moretti*[1], J. Stevens[1], K. Allen-Brady[1], A. Dotti[2], K. Figueroa[1], S. Pulst[1], L. Cannon-Albright[1]

[1]University of Utah, USA
[2]Midwestern University, USA

*Introduction:* Monogenic forms and genetic risk factors for Parkinson's disease (PD) have been previously identified, but together they explain only a fraction of familial and sporadic PD. High-risk pedigree studies offer a powerful method for identification of genetic variants affecting predisposition to PD.

*Objective:* To identify rare genetic variants associated with increased risk of PD in multi-generation, high-risk pedigrees.

*Methods:* We performed whole exome sequencing (WES) on previously sampled PD-affected relatives belonging to pedigrees exhibiting a statistically significant excess of PD. We identified pedigrees with high-risk of PD using the Utah Population Database (UPDB), a resource linking extensive genealogy information with medical record and other public health data sources. PD cases were identified by PD listed as a cause of death on death certificates. Sequencing results were compared to results in the PD DNA Variant Browser.

*Results:* We identified 2,357 clusters/pedigrees that included from 2 to 43 sampled individuals with PD-related deaths. From this group, we selected 379 high-risk clusters with 2-37 PD cases and significant excess of PD among pedigree members ($p<0.05$). We then selected 25/379 pedigrees with a significant excess of PD cases and at least one pair of cousins with DNA samples available. WES and bioinformatics analysis of the PD-affected cousin pairs from each high-risk pedigree identified 242 rare, shared variants in 221 genes. Of these, 16 genes showed significant association with PD risk in the PD DNA Variant Browser.

*Conclusions:* WES in pairs of related sampled PD cases from high-risk pedigrees led to the identification of shared DNA variants in 221 genes, 16 of which were identified in previous studies. Validation studies of some of these candidate PD predisposition variants in these families are currently underway.

## C17

### Olfactory neurons Substance P is overexpressed in Parkinson's disease and reflects gut dysfunction

*Tommaso Schirinzi*[1], D. Maftei[3], P. Grillo[1,2], R. Bovenzi[1], H. Zenuni[1], C. Simonetta[1], J. Bissacco[1], D. Mascioli[1], F.M. Passali[4], S. Di Girolamo[4], A. Stefani[1], R. Lattanzi[3], C. Severini[5], N.B. Mercuri[1]

[1]Unit of Neurology, Department of Systems Medicine, Tor Vergata University of Rome, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Department of Physiology and Pharmacology "V. Erspamer", Sapienza University of Rome, Rome, Italy
[4]Unit of ENT, Department of Clinical Sciences and Translational Medicine, Tor Vergata University of Rome, Rome, Italy
[5]Department of Biochemistry and Cell Biology, National Research Council of Italy, Rome, Italy

*Introduction:* Substance P is a neuropeptide whose expression in the gastrointestinal-nervous ascending pathway rises in response to various noxious stimuli. In Parkinson's disease (PD), Substance P might contribute to disease pathogenesis by mediating detrimental neuroinflammatory events, although direct proof is still lacking. Olfactory neurons can mirror central neuropathology, enabling the analysis of molecular processes implicated in the clinical-pathological progression of PD in vivo.

*Objective:* To understand the role of Substance P in PD through a molecular characterization of patients' olfactory neurons.

*Methods:* 30 patients and 20 sex/age-matched healthy controls underwent olfactory neuron withdrawal by the mucosa brushing. Gene expression levels of Substance P and its cognate receptor NK1 were comparatively measured by the Real Time-PCR. In addition, Substance P was quantified by immunofluorescence staining. Patients were evaluated by standard motor and non-motor scales, grouped per the presence of constipation, and specifically assessed with the Gastrointestinal Dysfunction Scale for Parkinson's Disease (GIDS-PD). Clinical parameters were correlated with biochemical data.

*Results:* In PD, olfactory neurons Substance P expression was significantly increased compared to controls. The expression levels directly correlated with the GIDS-PD score, also being higher in patients with constipation. Conversely, NK1 receptor levels did not differ between patients and controls.

*Conclusions:* The overexpression of Substance P within the olfactory neurons in association to gastrointestinal dysfunction suggests a main role for the tachykinergic system in PD. Specifically, Substance P might mediate the neuroinflammation in the "body-first" pathogenic trajectory, contributing to neurodegeneration. Substance P thus emerges as a novel target in PD either for biomarker or therapeutic purposes, with a peculiar specificity for the "body-first" subtype.

## C18

**Deep brain stimulation of GPi and STN stimulation in Parkinson's disease: a multicenter, retrospective study of efficacy and safety**

*Michele Mainardi*[1], D. Ciprietti[1], M. Pilleri[3], G. Bonato[1], L. Weis[1], V. Cianci[1], R. Biundo[2,1], F. Ferreri[1], M. Piacentino[4], A. Landi[5], A. Antonini[1]

[1]Parkinson and Movement Disorders Unit, Study Center for Neurodegeneration (CESNE), Department of Neuroscience, University of Padua, Padua, Italy
[2]Department of General Psychology, University of Padua, Padua, Italy
[3]Service of Neurology, Villa Margherita-Santo Stefano Private Hospital, Arcugnano, Italy
[4]Department of Neurosurgery, AULSS 8 Berica Ospedale San Bortolo, Vicenza, Italy
[5]Academic Neurosurgery, Department of Neurosciences, University of Padova, Padova, Italy

*Background*: Deep Brain Stimulation (DBS) is an established therapeutic option in advanced Parkinson's disease. Literature data and recent guidelines are controversial about efficacy of two well established targets Globus Pallidus internus (GPi) and Subthalamic Nucleus (STN) and our study aims at providing additional evidence by comparing retrospectively clinical outcome in two cohorts of PD who had DBS at two referral institutions in the Veneto region.

*Methods*: We retrospectively reviewed outcome of 48 DBS-implanted patients (33 STN and 15 GPi at two time points: short-term (within 1 years from surgery) and long-term (2-5years). We performed a genetic screening using an NGS panel for PD genes in patients with early onset and/or positive family history for dementia or PD. Concerning safety outcomes we considered the frequencies of 1) post-operative surgical complications such as infections, brain lesions, ischemic strokes or hemorrhages; 2) onset of severe side effects due to stimulation, such as suicide acts or other psychiatric disorders (e.g. delusions, ICD). We didn't collect the mild site effects related to stimulation (such as transient sensory problems or speech disorders).

*Results*: We found that motor and non-motor outcome was almost equivalent between GPi and STN treated PD but only in the STN-DBS cohort oral therapy doses were reduced. Genetic testing performed in 29 patients showed presence of mutation or variants in 11 cases (38%). We observed severe adverse events in 5 cases all among STN-DBS patients including 2 suicides, one in a PD carrying a GBA mutation.

*Conclusion*s: DBS is an effective treatment option for advanced Parkinson's disease. Both GPi and STN stimulation are effective in improving motor scales, but only STN stimulation resulted in significant oral therapy reduction. These results suggest that GPi and STN should be considered as equivalent in motor efficacy although the occurrence of two suicides in STN-treated patients deserves attention in target selection.

## C19

### Dystonic tremor as main manifestation of a large SCA21 family

*Vidal Yahya*[1], E. Monfrini[1], E. Moro[3], A.B. Di Fonzo[2]

[1]Dino Ferrari Center, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[3]Grenoble Alpes University, Division of Neurology, CHU of Grenoble, Grenoble Institute of Neurosciences, Grenoble, France

*Introduction:* Spinocerebellar ataxia 21 (SCA21) is a slowly progressive early-onset autosomal dominant cerebellar ataxia variably combined with cognitive impairment, parkinsonism, dystonia, and myoclonus. Pathogenic variants in the *TMEM240* gene are the cause of SCA21. Around 60 cases of TMEM240-related disease were reported to date, with the P170L variant recurring in several families with independent origin and different clinical phenotype: the most common manifestations are ataxia and cognitive impairment though in some cases dystonia has been reported as presenting feature. [1-10]

*Objective:* To identify the genetic cause of disease in a French family with multiple members affected by autosomal dominant dystonic tremor.

*Methods:* Seven subjects were clinically evaluated by neurologists with additional training in movement disorders and a whole-exome sequencing (WES) was performed.

*Results:* Six subjects, four female and two male, belonging to three consecutive generations, presented an autosomal dominant tremulous dystonia with disease onset at 4-6 years. They displayed dystonic tremor of upper and lower limbs, neck, and head, as well as writer's cramp and foot dystonia. Additional neurological signs interested some subjects including minimal dysmetria at finger-nose test, action tremor, bradykinesia, saccade impairment, dysphagia, autism spectrum disorder, and learning disability. All of them presented the recurrent P170L *TMEM240* variant at WES and at Sanger sequencing confirmation. All instrumental examinations including brain MRI, DaTscan, and EMG resulted normal. One additional subject complained hand tremor by the age of 12 years without dystonia nor ataxia. The *TMEM240* pathogenic variant was not present in this subject, thus she likely represents a phenocopy.

*Conclusions:* This work expands the clinical spectrum of *TMEM240*-related disease, including dystonic tremor as a main clinical presentation.

**References:**

[1] Delplanque, J. et al. TMEM240 mutations cause spinocerebellar ataxia 21 with mental retardation and severe cognitive impairment. Brain 137, 2657–2663 (2014).
[2] Ward, J. M. & la Spada, A. R. Identification of the SCA21 disease gene: remaining challenges and promising opportunities. Brain 137, 2626–2628 (2014).
[3] Zeng, S. et al. Spinocerebellar ataxia type 21 exists in the Chinese Han population. Sci Rep 6, 3–6 (2016).
[4] Yahikozawa, H. et al. A Japanese Family of Spinocerebellar Ataxia Type 21: Clinical and Neuropathological Studies. Cerebellum 17, 525–530 (2018).
[5] Traschütz, A. et al. The movement disorder spectrum of SCA21 (ATX-TMEM240): 3 novel families and systematic review of the literature. Parkinsonism Relat Disord 62, 215–220 (2019).
[6] Burdekin, E. D. et al. The Neurodevelopmental and Motor Phenotype of SCA21 (ATX-TMEM240). J Child Neurol 35, 953–962 (2020).
[7] Camargo, C. H. F., Piva-Silva, A. K. C., Munhoz, R. P., Raskin, S. & Teive, H. A. G. Spinocerebellar ataxia type 21 (TMEM240) with tremor and dystonia. Eur J Neurol 28, e63–e64 (2021).

[8] Cherian, A., Divya, K. P., Vijayaraghavan, A. & Krishnan, S. Pearls & Oy-sters: SCA21 Due to TMEM240 Variation Presenting as Myoclonus Dystonia Syndrome. Neurology 99, 531–534 (2022).
[9] Van der Put, J. et al. On Spinocerebellar Ataxia 21 as a Mimicker of Cerebral Palsy. Neurol Genet 8, 1–5 (2022).
[10] Park, D. G., Kim, M. S. & Yoon, J. H. The First Korean Family of Spinocerebellar Ataxia 21 (ATX-TMEM240) with Facial Dystonic Phenotype. Cerebellum 21, 6–8 (2022).

## C20

### Short-term plasticity of the motor cortex compensates for bradykinesia in Parkinson's disease

*Giulia Paparella*[1], A. Guerra[1,2], D. Colella[2], A. Cannavacciuolo[1], M. Giangrosso[2], G. Fabbrini[1,2], A. Berardelli[1,2], M. Bologna[1,2]

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

*Introduction:* Patients with Parkinson's disease (PD) show impaired short-term potentiation (STP) mechanisms in the primary motor cortex (M1) [1-4]. However, the role played by this neurophysiological abnormality in bradykinesia pathophysiology is unknown [2].

*Objectives:* In this study, we used a multimodal neuromodulation approach to test whether defective STP contributes to bradykinesia.

*Methods:* We evaluated STP by measuring motor-evoked potential facilitation during 5 Hz-repetitive transcranial magnetic stimulation (rTMS) [4] and assessed repetitive finger tapping movements through kinematic techniques [1, 3]. Also, we used transcranial alternating current stimulation (tACS) to drive M1 oscillations and experimentally modulate bradykinesia [3]. STP was assessed during tACS delivered at beta (β) and gamma (γ) frequency, and during sham-tACS [3]. Data were compared to those recorded in a group of healthy subjects.

*Results:* In PD, we found that STP was impaired during sham- and γ-tACS, while it was restored during β-tACS. Importantly, the degree of STP impairment was associated with the severity of movement slowness and amplitude reduction. Moreover, β-tACS-related improvements in STP were linked to changes in movement slowness and intracortical GABA-A-ergic inhibition during stimulation, as assessed by short-interval intracortical inhibition (SICI). Patients with prominent STP amelioration had greater SICI reduction (cortical disinhibition) and less slowness worsening during β-tACS. Dopaminergic medications did not modify β-tACS effects.

*Conclusions:* These data demonstrate that abnormal STP processes are involved in bradykinesia pathophysiology and return to normal levels when β oscillations increase. STP changes are likely mediated by modifications in GABA-A-ergic intracortical circuits and may represent compensatory mechanism against β-induced bradykinesia in PD.

**References:**

[1] Bologna M, Guerra A, Paparella G, et al. Neurophysiological correlates of bradykinesia in Parkinson's disease. Brain 2018;141(8):2432–2444.
[2] Bologna M, Paparella G, Fasano A, et al. Evolving concepts on bradykinesia. Brain 2020;143(3):727–750.
[3] Guerra A, Colella D, Giangrosso M, et al. Driving motor cortex oscillations modulates bradykinesia in Parkinson's disease. Brain 2022;145(1):224–236.
[4] Gilio F, Currà A, Inghilleri M, et al. Repetitive magnetic stimulation of cortical motor areas in Parkinson's disease: Implications for the pathophysiology of cortical function: Cortical Stimulation in Parkinson's Disease. Movement Disorders 2002;17(3):467–473.

**C21**

## Predictors of clinical response to MRgFUS VIM thalamotomy for treatment of tremor in a cohort of patients with Parkinson's disease and essential tremor: a 6-months perspective study

*Arianna Braccia*[1], N. Golfrè Andreasi[1], R. Cilia[1], L.M. Romito[1], A.E. Elia[1], V. Levi[2], G. Devigili[1], S. Rinaldo[1], E.F.M. Ciceri[3], M.G. Bruzzone[4], F. Ghielmetti[5], M. Fusar Poli[6], S. Prioni[6], P. Amami [6], S.H.M.J. Piacentini [6], M. Grisoli[4], M. Stanziano[4], R. Eleopra[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[2]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neurosurgery Department, Functional Neurosurgery Unit, Milan, Italy
[3]Fondazione IRCCS Istituto Neurologico Carlo Besta, Diagnostic Radiology and Interventional Neuroradiology, Milan, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neuroradiology Unit, Milan, Italy
[5]Fondazione IRCCS Istituto Neurologico Carlo Besta, Health Department, Milan, Italy
[6]Fondazione IRCCS Istituto Neurologico Carlo Besta, Clinical Neuropsychology Unit, Milan, Italy

*Introduction:* Unilateral VIM thalamotomy by Magnetic Resonance-guided Focal Ultrasound (MRgFUS) is a safe and effective treatment of tremor in Parkinson's disease (PD) and essential tremor (ET). Predictive factors of outcome are still debated.

*Objectives:* To investigate the role of clinico-demographic, procedural and neuroradiological variables in influencing tremor improvement by MRgFUS thalamotomy in a cohort of 118 patients with PD or ET.

*Methods:* We prospectively evaluated consecutive patients diagnosed with either PD or ET who underwent unilateral Vim thalamotomy by MRgFUS from January 2019 to August 2022, including n=66 patients with ET and 52 patients with P. Baseline and 6 months-follow up data included clinico-demographics (age, gender, disease duration and severity, skull density ratio), intra-procedural variables (n. of sonications, energy delivered, medium and maximum temperature reached at target) and neuroradiological characteristics of the lesion (position towards the intercommissural AC-PC line, calculated on the axial images). Disease severity and improvement were assessed using the TETRAS in ET and the MDS-UPDRS-III. For PD patients, we studied separately the effect of MRgFUS thalamotomy on action tremor and rest tremor.

*Results:* We found greater action tremor improvement in PD than ET. Younger age was a predictor of better outcome in ET patients but not in PD. Evaluating lesion's position towards AC-PC line on the axial plane, we established a significantly more anterior lesion's location in PD group.

*Conclusions:* Predictors of response to MRgFUS Vim thalamotomy could be distinct between ET and PD patients. Further research on others possible predictors is necessary to elucidate this field.

## C22

**Associations between sex hormones, clinical features and multimodal biomarkers in male patients with Parkinson's disease**

*Roberta Bovenzi*[1], G.M. Sancesario[2], M. Conti[1], P. Grillo[1], J. Bissacco[1], S. Minosse[3], M. Pierantozzi[1], A. Stefani[1,5], N.B. Mercuri[1,2], F. Di Giuliano[4], T. Schirinzi[1]

[1]Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]IRCCS Fondazione Santa Lucia, European Centre for Brain Research, Rome, Italy
[3]Department of Biomedicine and Prevention, University of Rome "Tor Vergata", Rome, Italy
[4]Neuroradiology Unit, Deparment of Biomedicine and Prevention, University of Rome "Tor Vergata", Rome, Italy
[5]UOSD Parkinson Centre, Tor Vergata University Hospital, Rome, Italy

*Introduction:* Epidemiology, clinical and pathophysiological features of Parkinson's disease (PD) differ between females and males, suggesting that hormonal factors are key-determinants of the disease [1-2]. However, human-based evidence is scarce.

*Objective:* To deepen into sex-dependent mechanisms of PD by analyzing the relationships between sex hormones, clinical features and multimodal biomarkers in a cohort of male PD patients.

*Methods:* We enrolled 63 male PD patients and 56 age-matched controls afferent to the Neurology Unit of Tor Vergata University Hospital (Rome - Italy). For each patient, comprehensive clinical evaluation, including motor, non-motor and cognitive scores was coupled to lumbar puncture for CSF biomarkers assay and blood sampling for sex hormones measurement. CSF levels of total α-synuclein (αSyn), amyloid-β-42 (Aβ42), amyloid-β-40 (Aβ40), total tau (t-tau) and phosphorylated-181-p tau (p-tau) were quantified. Aβ42/p-tau, Aβ42/Aβ40 ratios were also calculated. Serum total testosterone, estradiol, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were determined. 47 PD patients underwent 3T brain MRI for volumetric measurement of bilateral subcortical gray matter structures using a 3D T1-weighted MPRAGE sequence.

*Results:* Estradiol and testosterone levels were higher in PD patients than in controls, independently from age ($p=0.001$ and $p=0.003$, respectively). Estradiol inversely correlated with MDS-UPDRS-III ($p=0.006$) and with disease duration ($p=0.015$). Estradiol was significantly lower in patients with motor fluctuations (MDS-UPDRS IV >1, 17.33 ± 11.33 pg/ml) than in those without (27.9 ± 13.6) ($p=0.016$). Testosterone was inversely associated with α-syn CSF ($p=0.03$) and Right-Palladium volume ($p=0.024$). FSH and LH had a direct correlation with age (both $p<0.0001$) and an inverse correlation with Aβ42/Aβ40 ratio and cognitive scores, which were lost in the model adjusted for age.

*Conclusions:* This study provided evidence regarding the relationship within sex hormones and both clinical features and biomarkers of disease severity, laying the foundations for a possible therapeutic role in PD.

**References:**

[1] S. Cerri, L. Mus, F. Blandini, Parkinson's Disease in Women and Men: What's the Difference?, Journal of Parkinson's Disease. (2019). https://doi.org/10.3233/JPD-191683.
[2] K. Kompoliti, Estrogen and Parkinson's disease, Frontiers in Bioscience. (2003). https://doi.org/10.2741/1070.

**C23**

## Effects of probiotics on clinical symptoms and peripheral cytokines levels in Parkinson's disease: a pilot randomized placebo-controlled study

*Luca Magistrelli*[1], E. Contaldi[2,3], F. Leo[1], F. Vignaroli[1], F. Colombatto[1], A. Amoruso[4], M. Pane[4], L. Mogna[4], R. Cantello[1], C. Comi[5]

[1]Department of Translational Medicine, Section of Neurology, University of Piemonte Orientale and "Maggiore della Carità" University Hospital, Novara, Italy
[2]Parkinson Institute Milan, ASST-Pini-CTO, Milan, Italy
[3]PhD Program in Medical Sciences and Biotechnology, University of Piemonte Orientale, Novara, Italy
[4]Biolab Research Srl, Research and Development, Novara, Italy
[5]Neurology Unit, S. Andrea Hospital, Department of Translational Medicine, University of Piemonte Orientale, Vercelli, Italy

*Introduction:* Peripheral inflammation plays an important role in the pathophysiology of Parkinson's disease (PD) and may be involved in the development of both motor and non-motor symptoms, therefore representing a suitable therapeutic target. Preliminary in vitro studies demonstrated the immunomodulating properties of probiotics. The aim of this study is to evaluate the impact of probiotics on clinical symptoms and peripheral cytokines in a group of PD patients compared to placebo.

*Methods:* Patients were enrolled and blindly randomized to receive active probiotics (composed by Bifidobacterium animalis subsp. lactis BS01, Bifidobacterium longum 03, Bifidobacterium adolescentis BA02, Fructo-oligosaccharides and Maltodextrin) or placebo. Clinical evaluations (motor, non-motor and cognitive profile) were performed at enrolment, after 6 and 12 weeks. Plasmatic levels of cytokines (TNF-α, IFN-γ, IL17, IL10, IL4, IL6 and TGFβ) were also assessed. Anti-parkinsonian therapy was stable during the study.

*Results:* 40 PD patients were recruited (20 for each group, which did not differ for clinical and demographic data). After 12 weeks, the "active" group had a significant improvement of motor (UPDRS III: 13,89±4,08 vs 12,74±4,57, p = 0,028) and non-motor symptoms (NMSS: 34,32±21,41 vs 30,11±19,89, p = 0,041), particularly in the gastrointestinal subitem (3,79±4,14 vs 1,89±2,54, p = 0,021). Furthermore, a significant reduction of pro-inflammatory cytokines levels (IFN-γ and IL6) was detected in the active group (respectively $p<0.001$ and $p=0.002$).

*Conclusions:* Though preliminary, our data demonstrate that probiotics may modulate peripheral cytokines levels and improve clinical symptoms. Probiotics may therefore constitute an important add-on therapy to conventional anti-parkinsonian drugs.

**C24**

## Phenotypic variability in acquired and idiopathic dystonia

*Angelo Fabio Gigante*[1], R. Erro[2], D. Belvisi[3,4], M. Esposito[5], A. Trinchillo[6], G. De Joanna[5], R. Ceravolo[7,8], S. Mazzucchi[7,8], E. Unti[7,8], P. Barone[2], S. Scannapieco[2], M.S. Cotelli[9], M. Turla[9], M. Bianchi[9], L. Bertolasi[10], A. Pisani[11,12], F. Valentino[12], M.C. Altavista[13], V. Moschella[13], P. Girlanda[14], C. Terranova[14], F. Bono[15], G. Spano[15], G. Fabbrini[3,4], G. Ferrazzano[4], A. Albanese[16], A. Castagna[17], D. Cassano[18], M. Coletti Moja[19], R. Pellicciari[20], A.R. Bentivoglio[21,22], R. Eleopra[23], G. Cossu[24], T. Ercoli[25], M.M. Mascia[25], F. Di Biasio[26], S. Misceo[1], L. Magistrelli[27], M.C. Romano[28], C.L. Scaglione[29], M. Tinazzi[30], L. Maderna[31], M. Zibetti[32,33], A. Berardelli[3,4], G. Defazio[25]

[1]Section of Neurology, San Paolo Hospital, Bari, Italy
[2]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[3]IRCCS Neuromed, Pozzilli, Italy
[4]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[5]Clinical Neurophysiology Unit, Cardarelli Hospital, Naples, Italy
[6]Department of Neurosciences, Reproductive Sciences and Odontostomatology, “Federico II” University, Naples, Italy
[7]Parkinson and Movement Disorders Centre, Neurology Unit Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[8]Clinical and Experimental Medicine University of Pisa, Pisa, Italy
[9]Neurology Unit, ASST Valcamonica, Esine, Italy
[10]Neurology Unit, University Hospital, Verona, Italy
[11]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[12]IRCCS Mondino Foundation, Pavia, Italy
[13]Neurology Unit, San Filippo Neri Hospital, ASL Roma 1, Rome, Italy
[14]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[15]Center for Botulinum Toxin Therapy, Neurology Unit, A.O.U. Mater Domini, Catanzaro, Italy
[16]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[17]IRCCS Fondazione Don Carlo Gnocchi Onlus, Milan, Italy
[18]Unit of Neurology, Ospedale Maria Vittoria, Turin, Italy
[19]Departmentt of Neurology, Ospedale degli Infermi, Ponderano, Biella, Italy
[20]Department of Basic Medical Sciences, Neurosciences and Sense Organs, University of Bari “Aldo Moro”, Bari, Italy
[21]Agostino Gemelli IRCCS University Hospital Foundation, Rome, Italy
[22]Institute of Neurology, Università Cattolica del Sacro Cuore, Rome, Italy
[23]Neurology Unit 1, Fondazione IRCSS, Istituto Neurologico "Carlo Besta", Milan, Italy
[24]Neurology Service and Stroke Unit, Department of Neuroscience, AO Brotzu, Cagliari, Italy
[25]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari Italy
[26]Ospedale Policlinico San Martino IRCCS, Genoa, Italy
[27]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[28]Neurology Unit, Villa Sofia Hospital, Palermo, Italy
[29]IRCCS Institute of Neurological Sciences, Ospedale Bellaria, Bologna, Italy
[30]Neurology Unit, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy
[31]Department of Neuroscience, U.O. of Neurophysiology, IRCCS Istituto Auxologico Italiano, Milan, Italy
[32]Department of Neuroscience “Rita Levi Montalcini”, University of Torino, Torino, Italy
[33]Neurology 2 Unit, A.O.U. Città Della Salute e Della Scienza di Torino, Torino, Italy

*Background:* Differences in the clinical spectrum between acquired and idiopathic forms of dystonia have never been investigated [1-2-3].

*Objectives:* To compare demographic data and clinical features in patients with adult-onset acquired and idiopathic dystonias. We also compared these two groups with patients with dystonia combined with sporadic parkinsonism.

*Methods:* Patients were identified from among those included in the Italian Dystonia Registry, a multicenter Italian dataset of patients with adult-onset dystonia. Study population included 116 patients with adult-onset acquired dystonia, 651 patients with isolated adult-onset idiopathic dystonia, and 101 patients with sporadic parkinsonism.

*Results:* Comparison of acquired and idiopathic dystonia revealed differences in the body distribution of dystonia, with oromandibular dystonia, limb and trunk dystonia being more frequent in patients with acquired dystonia. The acquired dystonia group was also characterized by lower age at dystonia onset, greater tendency to spread, lower frequency of head tremor, sensory trick and eye symptoms, and similar frequency of neck pain associated with CD and family history of dystonia/tremor. Patients with sporadic parkinsonism were more similar to the acquired than idiopathic dystonia group for most phenomenological features.

*Conclusions:* The clinical phenomenology of dystonia may differ between acquired and idiopathic dystonia, particularly with regard to the body localization of dystonia and the tendency to spread. This dissimilarity raises the possibility of pathophysiological differences between etiologic categories [2-3]. The occurrence of family history of dystonia in a proportion of patients with acquired dystonia would support a genetic predisposition, as it has been hypothesized in idiopathic dystonia.

**References:**

[1] Albanese A, Bhatia K, Bressman SB, Delong MR, Fahn S, Fung VS, Hallett M, Jankovic J, Jinnah HA, Klein C, Lang AE, Mink JW, Teller JK. Phenomenology and classification of dystonia: a consensus update. Mov Disord. 2013 Jun 15;28(7):863-73. doi: 10.1002/mds.25475. Epub 2013 May 6. PMID: 23649720; PMCID: PMC3729880.

[2] Neychev VK, Gross RE, Lehéricy S, Hess EJ, Jinnah HA. The functional neuroanatomy of dystonia. Neurobiol Dis. 2011 May;42(2):185-201. doi: 10.1016/j.nbd.2011.01.026. Epub 2011 Feb 12. PMID: 21303695; PMCID: PMC3478782.

[3] Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? Brain. 2007 May;130(Pt 5):1183-93. doi: 10.1093/brain/awl355. Epub 2007 Jan 22. PMID: 17242025.

## C25

### Synaptic density and α-synuclein oligomers in skin biopsies: differences between idiopathic and GBA-linked Parkinson's disease

*Elena Contaldi*[1*], S. Mazzetti[2,3], M. Basellini[2,3], V. Ferri[1,3], E. Cereda[4], I.U. Isaias[1,5], G. Pezzoli[1], G. Cappelletti[2,6]

[1]Parkinson Institute Milan, ASST G. Pini-CTO, Milan, Italy
[2]Department of Biosciences, Università degli Studi di Milano, Milan, Italy
[3]Fondazione Grigioni per il Morbo di Parkinson, Milan, Italy
[4]Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[5]Department of Neurology, University Hospital of Würzburg and Julius Maximilian University of Würzburg, Würzburg, Germany
[6]Center of Excellence on Neurodegenerative Diseases, Università degli Studi di Milano, Milan, Italy

*Introduction:* Previous research [1] reported α-synuclein oligomers within synaptic terminals of autonomic fibers in skin biopsies from idiopathic Parkinson's disease (PD) patients employing the proximity ligation assay (PLA), but no information in glucocerebrosidase (GBA)-mutated PD is available.

*Objective:* To compare α-synuclein oligomers and synaptic density (SD) in skin biopsies from PD and GBA-PD.

*Methods:* We collected genetic and clinical data and skin biopsies in 35 patients with PD and 27 with GBA-PD (7 with N370S, 12 with L444P, 8 with compound heterozygous/homozygous mutations or other risk variants). Quantitative analysis was conducted in all the samples containing the sweat gland, which displayed the greatest quantity of autonomic synaptic terminals. The SD was calculated as the ratio between total synaptic terminals and the area of the sweat gland [2], and the α-synuclein oligomers were quantified as the area of PLA signal within synapses normalized for SD.

*Results:* GBA-PD were younger, had an earlier age at PD onset, and had longer disease duration compared with PD. Orthostatic hypotension was reported in 25.9% of GBA-PD and 20% of PD ($p=0.23$). No difference in PLA score could be detected between GBA-PD and PD, as well as between different GBA-PD subgroups. Concerning SD, significantly higher values were found in GBA-PD than PD ($p<0.001$). After controlling in multivariate regression analysis for the effect of age, sex, disease duration, UPDRS-III scores, and Hoehn and Yahr stage, the effect of genetic status was confirmed as a predictor for SD (beta=0.645, 95% CI 0.298-0.752, $p<0.001$). Interestingly, GBA-PD carrying the N370S mutation displayed higher SD compared with L444P-mutated patients ($p=0.05$), whereas α-synuclein oligomers did not differ between groups ($p=0.8$). ROC curve analysis of the SD values showed reliable specificity and sensitivity in detecting GBA-PD (AUC=0.855, $p<0.001$, sensitivity=85.2%, specificity=77.1%).

*Conclusions:* The SD values may help to discriminate between GBA-PD and PD.

**References:**

[1] Mazzetti S, Basellini MJ, Ferri V, et al (2020) α-Synuclein oligomers in skin biopsy of idiopathic and monozygotic twin patients with Parkinson's disease. Brain 143:920–931. doi.org/10.1093/brain/awaa008.
[2] Navarro-Otano J, Casanova-Mollà J, Morales M, et al (2015) Cutaneous autonomic denervation in Parkinson's disease. J Neural Transm (Vienna) 122:1149–1155. doi.org/10.1007/s00702-014-1355-3.

## C26

**Associations between fatigue and functional connectivity of dopamine and noradrenaline circuits in Parkinson's disease**

*Ilaria Antonella Di Vico*[1,2], M. Moretto[3,4], A. Tamanti[1], G. Tomelleri[1], D. Martins[5], O. Dipasquale[5], M. Veronese[3,5], A. Bertoldo[3,6], S. Ottaviani[1], F. Pizzini[1,7], M. Castellaro[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]The Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, NYU Langone Health, New York, USA
[3]Department of Information Engineering, University of Padua, Padua Italy
[4]Center for Mind/Brain Sciences, University of Trento, Trento, Italy
[5]Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[6]Padova Neuroscience Center, University of Padua, Padua, Italy
[7]Department of Diagnostics and Public Health, University of Verona, Verona, Italy

*Background:* Fatigue affects up to 50% of patients with Parkinson's disease (PD), significantly decreasing their quality of life [1]. Unfortunately, pathophysiological mechanisms and treatment options for fatigue are largely unknown. Functional MRI studies have shown abnormal connectivity in the Supplementary Motor Area in *de novo* PD, and multiple neurotransmitter systems have been involved in the pathogenesis of fatigue in PD [2-3].

*Aim:* We aimed to investigate associations between fatigue and functional connectivity within dopamine and noradrenaline functional networks in PD patients.

*Methods:* We enrolled 29 patients with PD, Hoehn and Yahr stages I-III, without significant cognitive decline or severe neuropsychiatric symptoms. Fatigue was measured with the Fatigue Severity Scale (FSS). We used resting-state MRI data and functional connectivity within dopamine transporter (DAT) and noradrenaline transporter (NET)-defined functional networks by applying a recently developed multimodal framework: "Receptor-Enriched Analysis of Functional Connectivity by Targets."

*Results:* We found a negative linear correlation between fatigue and noradrenaline-enriched functional connectivity in regions of the sensorimotor and salience networks and a positive linear trend between fatigue and dopamine-enriched functional connectivity in regions of the default mode network. FSS scores and NET-enriched functional connectivity were anticorrelated (Pearson's r=-0.48), while a positive correlation was found between FSS scores and DAT-enriched functional connectivity (Pearson's r=0.33).

*Conclusion:* These preliminary findings might suggest that fatigue in Parkinson's patients is sustained by a disruption in the sensory-motor circuits and a dysfunction of monoaminergic NET and DA-related connectivity.

**References:**

[1] Di Vico IA, Cirillo G, Tessitore A, Siciliano M, Venturelli M, Falup-Pecurariu C, Tedeschi G, Morgante F, Tinazzi M. Fatigue in hypokinetic, hyperkinetic, and functional movement disorders. Parkinsonism Relat Disord. 2021 May;86:114-123. doi: 10.1016/j.parkreldis.2021.03.018. Epub 2021 Mar 29. PMID: 33839028.
[2] Siciliano M, De Micco R, Giordano A, Di Nardo F, Russo A, Caiazzo G, De Mase A, Cirillo M, Tedeschi G, Trojano L, Tessitore A. Supplementary motor area functional connectivity in "drug-naïve" Parkinson's disease patients with

fatigue. J Neural Transm (Vienna). 2020 Aug;127(8):1133-1142. doi: 10.1007/s00702-020-02219-6. Epub 2020 Jun 27. PMID: 32594249.
[3] Tessitore A, Giordano A, De Micco R, Caiazzo G, Russo A, Cirillo M, Esposito F, Tedeschi G. Functional connectivity underpinnings of fatigue in "Drug-Naïve" patients with Parkinson's disease. Mov Disord. 2016 Oct;31(10):1497-1505. doi: 10.1002/mds.26650. PMID: 27145402.

**C27**

## Memory phenotypes in early *de novo* Parkinson's disease patients with mild cognitive impairment

*Mattia Siciliano*[1,2,3], R. De Micco[1], A.G. Russo[1], F. Esposito[1], V. Sant'Elia[1], L. Ricciardi[3], F. Morgante[3], A. Russo[1], J.G. Goldman[4,5], C. Chiorri[6], G. Tedeschi[1], L. Trojano[2], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences - MRI Research Center Vanvitelli-FISM, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[3]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[4]Parkinson's Disease and Movement Disorders, Shirley Ryan AbilityLab, Chicago, USA
[5]Departments of Physical Medicine and Rehabilitation and Neurology, Northwestern University Feinberg School of Medicine, Chicago, USA
[6]Department of Educational Sciences, University of Genova, Genova, Italy

*Introduction:* Memory deficits in Mild Cognitive Impairment related to Parkinson's disease (PD-MCI) are quite heterogeneous, and there is no general agreement on their genesis [1-2-3].

*Objectives:* To define memory phenotypes in PD-MCI and their associations with motor and nonmotor features and patients' quality of life.

*Methods:* From a sample of 183 early *de novo* patients with PD, cluster analysis was applied to neuropsychological measures of memory function of 82 patients with PD-MCI (44.8%). Cognitive measures and structural magnetic resonance imaging-based neural correlates of memory function were employed to substantiate the results.

*Results:* A three-cluster model produced the best solution. Cluster A (65.85%) included memory unimpaired patients; Cluster B (23.17%) included patients with mild episodic memory disorder related to a prefrontal-dependent executive phenotype; Cluster C (10.97%) included patients with severe episodic memory disorder related to a 'hybrid' phenotype, where hippocampal-dependent deficits co-occurred with prefrontal-dependent dysfunctions. Cognitive and structural imaging neural correlates substantiated the findings. The three phenotypes did not differ in terms of motor and nonmotor features, but the attention/executive deficits progressively increased from Cluster A, through Cluster B, to Cluster C. This last cluster had worse quality of life compared to others.

*Conclusions:* Our results demonstrated the memory heterogeneity of PD-MCI, suggesting the existence of three distinct memory-related phenotypes [4]. Identification of such phenotypes can be fruitful in understanding the pathophysiological mechanisms underlying PD-MCI and its subtypes and guiding appropriate treatments.

**References:**

[1] Litvan I, Goldman JG, Tröster AI, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord 2012; 27: 349-356.
[2] Litvan I, Aarsland D, Adler CH, et al. MDS Task Force on mild cognitive impairment in Parkinson's disease: critical review of PD-MCI. Mov Disord 2011; 26: 1814-1824.
[3] Goldman JG, Holden SK, Litvan I, McKeith I, Stebbins GT, Taylor JP. Evolution of diagnostic criteria and assessments for Parkinson's disease mild cognitive impairment. Mov Disord 2018; 33: 503-510.
[4] Weintraub D, Moberg PJ, Culbertson WC, Duda JE, Stern MB. Evidence for impaired encoding and retrieval memory profiles in Parkinson disease. Cogn Behav Neurol 2004; 17: 195-200.

## C28

**Iron deposition within the basal ganglia and thalamus in early drug-naïve Parkinson's disease patients with and without REM behavioral disorders**

*Martina D'Anna*[1], R. De Micco[1], N. Piramide[1], F. Di Nardo[1], M. Siciliano[1,2], G. Caiazzo[1], G. Tedeschi[1], F. Esposito[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]Neuropsychology Laboratory, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

*Introduction:* Iron deposition using Quantitative Susceptibility Mapping (QSM) has been reported in several cortical and subcortical areas within the dopaminergic pathways in patients with Parkinson's disease (PD), and a relationship with cognitive decline has been proposed. REM sleep behavior disorder (RBD) is a parasomnia wherein a loss of REM sleep atonia manifests as dream-enactment, often violent. Epidemiological studies suggest that PD patients with RBD present an increased risk of worse motor progression and dementia.

*Objective:* In this study, we aimed at exploring the whether RBD are associated with a specific pattern of iron deposition in early drug-naïve PD patients.

*Methods:* 3T MRI images of 58 drug-naïve PD patients (29 PD-RBD+ and 29 PD-RBD-), were analyzed and compared. QSM values were extracted from several subcortical deep gray matter nuclei and 16 thalamic subregions. A partial correlation analyses were run between MRI metrics and clinical data. Finally, a ROC curve was performed to test the ability of QSM values in distinguishing PD-RBD+ from PD-RBD- patients.

*Results:* Compared to PD-RBD-, PD-RBD+ patients showed higher susceptibility values within the right putamen, right red nucleus, left subthalamic nucleus, bilateral medial and anterior pulvinar, right lateral pulvinar and left ventral anterior nucleus of the thalamus. QSM values were found to be associated with the cognitive outcome. The ROC curve analysis showed that QSM values could significantly and accurately identify the presence of RBD in drug-naïve PD.

*Conclusions:* This study provides evidences that higher iron deposition within different subcortical nuclei may differentiates PD patients with RBD even in the early stages. We hypothesize that these findings may reflect the presence of more diffuse neuropathological changes occurring at the disease onset, potentially leading to altered cognitive processing and increased vulnerability to the future development of dementia.

**C29**

## Local Field Potentials (LFPs) beta power and neuroimaging predict the clinical DBS programming scheme in Parkinson's disease

*Lazzaro di Biase*[1,2,3], C. Piano[4,5], F. Bove[4], L. Ricci[1,2], M.L. Caminiti[1,2], A. Stefani[6], F. Viselli[7], N. Modugno[8], R. Cerroni[6], P. Calabresi[4,5], A.R. Bentivoglio[4,5], T. Tufo [9,10], V. Di Lazzaro[1,2] and Lazio DBS Study Group

[1]Research Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Roma, Italy
[2]Operative Research Unit of Neurology, Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[3]Brain Innovations Lab, Università Campus Bio-Medico di Roma, Rome, Italy
[4]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[5]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[6]Department of System Medicine, Unità Operativa Semplice Dipartimentale (UOSD) Parkinson, University of Rome Tor Vergata, Rome, Italy
[7]Department of Neurology, St John the Baptist Hospital, ACISMOM, Rome, Italy
[8]Neuromed Institute IRCCS, Pozzilli, IS, Italy
[9]Neurosurgery Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[10]Neurosurgery Department, Fakeeh University Hospital, Dubai Silicon Oasis, Dubai

*Introduction:* Directional Deep Brain Stimulation (DBS) leads improved the fine-tuning control of the stimulation field. Conversely, a possible drawback of this new technology could be an increase of the DBS programming time, due to the higher number of the possible scheme combinations compared to standard non-directional electrodes.

*Objectives:* The aim of the present study is to evaluate the performance in predicting the chronic contact selection of clinical programming DBS scheme in Parkinson's disease (PD) patients by using as predictors the intra-operative LFPs beta power and neuroimaging reconstructions.

*Methods:* In this retrospective, multicenter study, were enrolled 14 PD patients. Intra-operative LFPs were recorded from all contacts in the subthalamic nucleus (STN), in order to analyze the beta band power for each contact. 3D Neuroimaging reconstruction allowed to detect the position of the lead contacts respect to the STN. In addition, were collected chronic clinical DBS programming scheme, after 1 year from the implant. Statistical analysis evaluated the diagnostic performance of LFPs beta band power and neuroimaging data for identification of the contacts selected with clinical programming.

*Results:* The diagnostic performance of the combined predictors, LFPs beta power and Neuroimaging reconstruction, showed a sensitivity and a negative predictive value of 87%, and a diagnostic odd ratio of 2.7 for predicting the clinically DBS more effective contacts.

*Conclusions:* The good performance of Intraoperative LFP recordings and neuroimaging reconstructions for DBS contact selection prediction could represent an investigative protocol to guide the clinician during the contact selection programming phase, with a possible impact in decreasing the DBS programming time and improve the accuracy.

## C30

**The effects of dopaminergic treatment on interhemispheric disinhibition and bradykinesia asymmetry in Parkinson's disease**

*Martina De Riggi*[1], G. Paparella[2], D. Colella[1], A. Cannavacciuolo[2], A. De Biase[1], L. Angelini[1], D. Birreci[1], D. Costa[1], A. Guerra[2], A. Berardelli[1,2], M. Bologna[1,2]

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

*Introduction:* Previous evidence demonstrated a reduced interhemispheric inhibition (IHI) in Parkinson's disease (PD), possibly related to the asymmetry of motor symptoms [1-3-5]. However, the effects of dopaminergic treatment on interhemispheric disinhibition and motor correlates in PD, have never been investigated.

*Objectives:* To investigate whether dopaminergic therapy modulates IHI and bradykinesia asymmetry in PD.

*Methods:* We enrolled seventeen PD patients (mean age ± standard deviation - SD: 67.5±9.2 years) and 15 healthy controls (HCs) (mean age ± SD: 64±8.1 years). Patients were studied with and without their dopaminergic therapy [2-5] (ON and OFF sessions, mean LEDD ± SD: 483.8±173.2). Paired-pulse transcranial magnetic stimulation (TMS) served to measure IHI, with an interstimulus interval (ISI) between the conditioning (CS) and the test stimulus (TS) of 10 (short-latency IHI, sIHI) and 40 ms (long-latency IHI, lIHI) [1-2-4-5]. Objective finger-tapping measurements were obtained bilaterally with a motion analysis system [5]. We compared data between patients and HCs, and between patients ON and OFF medication using t-tests. We also calculated asymmetry indices (AI) of neurophysiological data. Correlations analysis was performed to test possible relations between TMS and kinematic data.

*Results:* As compared to HC, PD OFF medication had a reduced sIHI from the most to the less affected hemisphere ($p=0.02$). Finger tapping was slower, more irregular and characterised by the sequence effect in PD OFF medication as compared to HCs (all $p<0.05$). Interhemispheric imbalance quantified by the sIHI-AI correlated with the sequence effect of the less affected side in patients OFF medication ($R=-0.5$, $p<0.03$). Although improving movement velocity ($p=0.009$), dopaminergic treatment did not modify sIHI or the sequence effect ($R=0.23$, $p>0.05$).

*Conclusions:* We here provided further evidence on the pathophysiological role of interhemispheric disinhibition in bradykinesia asymmetry in PD with a focus on the effects of dopaminergic treatment.

**References:**

[1] Li JY, Espay AJ, Gunraj CA, Pal PK, Cunic DI, Lang AE, Chen R. Interhemispheric and ipsilateral connections in Parkinson's disease: relation to mirror movements. Mov Disord. 2007 Apr 30;22(6):813-21. doi: 10.1002/mds.21386. PMID: 17290459.

[2] Lizarraga KJ, Saravanamuttu J, Baarbé JK, Lang AE, Chen R. Interhemispheric pathways in agenesis of the corpus callosum and Parkinson's disease. Brain Stimul. 2020 Mar-Apr;13(2):360-362. doi: 10.1016/j.brs.2019.11.003. Epub 2019 Nov 4. PMID: 31727582.

[3] Malling ASB, Morberg BM, Wermuth L, Gredal O, Bech P, Jensen BR. The effect of 8 weeks of treatment with transcranial pulsed electromagnetic fields on hand tremor and inter-hand coherence in persons with Parkinson's disease. J Neuroeng Rehabil. 2019 Jan 31;16(1):19. doi: 10.1186/s12984-019-0491-2. PMID: 30704504; PMCID: PMC6357382.

[4] Bologna M, Caronni A, Berardelli A, Rothwell JC. Practice-related reduction of electromyographic mirroring activity depends on basal levels of interhemispheric inhibition. Eur J Neurosci. 2012 Dec;36(12):3749-57. doi: 10.1111/ejn.12009. Epub 2012 Oct 4. PMID: 23033874.

[5] Bologna M, Guerra A, Paparella G, Giordo L, Alunni Fegatelli D, Vestri AR, Rothwell JC, Berardelli A. Neurophysiological correlates of bradykinesia in Parkinson's disease. Brain. 2018 Aug 1;141(8):2432-2444. doi: 10.1093/brain/awy155. PMID: 29901693.

## C31

### The role of the "Unfolded protein response" and the Perk pathway in Parkinson's disease: study of genetic polymorphisms

*Marika Alborghetti*[1], C. Strafella[2], E. Bianchini[1], D. Rinaldi[1], V. Caputo[2], E. Giardina[2], F. Nicoletti[3], F.E. Pontieri[1,2]

[1]Departments of Neuroscience Mental Health and Sensory Organs (NESMOS), University Sapienza of Rome, Italy
[2]Fondazione Santa Lucia, IRCCS, Rome, Italy
[3]Physiology and Pharmacology, University Sapienza of Rome IRCCS Neuromed, Pozzilli, Italy

*Background:* The accumulation of α-synuclein in Parkinson's disease (PD) leads to the stress of endoplasmic reticulum (ER). The resulting cellular response is called "Unfolded Protein Responce" (UPR), and is activated with the aim of reducing protein synthesis and stimulating the expression of chaperone proteins to prevent protein aggregation and the degradation of already aggregated proteins. UPR is controlled by several sensor proteins, including PERK (PKR-like ER kinase) [1-7].

*Aim of the study:* To study a possible association between the development of PD and the presence of polymorphisms of the genes coding for proteins involved in the UPR and in particular in the PERK pathway.

*Methods:* This analysis focused on the study and analysis of 180 genetic variants (SNV) in a cohort of 210 PD patients and 503 healthy controls. Of these, 27 concern genes coding for proteins involved in the UPR (EIF2AK3, LRRK2, ATF4, ATF6, XBP1, BCL2, EIF2A, ERN1). The DNA was extracted from the blood samples and the Open Array ™ technology allowed a massive and simultaneous genotyping of all the samples under examination.

*Results:* The analysis made it possible to find 51 SNVs with a statistically significant association with susceptibility to PD. Of these, 1 concern EIF2AK3 coding for PERK and 4 concern EIF2A coding for eIF2α.

*Conclusions:* Our study confirms the involvement of UPR and in particular of the PERK pathway in the development of PD. Further analyses will be necessary to correlate these polymorphisms not only with the pathophysiological mechanisms, but also with the clinical course of PD. The PERK pathway represents a potential target for the development of new therapeutic strategies for both neuroprotective and symptomatologic purposes [1-5-6].

**References:**

[1] Ghemrawi R, Khair M. Endoplasmic Reticulum Stress and Unfolded Protein Response in Neurodegenerative Diseases. Int J Mol Sci. 2020 Aug 25;21(17):6127.
[2] Höglinger GU, Melhem NM, Dickson DW, Sleiman PM, Wang LS, Klei L, Rademakers R, de Silva R, Litvan I, Riley DE, van Swieten JC, Heutink P, Wszolek ZK, Uitti RJ, Vandrovcova J, Hurtig HI, Gross RG, Maetzler W, Goldwurm S, Tolosa E, Borroni B, Pastor P; PSP Genetics Study Group, Cantwell LB, Han MR, Dillman A, van der Brug MP, Gibbs JR, Cookson MR, Hernandez DG, Singleton AB, Farrer MJ, Yu CE, Golbe LI, Revesz T, Hardy J, Lees AJ, Devlin B, Hakonarson H, Müller U, Schellenberg GD. Identification of common variants influencing risk of the tauopathy progressive supranuclear palsy. Nat Genet. 2011 Jun 19;43(7):699-705.
[3] Liu QY, Yu JT, Miao D, Ma XY, Wang HF, Wang W, Tan L. An exploratory study on STX6, MOBP, MAPT, and EIF2AK3 and late-onset Alzheimer's disease. Neurobiol Aging. 2013 May;34(5):1519.e13-7.
[4] Qu M, Tang F, Wang L, Yan H, Han Y, Yan J, Yue W, Zhang D. Associations of ATF4 gene polymorphisms with schizophrenia in male patients. Am J Med Genet B Neuropsychiatr Genet. 2008 Sep 5;147B(6):732-6.
[5] Toyofuku T, Okamoto Y, Ishikawa T, Sasawatari S, Kumanogoh A. LRRK2 regulates endoplasmic reticulum-mitochondrial tethering through the PERK-mediated ubiquitination pathway. EMBO J. 2020 Jan 15;39(2):e100875. doi: 10.15252/embj.2018100875. Epub 2019 Dec 10. Erratum in: EMBO J. 2020 Sep 15;39(18):e105826.

[6] Xiang C, Wang Y, Zhang H, Han F. The role of endoplasmic reticulum stress in neurodegenerative disease. Apoptosis. 2017 Jan;22(1):1-26.
[7] Yuan SH, Hiramatsu N, Liu Q, Sun XV, Lenh D, Chan P, Chiang K, Koo EH, Kao AW, Litvan I, Lin JH. Tauopathy-associated PERK alleles are functional hypomorphs that increase neuronal vulnerability to ER stress. Hum Mol Genet. 2018 Nov 15;27(22):3951-3963.

**C32**

## Influence of RBD onset on the clinical characteristics of Parkinson's disease patients: a retrospective study

*Calogero Edoardo Cicero*[1], *A. Luca*[1], *G. Mostile*[1,2], *G. Donzuso*[1], *L. Giuliano*[1], *M. Zappia*[1], *A. Nicoletti*[1]

[1]Department of Medical, Surgical Sciences and Advanced technologies G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[2]Oasi Research Institute-IRCCS, Troina, Italy

*Introduction:* In Parkinson's disease (PD), Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) might either precede the appearance of motor symptoms, or develop during the disease course.

*Objective:* To analyze the clinical characteristics of PD patients according to the timeline of RBD onset.

*Methods:* PD patients have been retrospectively enrolled. Presence and onset of probable RBD (pRBD) has been evaluated using RBD Screening Questionnaire (score ≥6). Presence of Mild Cognitive Impairment (MCI) at baseline has been evaluated using the MDS criteria level II. Presence of motor complications and hallucinations has been evaluated at a 5-year follow-up.

*Results:* At total of 115 PD patients (65 men, 56.5%; mean age 62.5±9.7 years; mean disease duration 3.7 ±3.9 years) have been enrolled. Out of these, 63 fulfilled the diagnosis of pRBD (54.8%) with 21 (33.3%) reporting the RBD onset before the onset of the motor symptoms (PD-RBDpre), and 42 (66.7%) after the motor symptoms (PD-RBDpost). At enrolment presence of MCI was associated with PD-RBDpre patients (OR 5.04; 95%CI 1.33-19.05; p-value 0.02). At follow-up, a higher risk of developing hallucinations was also associated with PD-RBDpre (OR 4.82;95%CI 1.30-17.85;p=0.018).

*Conclusions:* PD patients with RBD occurring before the onset of motor symptoms represent a subgroup of patients with a more severe cognitive phenotype and with a higher risk of developing hallucinations along the disease course, with significant implications in terms of prognostic stratification and therapeutic approach.

# Poster

**P1**

## Reduction of primacy effect as marker for cognitive decline in Parkinson's disease

*Paolo Amami*[1], B. Curti[1], S. Prioni[1], E. Bocchi[1], M. Fusar Poli[1], N. Golfrè Andreasi[2], R. Cilia[2], L.M. Romito[2], A.E. Elia[2], G. Devigili[2], O. Pino[3], R. Eleopra[2], S.H.M.J. Piacentini[1]

[1]Clinical Neuropsychology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[2]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[3]Neuroscience Unit, Medicine and Surgery Department, Università degli Studi di Parma, Parma, Italy

*Introduction:* From a neuropsychological standpoint, a dysexecutive syndrome is a feature of early Parkinson's disease (PD), while in patients who develop dementia associated to PD (PDD) also a declarative memory disorder may occur. The serial position effect (SPE) reflects the tendency of cognitively normal subjects to recall more words from the beginning (primacy effect) and the end of a list (recency effect) as compared to words in the middle. Alteration of SPE was found in patients with declarative memory disorder: a reduced primacy effect characterized Alzheimer's disease and a lower primacy effect predicted the conversion to dementia in mild cognitive impairment (MCI) patients. SPE was scarcely explored in PD and there are no data regarding PDD patients.

*Objective:* Aim of the study was to investigate SPE in PD patients with different degree of cognitive impairment and to determine if SPE can be useful in identifying PDD patients.

*Methods:* Three matched groups of PD patients were selected based on neuropsychological diagnosis: cognitively normal PD patients (PD-CN), PD patients with MCI (PD-MCI) and PDD patients. The groups were matched based on gender, age at disease onset and education and 27 patients belonged to each group. Declarative memory was evaluated with the Rey's auditory verbal learning test and SPE was estimated using the regional scoring method. Within-group, between-group and a ROC analysis were performed.

*Results:* PDD patients showed the worse performance in learning and delayed recall. In PDD patients the primacy effect disappeared, while it was still observable, even if decreased, in PD-MCI. PD-CN patients showed no alteration of SPE. The accurancy of the primacy effect in distinguishing PDD from PD-MCI and PD-CN patients was of 91% and the best cut-off was 0.4 (sensitivity 85.2% and specificity 88.9%).

*Conclusions:* The absence of the primacy effect was a marker of PDD patients. Longitudinal studies are necessary to ascertain if SPE could be a potential predictive factor for cognitive decline in PD.

**P2**

## Fist Palm Test (FiPaT): a quick bedside test to reveal cognitive dysfunction in Parkinson's disease

*Beatrice D'Arco*, S. Cuoco, C. Sorrentino, R. Bisogno, M. Picillo, M.T. Pellecchia, R. Erro, P. Barone

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

*Introduction:* The FiPaT is a non-verbal test useful to screen for global cognitive status, attention, and executive functions, and to predict the Mild Cognitive Impairment (MCI) [1]. Four types of errors are possible at FiPaT: Topography, Perseverance, Attention and Planning.

*Aims of this study:* (I) To reveal cognitive alteration in Parkinson's disease (PD) using FiPaT; (II) to analyze the relationship between FiPaT and cognitive/motor symptoms in PD.

*Methods:* 102 subjects [51 PD and 51 healthy controls (HC)] matched for age and educational, were administered both a comprehensive neuropsychological battery and FiPaT. PD patients were evaluated for motor symptoms using UPDRS-III and were tested for presence of cognitive alteration and divided in PD - normal cognition (PD-NC) or PD-MCI. These two groups were compared to HC for FiPaT. Subsequently, FiPaT was evaluated in different parkinsonian phenotypes including: postural instability gait difficulty (PIGD), tremor dominant (TD) and presence or absence of freezing of gait (FOG).

*Statistical analysis*: We measured global score and percentage of errors. The Mann Whitney's U test and contingency tables, were used to measure FiPaT errors between PD and HC, between sub-groups of PD and neuropsychological differences between PD with and without FiPaT errors. A binary logistic regression analysis, with Bootstrap method, was used to investigate the role of FiPaT and of specific errors in identifying MCI in PD patients.

*Results:* The PD patients performed worse than HC on FiPaT global score ($p = 0.006$). The percentage of errors in topography, perseveration and planning is significantly higher in PD than in HC ($p<0.05$). No difference in FiPaT global score was found between HC and PD-NC; PD-MCI performed significantly worse on FiPaT than PD-NC ($p=0.002$). As compared with PD patients with normal FiPat, PD patients with altered FiPaT performed worse on neuropsychological tests measuring memory, visuospatial and executive skills, but not ideomotor apraxia. UPDRS-III motor score no difference was found between two groups. The logistic regression analysis showed that the FiPaT predicted the presence of MCI in PD with a variance of 24% ($p=0.023$). Topographic and attentional errors predicted the presence of MCI in PD, with a variance of 31% ($p<0.021$ e $p<0.013$, respectively). There were not significant differences on FiPaT between motor PD sub-groups but the TD subgroup showed more planning errors than the PIGD ($p = 0.014$). Patients with FOG had significantly higher percentage of attention errors at FiPat than patients without FOG ($p = 0.023$).

*Discussion*: The FiPaT is a bedside test useful to reveal cognitive dysfunction in PD. Worse performance on FiPaT is associated with worse cognitive performance. Different motor PD phenotypes are associated with specific errors in the FiPaT.

*Conclusions:* Nonketotic hyperglycemia is an unusual, potentially easily-treatable cause of chorea-ballismus. Early recognition is crucial in order to start a prompt management and prevent further complications. HHHS should always be suspected in new-onset chorea/hemichorea, even in patients with no history of diabetes. The prognosis is excellent in most of the cases.

**References:**

[1] Cuoco S, Erro R, Carotenuto I, Picillo M, Pellecchia MT, Barone P. Fist-Palm Test (FiPaT): a bedside motor tool to screen for global cognitive status [published online ahead of print, 2022 May 30]. Neurol Sci. 2022;10.1007/s10072-022-06129-1. doi:10.1007/s10072-022-06129-1.

**P3**

## Gender differences and cognitive reserve in people with Parkinson's disease: possible interactions and effects on cognitive domains

*Francesca Lea Saibene*[1], S. Di Tella[1,2], A. Salvatore[1], P. Arcuri[1], A. Castagna[1], E. Farina[1], M. Alberoni[1], E. Calabrese[1], J.S. Navarro[1], M. Mario[1,3]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy
[3]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy

*Introduction:* Although there are several studies on Cognitive Reserve (CR) and Gender Differences (GDs) in the phenotypical expression of Parkinson's Disease (PD) [1-2], the results are still controversial.

*Objective:* To investigate the effects of GDs and CR on global cognitive functioning and different cognitive domains in People with PD (PwPD).

*Methods:* Fifty-six PwPD (Age: 69.48±6.68ys, H&Y: 1.50-3, Male/Female=29/27) were recruited at IRCCS Don Carlo Gnocchi Foundation (Milan). Motor and overall cognitive functioning were assessed respectively by the MDS-UPDRS-Part III [3] and the Montreal Cognitive Assessment (MoCA Test) [4] while the CS was evaluated through the Cognitive Reserve Index-questionnaire (CRI-q) [5]. Median of CRI-q global score was used to split participants in two groups: high-CR and low-CR PwPD. Linear models were performed on each neuropsychological test to explore the impact of CRIq (high/low), gender (male/female) and interaction CRIq*Gender, including age as covariat

*Results:* A significant impact of CR was observed for several MoCA sub-scores, visuospatial (p=0.049) and executive (p=0.022) abilities, attention (p=0.032), Raven's Matrices (p=0.015), verbal span forward (p=0.023) and backward (p=0.004), copy of Rey's Figure (p=0.047), test of imitation gestures (p=0.023) and verbal fluency (p=0.023). A main effect of gender was reported for Immediate free recall (p=0.014) and delayed free recall (p=007) with female PwPD showing a better performance than male PwPD. A significant interaction CRIq*Gender was obtained in attentional matrices (p=0.058), TMT part B (p=0.019), TMT part B-A (p=0.035), Symbol Digit Modalities Test (SDMT) (p=0.064) and Immediate free recall (p=0.031).

*Conclusions:* Higher CR might be correlated with better cognitive functions on several domains regardless of gender, supporting that CR may help to cope with the initial PD cognitive difficulties. Furthermore, a higher level of CR was found to be beneficial in female rather than in men PwPD. Further studies are necessary to investigate how CR and GDs modulate cognitive impairment in PD.

**References:**

[1] Cholerton, B., Johnson, C. O., Fish, B., Quinn, J. F., Chung, K. A., Peterson-Hiller, A. L., ... & Edwards, K. L. (2018). Sex differences in progression to mild cognitive impairment and dementia in Parkinson's disease. Parkinsonism & related disorders, 50, 29-36.
[2] Cerri, S., Mus, L., & Blandini, F. (2019). Parkinson's disease in women and men: what's the difference? Journal of Parkinson's disease, 9(3), 501-515.
[3] Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., ... & LaPelle, N. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Movement disorders: official journal of the Movement Disorder Society, 23(15), 2129-2170.
[4] Santangelo, G., Siciliano, M., Pedone, R., Vitale, C., Falco, F., Bisogno, R., ... & Trojano, L. (2015). Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36, 585-591.

[5] Nucci, M., Mapelli, D., & Mondini, S. (2012). Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. Aging clinical and experimental research, 24, 218-226.

**P4**

## Psychometric properties and clinical correlates of the Frontal Behaviour Inventory in progressive supranuclear palsy: data from the PSP-NET

*Arianna Cappiello*, S. Cuoco, P. Barone, M. Picillo per PSP-NET group

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, University of Salerno, Salerno, Italy

*Objectives:* Behavioural symptoms, such as apathy, disinhibition, dysphoria and anxiety are frequent complains in progressive supranuclear palsy (PSP) [1]. Specific scales evaluating neuropsychiatric disturbances in PSP are lacking. The Frontal Behaviour Inventory (FBI) is widely used to evaluate behavioural issues in dementia. Aims of the present study were to (I) report the psychometric properties of the FBI in PSP and (II) describe the clinical correlates of behavioural symptoms in PSP patients. Design, setting and participants: PSP patients diagnosed according to the Movement Disorder Society Criteria underwent a clinical interview, a motor evaluation, cognitive and behaviour testing. Data were collected from several centres throughout Italy within the PSP-NET supported by Fondazione LIMPE.

*Results:* Two-hundred and eight subjects, with mean (± DS) age of 63.90 ± 12.25 years and mean (± DS) education of 9.82 ± 3.98, were screened for the present study. One-hundred-twenty-two were men (67,80%) and 59 were women (32,60%). The internal consistency was high (Cronbach's alpha = 0.868) and corrected item-total correlation was > 0.40 for the majority of items. Principal component analysis revealed that five factors with the highest eigenvalues accounted for 54.92% of the total variance. Behavioural aspects measured with FBI associated with less education and more aggressive and apathetic symptoms.

*Conclusion:* The FBI is a reliable tool for the assessment of behavioural symptoms in PSP. Higher behavioural symptoms scores may represent a marker of prevalence of aggressive and apathetic aspects in PSP. The lack of items exploring depressive symptoms in the FBI may justify the low total variance displayed by factor analysis.

**References:**

[1] Agarwal S., Gilbert R. Progressive Supranuclear Palsy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. 2022 Apr 3. PMID: 30252354. Bookshelf ID: NBK526098.

**P5**

## Recognition of emotional faces and judgment of affective scenes in Parkinson's disease

*Gennaro Saporito*[1], F. Pistoia[1], S. Toro[1], F. Salfi[1], G. Montaruli[1], M. Conson[2], C. Marini[3], M. Ferrara[1], P. Sucapane[4]

[1]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[2]Department of Psychology, University of Campania Luigi Vanvitelli, Caserta, Italy
[3]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[4]Department of Neurology, San Salvatore Hospital, L'Aquila, Italy

*Introduction:* Non-motor symptoms in Parkinson's disease (PD) include emotional dysfunctions.

*Objectives:* This study aimed to investigate PD patients' ability to recognize the emotional valence of others' facial expressions and evaluate the congruity between their own emotional responses and the affective content of scenes.

*Methods:* Forty PD patients (mean age ± SD 64.50 8.19 years; 27 men) were included in the study. Exclusion criteria were a previous history of psychiatric disorders, treatment with Deep Brain Stimulation and the presence of cognitive impairment. Forty healthy individuals (64.95±8.25 years; 27 men) were the control group. All subjects were evaluated through the Ekman 60-Faces test and the International Affective Picture System (IAPS) test [1-2]. The accuracy in recognizing the emotional valence of facial expressions and affective scenes was compared between groups using linear mixed models. Pearson's correlation was performed to test the association between accuracy measures.

*Results:* The groups did not differ in sex composition, age, education years, and Mini-Mental State Examination scores. Patients showed a lower recognition accuracy of facial expressions (68.54% ± 15.83%) than healthy participants (78.67% ± 12.04%; $p < 0.001$). Patients showed lower recognition accuracy for faces expressing fear, sadness, and anger than the control group (all $p < 0.020$). No difference was detected for faces expressing disgust, surprise, and happiness (all $p \geq 0.25$). PD patients showed lower accuracy in recognizing the emotional valence of affective scenes (66.75% ± 14.59%) than healthy participants (74.83% ± 12.65%; $p = 0.010$). Pearson's correlations indicated that higher accuracy in recognizing the emotional facial expressions was associated with higher accuracy in classifying the valence of affective scenes in patients ($r = 0.57$, $p < 0.001$) and healthy participants ($r = 0.57$, $p < 0.001$).

*Conclusions:* Lower accuracy in PD patients may reflect maladaptive affective processing within specific neural networks.

**References:**

[1] Ekman P, Friesen WV (1976) Pictures of facial affect (Consulting Psychologists, Palo Alto, CA).
[2] Lang PJ, Bradley MM, Cuthbert BN (1997) International affective picture system (IAPS): technical manual and affective ratings (NIMH Center for the Study of Emotion and Attention, University of Florida, Gainesville, FL).

**P6**

## Prospective memory in Parkinson's Disease: a longitudinal study

*Giovanni Luca di Benedetto*[1], A. D'Iorio[1], M.P. Idropico[1], C. Alves[1], C. Vitale[2,3], M. Amboni[3,4], G. Santangelo[1]

[1]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Department of Motor Sciences and Wellness, University "Parthenope", Naples, Italy
[3]Institute of Diagnosis and Care (IDC), Hermitage-Capodimonte, Naples, Italy
[4]Department of Medicine, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Salerno, Italy

*Introduction:* Prospective Memory (PM) is defined as the memory for future intentions and it is typically divided into time-based and event-based PM. PM deficits, especially time-based ones [1], have been widely reported in patients with Parkinson's disease (PD) but, until now, no study has yet explored PM functioning over time.

*Objectives:* The present longitudinal study aimed at exploring the evolution of PM deficits, both time-based and event-based, in PD patients.

*Methods:* Thirteen non-demented PD patients were enrolled. They underwent the first assessment between January 2017 and December 2018 (T0). Then, between January and December 2022 (T1), they were contacted again and asked to complete the second assessment. All patients underwent a neuropsychological battery to assess PM functioning, verbal memory, executive functions, the frequency of prospective and retrospective memory failures, the subjective memory complaints, the occurrence of apathetic symptoms and the functional impact of cognitive impairment.

*Results:* Results of the Wilcoxon signed-rank test showed that PM scores changed between T0 and T1. At T1, PD patients performed worse on both time-based ($Z=-2.365$; $p=0.018$) and event-based ($Z=-2.431$; $p=0.015$) PM tasks. Moreover, at T1 lower scores on tasks assessing executive functions and a worsening of functional autonomy and apathetic symptoms were also highlighted. Scores on tasks assessing memory functions did not change between T0 and T1.

*Conclusion:* In the present study no worsening of verbal memory abilities was found in PD patients. Contrariwise, a worsening of PM functions, functional autonomy and apathetic symptoms were reported. These evidences seem to suggest that executive dysfunctions and behavioral disturbances related to a frontal damage were significantly associated to a reduced performance on PM tasks as a consequence of the progressive neurodegeneration primarily involving prefronto-subcortical circuitries.

**References:**

[1] D'Iorio A, Maggi G, Vitale C, Amboni M, Di Meglio D, Trojano L, Santangelo G. Prospective memory in Parkinson's disease: the role of the motor subtypes. J Neurol. 2019;266(10):2505-251.

**P7**

## Cognitive decline in patients with Parkinson's disease and GBA mutation: preliminary results of a longitudinal neuropsychological study

*Chiara Longo*[1,2], R. Bacchin[1], C. Papagno[3], A. Martinelli[1], M. Fronza[1], D. Ottaviani[4], C. Zizzo[5], A.B. Di Fonzo[6], M.C. Malaguti[1]

[1]Department of Neurology, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[2]Department of Psychology, University of Milano-Bicocca, Milan, Italy
[3]Center of Neurocognitive Rehabilitation (CeRiN), CIMeC, University of Trento, Rovereto, Italy
[4]Department of Neurology, Santa Maria del Carmine Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Rovereto, Italy
[5]Institute for Biomedical Research and Innovation (IRIB) National Research Council (CNR), Palermo, Italy
[6]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy

*Introduction:* Mutations of glucocerebrosidase (GBA) are associated with an increased incidence of Parkinson's disease (PD) [1]. Moreover, studies showed that PD patients with GBA mutation (mPD) present a more severe cognitive decline compared to PD patients without GBA mutation (iPD) [2]. However, neuropsychological profile of mPD patients have been poorly defined: only three studies evaluated patients with an extensive neuropsychological assessment, and only two studies included a control group of iPD.

*Aim:* Profiling and follow-up of cognitive performance of mPD compared to iPD.

*Methods:* 5 mPD and 5 iPD patients underwent a neurological and a II level cognitive assessment at baseline (T0) and after one year (T1). The data were analysed retrospectively, using non-parametric analyses; mPD and iPD (i) with dementia and psychosis at T0, (ii) without cognitive follow-up, and (iii) with neurological comorbidities were excluded. At T0, mPD and iPD were matched for all the clinical-demographic variables, but they differed in Digit Span Backward performance (p=0.045).

*Results:* Analysis of variance between T0 e T1 showed significant different performances in mPD and iPD in Digit Span Backward (p=0.010), Rey Auditory Verbal Learning Test-Delayed Recall (p=0.017), and Unknown Face Recognition (p=0.014). Specifically, post-hoc analysis for these tests showed a Group effect with worse performance for mPD. Notably, in the mPD group two patients remained cognitively unimpaired (CU), two changed from single domain MCI (sdMCI) to multi-domain MCI (mdMCI), while 1 from CU became mdMCI. Instead, all iPD remained CU. Considering emotional symptomatology, mPD and iPD differed in GDS and PAS, particularly mPD compared to iPD group showed more anxiety-depressive symptoms.

*Conclusions:* Preliminary results showed higher cognitive decline in mPD compared to iPD at one-year follow-up, particularly in working memory, verbal long-term memory and visual-perceptual abilities. Although preliminary, these data support the relevance to cognitively evaluate mPD to better understand the profile associated with the type of GBA mutation and to better organize the treatment process.

**References:**

[1] Riboldi GM, Di Fonzo A. (2019). GBA, Gaucher Disease, and Parkinson's Disease: From Genetic to Clinic to New Therapeutic Approaches. Cells. doi:10.3390/cells8040364.
[2] Planas-Ballvé A, Vilas D. (2021). Cognitive Impairment in Genetic Parkinson's Disease. Parkinsons Dis. doi:10.1155/2021/8610285.

**P8**

## Italian version of the Parkinson's disease - Cognitive Functional Rating Scale: a multicenter validation study

*Antònia Siquier*[1], L. Weis[2], E. Fiorenzato[3,4], F. Pistonesi[2], V. Cianci[2], M. Canesi[6], F. Pesce[6], E. Reali[7], B. Pozzi[7], I.U. Isaias[7], C. Siri[6,7], G. Santangelo[9], S. Cuoco[10], P. Barone[10], A. Antonini[2,4], R. Biundo[3,4,5]

[1]Neuropsychology and Cognition Research Group, Department of Psychology, University of the Balearic Islands, Palma, Spain
[2]Parkinson's Disease and Movement Disorders Unit, Department of Neuroscience, University of Padova, Padova, Italy
[3]Department of General Psychology, University of Padova, Padova, Italy
[4]Study Center for Neurodegeneration (CESNE), University of Padova, Padova, Italy
[5]IRCCS San Camillo Hospital, Venezia, Italy
[6]Department of Parkinson's Disease and Movement Disorders, Moriggia Pelascini Hospital, Gravedona ed Uniti, Italy
[7]Parkinson Institute, ASST G. Pini-CTO Milan, Italy
[9]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[10]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Odontology "Scuola Medica Salernitana", University of Salerno, Salerno, Italy

*Introduction:* Significant functional decline resulting from cognitive impairment remains a primary feature in differentiating dementia from mild cognitive impairment (MCI) in Parkinson's disease (PD). The Parkinson's Disease-Cognitive Functional Rating Scale [1] (PD-CRFS) was designed to measure functional disability related to cognitive impairment in PD while reducing possible biases derived from motor alterations.

*Objective:* The aim of this multicenter study was twofold. First, to validate the Italian version of the PD-CFRS on a large cohort of PD patients. Second, to determine optimal cut-off scores for detecting MCI and dementia in PD.

*Methods:* 669 PD patients were enrolled from 4 Italian movement disorders centers (Venice, Milan, Gravedona, and Salerno). They were cognitively characterized based on Level-II cognitive evaluation, resulting in: 282 PD-NC, 310 PD-MCI, 77 PDD. Clinimetric properties, applicability, and responsiveness of the PD-CFRS were analyzed.

*Results:* PD-CFRS was free from floor and have only a 5% ceiling effects. It showed strong internal consistency (Cronbach's $\alpha = 0.738$) and higher coefficient of variation to detect dysfunction in PD-MCI patients (PD-CFRS 96% vs IADL 22.5%). Test-retest reliability reached 0.854. Convergent validity with the IADL was r= -0.638 and -0.527 ($p< 0.0001$) in male and female, respectively. PD-CFRS total score negatively correlated with global cognition (moca corrected score r = -0.61; $p <0.001$). PD-CFRS optimal cut-off score for detecting functional impairment in PD-MCI was > 0 (Sensitivity = 80%; Specificity = 39%) and the screening cut-off was >1 (Sensitivity=68%; Specificity=69%) (AUC=0.695). A cut-off score of > 6.5 (Sensitivity= 90%; Specificity =88%) was the optimal for detecting PDD (AUC = 0.959).
*Conclusions:* The Italian version of the PD-CFRS demonstrated to be a valid and reliable tool for capture functional impairment due to cognitive decline in PD and would be a useful instrument that can aid for the diagnosis of MCI and dementia in PD.

**References:**

[1] Kulisevsky, J., Fernández de Bobadilla, R., Pagonabarraga, J., Martínez-Horta, S., Campolongo, A., García-Sánchez, C., Pascual-Sedano, B., Ribosa-Nogué, R., & Villa-Bonomo, C. (2013). Measuring functional impact of cognitive impairment: validation of the Parkinson's disease cognitive functional rating scale. Parkinsonism & related disorders, 19(9), 812–817. Https://doi.org/10.1016/j.parkreldis.2013.05.007.

**P9**

## Prospective memory in Parkinson's disease: a meta-analysis

*Chiara Giacobbe*, G. Maggi, G. Santangelo

Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Prospective memory (PM) is defined as memory for future intentions, and it is typically divided into time-based (TBPM) and event-based (EBPM) [1]. Deficit of PM has been reported in patients with Parkinson's disease (PD) but it is still unclear the extent of PM deficits as well as the possible dissociation between the two sub-components. Hence, we designed a meta-analytic study to unravel the nature of PM deficits in PD by comparing their performance with those of healthy controls (HCs).
A systematic literature search was conducted using PubMed, Scopus, and Web of Science using "Parkinson's disease" and "prospective memory" as keywords.
Articles were screened for titles and abstracts and subsequently evaluated through full-texts examination. We extracted from each selected study: number of participants and demographic, clinical, neuropsychological and neuropsychiatric data. Effect sizes (ES) from cross-sectional data investigating the PM performance for PD patients compared to HCs were computed. Several meta-regressions were performed to investigate the impact of socio-demographical and clinical variables on the results.
Thirteen articles were included in the meta-analysis. Among them, 7 explored differences on both PM sub-components while 6 studies investigated only EBPM sub-component.
PD patients reported worse scores in both TBPM (ES = -0.71) and EBPM (ES= -0.44) PM tasks compared to HCs. No demographical and clinical variables impacted on these results.
Overall, our findings revealed PM deficits in PD patients with a major impairment in TBPM sub-component. Moreover, PM deficits would be independent from age-related processes and PD progression and then, they might be the consequence of executive and working memory dysfunctions [2].
Deficits of PM heavily limit PD patients' everyday functioning impacting on their medical adherence and functional autonomy [3]. Therefore, we underline the need to use compensatory strategies to sustain PM along with the implementation of non-pharmacological interventions to improve these abilities in PD and other neurodegenerative disorders.

**References:**

[1] Ramanan, S., & Kumar, D. (2013). Prospective memory in Parkinson's disease: A meta-analysis. Journal of the International Neuropsychological Society, 19(10), 1109–1118. doi:10.1017/ S1355617713001045.

[2] Katai, S., Maruyama, T., Hashimoto, T., & Ikeda, S. (2003). Event based and time based prospective memory in Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 74(6), 704-709. doi:10.1136/jnnp.74.6.704.

[3] Pirogovsky, E., Woods, S. P., Filoteo, J. V., & Gilbert, P. E. (2012). Prospective memory deficits are associated with poorer everyday functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 18(6), 986-995. doi:10.1017/S1355617712000781.

**P10**

## Effect of cognitive reserve on cognitive function in Parkinson's disease: a preliminary analysis

*Eleonora Zirone*, M. Takeko Molisso, R. Girlando, F. Ruggiero, S. Barbieri, F. Mameli

Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

*Introduction:* Cognitive reserve (CR) has been proposed to explain the difference between the degree of brain pathologies and the clinical outcome of the cognitive profile. However, the available studies on Parkinson's disease (PD) have mainly investigated CR through only one proxy measure, such as education level, and not as a multidimensional factor.

*Objective:* We examined the possible effect of the CR, measured through a standardized tool, on the neuropsychological function of PD patients.

*Methods:* A total of 16 patients with PD (5 female, mean [±SD] age 57 ± 6.73 years) were included in this study. All patients underwent the Montreal of Cognitive Assessment (MoCA) [1] to assess cognitive function and CR was evaluated by Cognitive Reserve Index questionnaire (CRIq) [2]. According to CRIq score, patients were divided into two subgroups: low-medium score (≤ 114) vs. medium-high score (> 114).

*Results:* Univariate linear regression analysis showed a significant association between CR and cognitive function ($\beta = 0.037$; SE = 0.013; t-value 2.728; $p = 0.016$). Comparison between subgroups showed that PD patients with medium-high CRIq scores had better cognitive performance (CRIq score ≤ 114 vs. CRIq score > 114; mean ± SD raw MoCA score 24.25 ± 1.28 vs. 26.63 ± 1.30; $p = 0.012$) and longer disease duration (CRIq score ≤ 114 vs. CRIq score > 114; mean ±SD 8.88 ± 2.36 vs. 11.63 ± 2.39; $p = 0.036$).

*Discussion:* Our preliminary results suggest that higher CR might be correlated with better cognitive function and a lower risk of longitudinal progression to Mild Cognitive Impairment in PD. More systematic and longitudinal studies in large PD cohorts are needed to better understand the relationship between CR and neuropsychological outcome.

**References:**

[1] Santangelo et al. (2015) Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36(4), 585-591.

[2] Nucci et al. (2012) Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. Aging Clin Exp Res 24(3):218-26.

**P11**

## MRgFUS thalamotomy in dystonic and essential tremor: a prospective study with one year follow up

*Nico Golfrè Andreasi*[1], A. Braccia[1], F. Ghielmetti[2], F. Paio[1], L.M. Romito[1], R. Cilia[1], G. Messina[3], V. Levi[3], A.E. Elia[1], G. Devigili[1], S. Rinaldo[1], M. Grisoli[4], M. Stanziano[4], R. Gianneri[4], S. Prioni[5], M. Fusar Poli[5], P. Amami[5], S.H.M.J. Piacentini[5], E.F.M. Ciceri[6], M.G. Bruzzone[4], R. Eleopra[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milano (Italy)
[2]Fondazione IRCCS Istituto Neurologico Carlo Besta, Health Department, Milano (Italy)
[3]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neurosurgery Department, Functional Neurosurgery Unit; Milano (Italy)
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Neuroradiology Unit, Milano (Italy)
[5]Fondazione IRCCS Istituto Neurologico Carlo Besta, Clinical Neuropsychology Unit, Milano (Italy)
[6]Fondazione IRCCS Istituto Neurologico Carlo Besta, Diagnostic Radiology and Interventional Neuroradiology, Milano (Italy)

*Introduction:* MRgFUS thalamotomy has been shown to be a safe and effective surgical option for treating disabling tremor in patients with Essential Tremor (ET) and Parkinson's Disease. Thalamic VIM nucleus is the target of choice for surgical therapies in drug-resistant ET. Currently, there is no consensus on the best target for the surgical treatment of Dystonic Tremor (DT) [1].

*Objective:* To investigate effectiveness, safety and lesion coordinates of MRgFUS thalamtomy in patients with DT compared with ET.

*Methods:* Between January 2019 and January 2022, 55 patients with ET and 12 with DT underwent MRgFUS thalamotomy in our Institute. Patients were evaluated before surgery and after 1, 6 and 12 months from thalamotomy. Initial targeting for thalamotomy followed previous indications in literature [2]. During the visits we evaluated the clinical severity of tremor with The Essential Tremor Rating Assessment Scale (TETRAS) and collected the adverse events. The position of the lesion was determined on 3T T1-weighted MRI performed one month after thalamotomy.

*Results:* 10 patients with DT and 35 with ET completed the one-year evaluations and were included. Effectiveness of MRgFUS thalamotomy in significantly improve activities of daily living (ADL) and tremor scores resulted similar between the two groups. The thalamotomic lesion was positioned significantly more anterior in DT compared with ET. No significant difference in the incidence of adverse events related to thalamotomy was found between the two groups. However, considering the whole sample, a more anterior placement of the lesion was associated with a reduced odds ratio for incident adverse events.

*Conclusions:* MRgFUS thalamomy is safe and efficacious in patients with DT and ET; a more anterior initial targeting may be considered for DT patients [2-3], instead of classical Vim coordinates. This may allow improvement in ADL and tremor with a particularly safe adverse event profile in DT.

**References:**

[1] Mongardi L, Rispoli V, Scerrati A, et al (2020) Deep brain stimulation of the ventralis oralis anterior thalamic nucleus is effective for dystonic tremor. Parkinsonism Relat D 81:8–11. https://doi.org/10.1016/j.parkreldis.2020.09.040.
[2] Chang WS, Jung HH, Kweon EJ, et al (2015) Unilateral magnetic resonance guided focused ultrasound thalamotomy for essential tremor: practices and clinicoradiological outcomes. J Neurology Neurosurg Psychiatry 86:257. https://doi.org/10.1136/jnnp-2014-307642.
[3] Tsuboi T, Wong JK, Eisinger RS, et al (2021) Comparative connectivity correlates of dystonic and essential tremor deep brain stimulation. Brain 144:1774–1786. https://doi.org/10.1093/brain/awab074.

**P12**

## Deep brain stimulation in Parkinson's disease: cognitive outcomes one year after surgery

*Chiara Longo*[1,2], L. Zigiotto[3], M.C. Malaguti[1], M. Pellegrini[1], R. Bacchin[1], S. Sarubbo[3], F. Corsini[3], U. Rozzanigo[4], B. Bertoldi[5], C. Papagno[5]

[1]Department of Neurology, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[2]Department of Psychology, University of Milano-Bicocca, Milan, Italy
[3]Department of Neurosurgery, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[4]Department of Neuroradiology, Santa Chiara Hospital, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[5]Center of Neurocognitive Rehabilitation (CeRiN), CIMeC, University of Trento, Rovereto, Italy

*Introduction:* Deep Brain Stimulation (DBS) is a valid treatment for motor symptoms in patients with Parkinson's disease (PD). However, a recent meta-analysis [1] has shown that this can have adverse effects on cognition, but most of the included studies do not have level II cognitive assessments and lack a control group.

*Objective:* The study aims to evaluate the effects of DBS on the subthalamic nucleus (STN) one year after surgery by comparing DBS and non-DBS patients in level II cognitive assessment.

*Methods:* Eight PD patients undergoing STN-DBS and eight pharmacologically treated patients (MED) were administered a neurological exam and an extensive battery of neuropsychological tests. Both groups were evaluated at baseline (T0) and after one year (T1), a time long enough to avoid effects due to surgical micro-injuries and short enough to avoid measuring possible cognitive decline.

*Results:* At baseline, the two groups differ in levodopa taken per day (LEDD) but not in other demographic, cognitive, and motor variables. Considering T0 and T1 of each group, the DBS shows a worsening in Attentive Matrices, Semantic Verbal Fluency, and Stroop Test. Even MED worsen Attention Matrices but improve Semantic Verbal Fluency. Furthermore, only MEDs increase depressive symptoms. Using the simple discrepancy score (SDS), the comparison between DBS and MED shows that the two groups no longer differ in LEDD, but there is a difference in the Semantic Verbal Fluency about one year after the intervention, in which DBS scores significantly lower than MEDs.

*Conclusions:* Preliminary results indicate that, after about a year, STN-DBS patients compared to MEDs presented a reduction of LEDD and stability in most cognitive tests while worsening in Semantic Verbal Fluency. This finding needs further neuroimaging and behavioral investigations and emphasizes the need to integrate cognitive assessment into the pre- and post-operative routine of DBS patients.

**References:**

[1] Bucur M., Papagno C. (2022). Deep Brain Stimulation in Parkinson's Disease: A Meta-analysis of the Long-term Neuropsychological Outcomes. Neuropsychological Review. DOI: 10.1007/s11065-022-09540-9.

**P13**

## Procedure-related pain in MRgFUS for the treatment of tremor in PD and ET patients

*Paolo Amami*[1], S. Prioni[1], M. Fusar Poli[1], E. Bocchi[1], N. Golfrè Andreasi[2], R. Cilia[2], L.M. Romito[2], A.E. Elia[2], G. Devigili[2], S. Rinaldo[2], G. Messina[3], V. Levi[3], M. Grisoli[4], M. Stanziano[4], F. Ghielmetti[5], E.F.M. Ciceri[6], M.G. Bruzzone[4], R. Eleopra[2], S.H.M.J. Piacentini[1]

[1]Clinical Neuropsychology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[2]Parkinson and Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[3]Functional Neurosurgey Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[4]Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[5]Health Physics Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[6]Interventional Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy

*Introduction:* Magnetic resonance-guided focused ultrasound (MRgFUS) targeting the ventral intermediate nucleus of the thalamus (Vim) is an effective treatment for medically refractory tremor in patients with essential tremor (ET) and tremor-dominant Parkinson's disease (PD). MRgFUS is an awake procedure in which the patient's cooperation with the clinician is pivotal for the treatment outcome. Pain during sonication and frame positioning are among the more frequent transient adverse events of the MRgFUS procedure. Pain can become so severe that the ablation has to be stopped prematurely, leading to incomplete ablation and reducing the effectiveness of the treatment.

*Objective:* The study aimed to investigate pain perception during the MRgFUS procedure and to identify factors that affect it.

*Methods:* Consecutive patients with ET and PD treated with unilateral MRgFUS of the Vim were enrolled. Pain perception during sonication and frame positioning was assessed using a visual analog scale (VAS) within one month of the surgery. Between-group and correlational analyses were performed.

*Results:* A total of 73 patients (34 PD and 39 ET) were enrolled. One-third (33%) of patients experienced "strong" to "heartbreaking" pain during sonication and 47% during frame positioning. There was no difference in pain intensity during MRgFUS depending on gender, side of the lesion, or disease. The perception of pain showed the strongest correlation with the skull density ratio (SDR) and significant correlations with the peak of the temperature, treatment duration, and pain during helmet placement. The number of sonications, the peak of the power (Watt), the cranial surface, mood symptoms, and anxiety symptoms before surgery were unrelated.

*Conclusions:* SDR is the main factor influencing pain intensity perception. During MRgFUS, attention must be paid to pain management, particularly for patients with low SDR scores.

**P14**

## Levodopa-carbidopa intestinal gel infusion associated complications: a retrospective study

*Gennaro Saporito*[1], F. Pistoia[1], C. Marini[2], D. Cerone[3], T. Russo[3], P. Sucapane[3]

[1]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[2]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[3]Department of Neurology, San Salvatore Hospital, L'Aquila, Italy

*Introduction:* Intra-duodenal infusion of levodopa-carbidopa intestinal gel (LCIG) is used in advanced Parkinson's disease (DS) to reduce motor fluctuations when oral therapy is no longer effective or tolerated. Although generally safe [1-2], LCIG may be associated with complications.

*Objectives:* This study aimed to investigate the clinical characteristics of PD patients treated with LCIG and the most common complications encountered in the follow-up.

*Methods:* We reviewed the medical files of PD patients treated with LCIG at the Clinical Neurological Unit of L'Aquila in the last five years. Adverse events (AE) were divided into 2 categories: percutaneous endoscopic gastrostomy (PEG)-related events (owing to the procedure environment) and LCIG-related events (owing to the effects of the medical treatment).

*Results:* 40 patients (57% male; mean age at LCIG start: 67.7 years-range 51-86) received LCIG infusion. The mean disease duration at LCIG start was 12.3 years. Rigidity and bradykinesia were the main symptoms in most of the patients (n=35; 87%) while tremor-dominant PD was recognized in the remainder (n=5; 13%). LCIG infusion was performed during daytime and stopped at bedtime: the mean morning dose was 7.9±2.2 ml, the mean continuous maintenance dose 3.1±0.9 ml/h and the mean extra dose 1.9±0.7 ml. During follow-up nine patients died (22%) while three patients discontinued the treatment (7.5%). Death was caused by aging-associated biological decline, except for one patient showing procedure-related bowel perforation. Treatment discontinuation was due to accidental removal of the J-tube (n=2; 5%) or poor compliance (n=3; 7.5%). PEG-related AE included peristomal (n=3; 7.5%) and tube complications (n=16; 40%): the most severe complications were postoperative pneumo-peritoneum (n=1; 2%), buried bumped syndrome (n=1; 2%) and bezoar formation (n=5; 12.5%). The most frequent LCIG-related event was weight loss (n=3; 7.5%).

*Conclusions:* Patients receiving LCIG should be carefully selected and monitored during the whole follow-period, to promptly face LCIG related complications.

**References:**

[1] Antonini A, Poewe W, Chaudhuri KR, Jech R, Pickut B, Pirtošek Z, Szasz J, Valldeoriola F, Winkler C, Bergmann L, Yegin A, Onuk K, Barch D, Odin P and the GLORIA study co-investigators. Levodopa-carbidopa intestinal gel in advanced Parkinson's: Final results of the GLORIA registry. Parkinsonism Relat Disord 2017;45:13-20.
[2] Zibetti M, Merola A, Artusi CA, Rizzi L, Angrisano S, Reggio D, De Angelis C, Rizzone M, Lopiano L. Levodopa/carbidopa intestinal gel infusion in advanced Parkinson's disease: a 7-year experience. Eur J Neurol. 2014 Feb;21(2):312-8.

**P15**

## Magnetic Resonance guided Focused UltraSound as interventional therapy in movement disorders: design and management of a highly complex pathway

*Sara Rinaldo*[5], M. Gammone[5], M. Catotti[5], N. Golfrè Andreasi[1], M. Fusar Poli[7], L.M. Romito[1], V. Levi[3], F. Colucci[1], A. Braccia[1], M. Stanziano[2], M. Grisoli[2], V. Caldiera[8], F. Ghielmetti[6], E. De Martin[6], M.L. Fumagalli[6], M. Corradi[1], F. Epifani[2], S. Prioni[7], P. Amami[7], S.H.M.J. Piacentini[7], V. Nazzi[3], F. Dimeco[4], E.F.M. Ciceri[8], M.G. Bruzzone[2], G.C. Moreschi[5], R. Eleopra[1]

[1]Department of Clinical Neurosciences, Movement Disorders Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Department of Diagnostics and Technology, Diagnostic Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[3]Neurosurgery Department, Functional Neurosurgery Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Neurosurgery Department, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[5]SITRA (nursing, technical and riabilitation service), Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[6]Medical Physics Service, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[7]Clinical Neuropsychology, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[8]Interventional Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

*Introduction:* High-intensity focused ultrasound ablation therapy under Magnetic resonance guidance (MRgFUS) is a non-invasive modality for the treatment of essential tremors and unilateral tremors in Parkinson's Disease [1]. Fondazione IRCCS Carlo Besta of Milan is one of the Italian institutes where it is available the 1.5T MRI for ablation treatments and where, since 2019, we perform the procedure.

*Objective:* To develop and apply a diagnostic-therapeutic care pathway (PDTA) for patients with movement disorders who are candidates for MRgFUS treatment. The secondary objective is to define and verify indicators that measure: appropriateness in the selection phase, correctness of the selection modalities, and effectiveness of the intake and follow-up phase.

*Methods:* A literature review was conducted that considered different study designs, including scientific evidence regarding Health Technology Assessment, which was examined and discussed. Based on the collected data [2], validated protocols, and analysis tools, the new PDTA was constructed and tested.

*Results:* First, a systematic and rigorous in-progress assessment process was set up as a basis for the analysis of context and environmental factors. Then a 3-stage PDTA (screening/treatment/follow-up) was developed, defining specific outcome indicators for each. Since 2020, more than 500 patients have been referred to our center: each year, the indicators have remained above the established threshold (>0.85). No adverse events, near missing, or sentinel events were reported; data on procedure-related side effects and remission times are similar to data reported in the literature.

*Conclusions:* The MRgFUS PDTA has created a new cross-sectional operating model. Given the multidisciplinary characteristics of the highly complex pathway, a coordination figure was implemented, which proved to be a strategic figure in the PLAN, DO, CHEK, and ACT phases.

**References:**

[1] Yamamoto K, Sarica C, Loh A, Vetkas A, Samuel N, Milano V, Zemmar A, Germann J, Cheyuo C, Boutet A, Elias GJ, Ito H, Taira T, Lozano AM. Magnetic resonance-guided focused ultrasound for the treatment of tremor. Expert Rev Neurother. 2022 Oct;22(10):849-861. doi: 10.1080/14737175.2022.2147826. Epub 2022 Dec 5. PMID: 36469578.

[2] Lorenz D, Poremba C, Papengut F, Schreiber S, Deuschl G. The psychosocial burden of essential tremor in an outpatient- and a community-based cohort. Eur J Neurol. 2011 Jul;18(7):972-9. doi: 10.1111/j.1468-1331.2010.03295.x. Epub 2011 Jan 18. PMID: 21244579.

**P16**

## Subthalamic Nucleus - Deep Brain Stimulation deteriorates speech in Parkinson's disease: a machine learning study

*Francesco Asci*[1,2], G. Costantini[3], F. Bove[4], C. Piano[4], F. Pistoia[5,6], R. Cerroni[7], L. Brusa[8], V. Cesarini[3], S. Pietracupa[1,2], N. Modugno[2], A. Zampogna[1], P. Sucapane[6], M. Pierantozzi[7], T. Tufo[9,10], A. Pisani[11,12], A. Peppe[13], A. Stefani[7], P. Calabresi[4], A. Rita Bentivoglio[4], G. Saggio[3], A. Suppa[1,2] and Lazio DBS Study Group

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed Institute, Pozzilli, Italy
[3]Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy
[4]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[5]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[6]Neurology Unit, San Salvatore Hospital, L'Aquila, Italy
[7]Department of System Medicine, University of Rome Tor Vergata, Rome, Italy
[8]Neurology Unit, S. Eugenio Hospital, Rome, Italy
[9]Neurosurgery, Policlinico A. Gemelli University Hospital Foundation IRCSS, Rome, Italy
[10]Neurosurgery Department, Fakeeh University Hospital, Dubai, UAE
[11]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[12]IRCCS Mondino Foundation, Pavia, Italy
[13]IRCSS Fondazione Santa Lucia, Rome, Italy

*Introduction:* Deep brain stimulation of the subthalamic nucleus (STN-DBS) can worsen speech in Parkinson's disease (PD).

*Objective:* We here examined voice impairment objectively in STN-DBS patients, by using artificial intelligence.

*Methods:* We enrolled 108 controls and 101 patients (50 with STN-DBS and 51 under the best medical treatment). Voice was clinically evaluated using the Unified Parkinson's Disease Rating Scale part-III subitem for voice (UPDRS-III-v). We recorded and then analysed voices using specific machine-learning algorithms. The likelihood ratio (LR) was also calculated as an objective measure for clinical-instrumental correlations.

*Results:* Clinically, voice impairment was greater in STN-DBS patients than in those under oral treatment. Machine-learning discriminated voices recorded from STN-DBS patients and those under oral treatments, objectively and with high accuracy. We also found significant clinical-instrumental correlations since the greater LRs, the higher UPDRS-III-v scores.

*Conclusions:* STN-DBS deteriorates speech in patients with PD as objectively demonstrated by machine-learning voice analysis.

**P17**

## Evaluation of factors affecting tremor recurrence after MRgFUS thalamotomy

*Patrizia Sucapane*[1], G. Saporito[2], C. Marini[3], D. Cerone[1], T. Russo[1], F. Bruno[2], A. Catalucci[4], A. Splendiani[2], F. Pistoia[1,2]

[1]Neurology, San Salvatore Hospital, 67100 L'Aquila, Italy
[2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[3]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[4]Neuroradiology and Interventional Radiology, San Salvatore Hospital, L'Aquila, Italy

*Background:* MRgFUS thalamotomy is a new treatment minimal invasiveness for intractable tremor due to Essential Tremor (ET) or Parkinson's Disease (PD). Objective our study is to identify possible relevant factors contributing to tremor relapse (defined an increase in the FTM score of > 5 points compared to baseline) after MRgFUS thalamotomy in patients with essential tremor (ET) and Parkinson's disease (PD).

*Methods:* We identified patients with tremor relapse from a series of 80 patients treated with MRgFUS in the institute of L'Aquila. The demographic and clinical characteristics of the study group patients were compared to those of patients who did not relapse in the same follow-up period. Imaging and procedural factors were compared using a control group matched for clinical and demographic characteristics.

*Results:* Concerning clinical and demographic characteristics, we did not find statistically significant differences in gender and age. Seventy-three percent of patients with tremor relapse were Parkinson's disease patients. Using MRI, we found larger thalamotomy lesions at the 1-year follow-up in the control group with stable outcomes, compared to patients with tremor relapse. In the tractography evaluation, we found a more frequent eccentric position of the DRTt in patients with tremor relapse.

*Conclusions:* The most relevant determining factors for tremor relapse after MRgFUS thalamotomy appear to be tremor from Parkinson's disease and inaccurate thalamic targeting. Size of the thalamotomy lesion can also influence the outcome of treatment.

**P17**

## Evaluation of factors affecting tremor recurrence after MRgFUS thalamotomy

*Patrizia Sucapane*[1], G. Saporito[2], C. Marini[3], D. Cerone[1], T. Russo[1], F. Bruno[2], A. Catalucci[4], A. Splendiani[2], F. Pistoia[1,2]

[1]Neurology, San Salvatore Hospital, 67100 L'Aquila, Italy
[2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[3]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[4]Neuroradiology and Interventional Radiology, San Salvatore Hospital, L'Aquila, Italy

*Background:* MRgFUS thalamotomy is a new treatment minimal invasiveness for intractable tremor due to Essential Tremor (ET) or Parkinson's Disease (PD). Objective our study is to identify possible relevant factors contributing to tremor relapse (defined an increase in the FTM score of > 5 points compared to baseline) after MRgFUS thalamotomy in patients with essential tremor (ET) and Parkinson's disease (PD).

*Methods:* We identified patients with tremor relapse from a series of 80 patients treated with MRgFUS in the institute of L'Aquila. The demographic and clinical characteristics of the study group patients were compared to those of patients who did not relapse in the same follow-up period. Imaging and procedural factors were compared using a control group matched for clinical and demographic characteristics.

*Results:* Concerning clinical and demographic characteristics, we did not find statistically significant differences in gender and age. Seventy-three percent of patients with tremor relapse were Parkinson's disease patients. Using MRI, we found larger thalamotomy lesions at the 1-year follow-up in the control group with stable outcomes, compared to patients with tremor relapse. In the tractography evaluation, we found a more frequent eccentric position of the DRTt in patients with tremor relapse.

*Conclusions:* The most relevant determining factors for tremor relapse after MRgFUS thalamotomy appear to be tremor from Parkinson's disease and inaccurate thalamic targeting. Size of the thalamotomy lesion can also influence the outcome of treatment.

**P19**

## Low frequency reduces interference of cognitive workload on gait in subthalamic nucleus DBS for advanced Parkinson's disease

*Vittorio Rispoli*[1], F. Colucci[2,3], G. Ferraresi[4], M. Morelli[4], A. Gozzi[2,3], P. Antenucci[2,3], M. Cosma[4], M.A. Cavallo[5], M. Sensi[3]

[1]Neurology, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy
[3]Neurology, Department of Neuroscience and Rehabilitation, Azienda Ospedaliero-Universitaria S. Anna, Ferrara, Italy
[4]Movement Analysis Laboratory, Neuroscience and Rehabilitation Department, University Hospital S. Anna, Ferrara, Italy
[5]Neurosurgery, Department of Morphology, Surgery and Experimental Medicine, University Hospital S. Anna, Ferrara, Italy

*Background:* The clinical benefits of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) for advanced Parkinson's disease (aPD) may be reduced by gait disorders onset occurring months or years after the implant. Little is known about their pathophysiology and the management is usually difficult and not fruitful. Literature suggests reducing the stimulation frequency below 100 Hz and the reported efficacy of this approach for freezing of gait is variable.

*Objectives:* (1) To explore how low frequency stimulation change gait in aPD compared to conventional high frequency stimulation (HF); (2) To uncover possible pathophysiological mechanisms for LF-related gait improvement compared to HF.

*Methods: P*atients complaining freezing of gait and affected by aPD with bilateral STN DBS implant without cognitive impairment (MoCA >26/30) were enrolled. As per protocol, each participant was assessed at baseline in OnMeds/OffStim and OnMeds/ONStim with HF as well as one month after switching to LF, namely 80 Hz. Motor symptoms and gait were evaluated in each therapeutic condition through UPDRS-III, Modified Hoehn & Yahr Scale (H&Y) and gait analysis. The latter was performed by employing 3 accelerometers (one in each foot and one at L2 lumbar level) in the 2-Minute-Walk-Test as a single motor task, as a dual motor task and with a cognitive interfering task. Moreover, participants were asked to perfomed a modified timed-up-and-go (mTUG). Finally, PDQ-39, DBS-IS, UPDRS-I, UPDRS-II and FOG-Q were administrated at baseline and at follow-up.

*Result:* No significant changes were detected by mTUG and clinical scales. Conversely, gait analysis disclosed a remarkable improvement in a number of gait microparameters when comparing LF to HF and LF vs OFFstim condition, only. In fact, no significant differences were found when comparing these therapeutic conditions for gait as single motor task or during a concomitant motor task.

*Conclusions:* 80 Hz STN DBS improves gait disorders during interfering cognitive workload as compared to HF and OFFstim in aPD without dementia. These findings may be of help in drawing more effective flow-chart in treating gait disorders occurring after STN-DBS.

**P20**

## The acute effects of DBS on cardiovascular autonomic and sudomotor function

*Kristi Meksi*[1], L. Brusa[2], C. Piano[3], F. Bove[3], E. Garasto[1], R. Cerroni[4], N.B. Mercuri[1], A. Stefani[4], C. Rocchi[1]

1 Neurology Unit, Policlinico Tor Vergata, University of Rome "Tor Vergata", Rome, Italy
2 Neurology Unit, Ospedale S.Eugenio, Rome, Italy
3 Neurology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
4 Parkinson's Disease Center, Policlinico Tor Vergata, University of Rome "Tor Vergata", Rome, Italy

*Introduction:* Deep brain stimulation of the subthalamic nucleus (STN-DBS) is an effective treatment option for advanced Parkinson's disease (PD). Currently, there are few and contradictory data on the effects of DBS on the autonomic nervous system [1-2].

*Aim:* To examine the acute cardiovascular and sudomotor effect in 10 patients with advanced PD in whom electrodes had been implanted in the bilateral STN. Heart rate (HR), blood pressure (BP) and respiratory rate were continuously recorded under supine resting conditions and at the 3rd and 10th minute head-up tilt test at 65° (HUTT). Sudomotor function was assessed by means of the Sudoscan. Patients were examined under three conditions: with deep brain stimulation in progress and CAPIT condition (DBS on/Th off), 30 minutes after switching off the DBS, in CAPIT (DBS off /Th off) and 30 minutes after switching on the stimulator and in best on condition after administering melevodopa/carbidopa 100/25 mg (DBS on /Th on). The pre-HUTT supine (baseline) values of systolic and dystolic BP and HR and the changes expressed as delta (raw data) from baseline were compared with those recorded during HUTT at minute 3' and minute 10' by t-test. Statistical significance was set at $p<0.05$.

*Results:* A significant reduction in systolic BP was found at minute 10 of HUTT only in the DBS on/Th on condition. No other significant differences in HR, BP and sudomotor function were found among the three conditions.

*Conclusions:* STN stimulation has no significant impact on HR and BP under basal conditions and during orthostatic stress. Sudomotor function was also not affected. The reduction of systolic BP at 10 min in the DBS on/Th on condition is related to the effect of acute therapy. DBS may exert a positive effect on cardiovascular reactivity with indirect mechanism as it allows the levodopa load.

**References:**

[1] Kaufmann H, Bhattacharya KF, Voustianiouk A, Gracies JM. Stimulation of the subthalamic nucleus increases heart rate in patients with Parkinson disease. Neurology. 2002 Nov 26;59(10):1657-8. doi: 10.1212/01.wnl.0000034180.21308.c0. PMID: 12451221.
[2] Stemper B, Beric A, Welsch G, Haendl T, Sterio D, Hilz MJ. Deep brain stimulation improves orthostatic regulation of patients with Parkinson disease. Neurology. 2006 Nov 28;67(10):1781-5. doi: 10.1212/01.wnl.0000244416.30605.f1. PMID: 17130410.

**P21**

## Bilateral double beta peak activity is influenced by stimulation, levodopa concentrations and motor tasks in a Parkinson's disease patient on chronic deep brain stimulation

*Giulia Giannini*[1,2], L. Baldelli[2], G. Leogrande[3], I. Cani[2], P. Mantovani[4], G. Lopane[5], P. Cortelli[1,2], G. Calandra Buonaura[1,2], A. Conti[2,4]

[1]UOC Clinica Neurologica Rete Metropolitana NEUROMET, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[2]Department of Biomedical and NeuroMotor Sciences (DiBiNeM), Alma Mater Studiorum - University of Bologna, Italy
[3]Medtronic EMEA Corporate Technology & Innovation, Maastricht, The Netherlands
[4]Unit of Neurosurgery, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[5]Unit of Rehabilitation Medicine, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

*Introduction:* Subthalamic (STN) local field potentials (LFP) in the beta band are considered as potential biomarkers for closed-loop deep brain stimulation (DBS) in Parkinson's disease (PD). The beta band is further dissected into the low and the high frequency components with somewhat different functions, although their concomitance and association in the single patient is far to be defined. We present a 56-year old male PD patient undergoing DBS showing a double beta peak activity on both sides.

*Objective:* To investigate how low and high beta peaks were influenced by plasma levodopa (L-dopa) levels, stimulation and motor performances.

*Methods:* A systematic evaluation of raw LFP, plasma L-dopa levels and motor tasks was performed in the following four conditions: OFF medications/ON stimulation; OFF medications/OFF stimulation; ON medications/OFF stimulation; ON medications/ON stimulation.

*Results:* The analysis of the LFP spectra suggests the following results: 1) some PD patients show a double beta peak activity; 2) both the high and the low beta peaks are suppressed by stimulation; 3) the high beta peak is influenced also by plasma L-dopa concentration showing a progressive amplitude increment concordant with plasma L-dopa levels, while the low beta peak shows a different behaviour; 4) motor performances seem to impact beta peaks behaviour.

*Conclusions:* This single exploratory case study illustrates a complex behaviour of low and high beta peaks in a PD patient, in response to stimulation, L-dopa plasma levels and motor performances. Our results suggest the importance to investigate patient-specific individual LFP patterns in view of upcoming closed-loop stimulation.

**P22**

## Magnetic resonance imaging focused ultrasound thalamotomy, assesment of factors affecting risk of recurrence by Clinical Rating Tremor Scale scores: clinical and gender influence?

*Patrizia Sucapane*[1], G. Saporito[2], C. Marini[3], D. Cerone[1], T. Russo[1], F. Bruno[2], A. Catalucci[4], A. Splendiani[2], F. Pistoia[2]

[1]Department of Neurology, San Salvatore Hospital, L'Aquila, Italy
[2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[3]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[4]Neuroradiology and Interventional Radiology, San Salvatore Hospital, L'Aquila, Italy

*Introduction:* Magnetic resonance imaging-guided focused ultrasound (MRgFUS) thalamotomy is an innovative treatment for medically refractory tremor. The recurrence rate of tremor after thalamotomy is about 11% within six months after surgery. No studies comprehensively analyze the factors influencing tremor recurrence at follow-up.

*Objective:* To evaluate the influence of anagraphical and clinical parameters on post-treatment clinical outcomes.

*Methods:* We retrospectively evaluated all patients showing a tremor recurrence, defined as an increase in Clinical Rating Scale (CRST) score $\leq 2$ or $\geq 5$. All patients underwent clinical follow-up at one month, six months and one year after treatment.

*Results:* Forty-five patients (mean age 67.6±8.9; mean disease 15.7±14.3) with ET (n=24) and PD-related tremor (n=21) were included. Considering the whole sample, it was observed that one year after treatment both the total CRST (12.2%) as well as Part A (15.6%) showed a slight increase in scores. Stratifying the sample by gender, the analysis showed that women, at one year after treatment, presented a slight flare-up of tremor with a rate of 19.3% (16.6±13.4 Vs19.8±16.3) as compared to 10.4% (16.7±8.3 Vs 18.4±12.1) of men in total CRST scores. When considering patients separately a slight increase (19.8%) is recognized in PD patients at one year post treatment in total CRST scores (15.5±10.3 Vs 17.5±13.0) as well as in part A 19.2% (5.6±3.6 Vs 6.7±4.0) as compared to 11.7% (total CRST 17.7±8.6 Vs 19.7±12.9) and 12.9% (CRST part A 6.4±3.2 Vs 7.2±4.1) of ET patients. In contrast, stratifying the sample by gender and diagnosis a slight increase in CRST scores is observed in ET women (15.3±8.9 Vs 27.0±19.6) and PD men (14.8±7.7 Vs 18.0±12.7).

*Conclusions:* Clinical variable and gender, together with neuroradiological parameters, should be considered to investigate and predict the recurrence rate in patients undergoing MRgFUS thalamotomy.

**P23**

## Levodopa-induced orthostatic hypotension in parkinsonism: a red flag of autonomic failure

*Ilaria Cani*[1], P. Guaraldi[2], G. Giannini[1,2], L. Sambati[2], G. Barletta[2], P. Cortelli[1,2], G. Calandra Buonaura[1,2]

[1]Department of Biomedical and NeuroMotor Sciences (DIBINEM), Alma Mater Studiorum - University of Bologna, Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

*Introduction:* Levodopa (LD) is the main treatment for parkinsonism, but its use may be limited by a potential hypotensive effect.

*Objective:* To evaluate the cardiovascular and hemodynamic effect of LD in patients with parkinsonism on chronic LD treatment.

*Methods:* Head-up tilt test were performed before and 60 minutes after 100/25mg LD/dopa-decarboxylase inhibitor (pre-LD vs post-LD HUTT) in 164 patients. Features predictive of LD-induced orthostatic hypotension (OH) were assessed by logistic regression analysis.

*Results:* Basal supine blood pressure (BP) and heart rate (HR) decreased after LD. During post-LD HUTT, BP drop and HR increase were significantly greater than at pre-LD HUTT. A proportion of 37% of patients had OH at post-LD HUTT compared to 22% of patients presenting OH at pre-LD HUTT ($p<0.001$). Risk factors for LD-induced/worsened OH were pre-LD OH [odds ratio (OR): 36; 95% confidence interval (CI):10-131], absence of overshoot at Valsalva maneuver [OR: 9; CI:4-20] and pathological Valsalva ratio [OR: 6; CI:2-15]. Hemodynamic data showed a steady decrease in HR and left ventricular contractility after LD administration.

*Conclusion:* The 100/25mg LD/dopa-decarboxylase inhibitor administration caused hypotension in both supine and orthostatic conditions primarily mediated by a cardioinhibitory mechanism. Patients with cardiovascular autonomic failure had a higher risk of developing LD-induced OH. In clinical practice, LD-induced OH could represent a red flag for cardiovascular autonomic failure.

**P24**

## Progressive supranuclear palsy phenotyping: a data-driven approach from the PSP-NET

*Filomena Abate*, P. Barone, M. Picillo for PSP-NET

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Salerno, Italy

*Introduction:* Progressive supranuclear palsy (PSP) is an atypical parkinsonism diagnosed according to the Movement Disorder Society (MDS) criteria [1]. On the basis of expert opinion, different phenotypes have been identified [1]. However, phenotype attribution is often difficult and complex hierarchical rules are needed to overcome the frequent overlapping. Moreover, a data-driven approach to describe PSP phenotyping has not been explored yet.

*Objective:* To identify PSP phenotypes with unsupervised machine learning algorithms.

*Methods:* Three hundred eighty-one patients from the Italian PSP-NET supported by Fondazione LIMPE [3] were assessed by the PSP rating scale [4] and the Montreal Cognitive Assessment [5]. All records were systematically combined to obtain pre-specified PSP feature scoring and used as variables for a two-step cluster analysis. One-way ANOVA and Chi-squared test were used to determine differences among clusters in disease duration and MDS phenotype distribution.

*Results:* Four different clusters were found. Cluster 1 (n=70) presented prominent axial impairment, postural instability and oculomotor dysfunction. Cluster 2 (n=84) had mild PSP features with prominent appendicular involvement. Cluster 3 (n=131) presented major frontal and language impairment, with partial levodopa response. Cluster 4 (n=96) had freezing of gait with partial levodopa response. No significant differences were found in disease duration and MDS phenotype distribution among clusters (p=0.397 and p=0.8, respectively).

*Conclusions:* Four clinical clusters based on PSP clinical features have been identified. Interestingly, they do not completely overlap with classical MDS phenotypes. We hypothesize that specific combinations of features, each with a different weight, have a prominent role in the definition of phenotypes. As such, a simple hierarchical phenotype attribution may not represent the best solution to assign PSP phenotypes [1-2]. Nonetheless, this is a preliminary analysis and further studies are needed to define the reproducibility and the clinical significance of the proposed clusters.

**References:**

[1] Höglinger, G.U., Respondek, G., Stamelou, M., et al. Clinical diagnosis of progressive supranuclear palsy: the movement disorder society criteria. Mov Disord 2017; 32: 853–864.

[2] Grimm MJ, Respondek G, Stamelou M, et al.; Movement Disorder Society-endorsed PSP Study Group. How to apply the movement disorder society criteria for diagnosis of progressive supranuclear palsy. Mov Disord. 2019; 34(8): 1228-1232.

[3] https://www.fondazionelimpe.it/network-paralisi-sopranucleare-progressiva

[4] Golbe, L.I., Ohman-Strickland, P.A. A clinical rating scale for progressive supranuclear palsy. Brain 2007; 130: 1552-1565.

[5] Nasreddine Z.S., Phillips N.A., Bédirian V. et al. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. Journal of the American Geriatrics Society 2005; 53: 695-699.

**P25**

## Quantitative spatio-temporal gait parameters while walking and dual tasking in functional gait disorders: a possible new biomarker

*Giulia Bonardi*, M. Gandolfi, Z. Menaspà, C. Geroin, N. Smania, M. Fiorio, M. Tinazzi

Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Functional gait disorders (FGDs) are disabling symptoms of Functional Motor Disorders. Clinical observations show gait improvement with distraction suggesting an association with higher-level control mechanisms [1-2]. Dual tasking is a valuable tool for exploring the interplay between gait and cognition [3].

*Objective:* To identify measures of quantitative spatio-temporal gait parameters while walking and dual tasking in FGDs that best discriminate performance from healthy controls.

*Methods:* This observational cross-sectional study enrolled 76 patients with FGDs (77.63% females; mean age 41.85±15.26) and 42 healthy controls (59.52% females; mean age 42.14±16.03). An electronic walkway performed spatio-temporal gait analysis under a single task (ST), a motor DT (mDT), a cognitive DT (cDT), and a visual-fixation DT (vDT) [1-3]. Outcome measures included gait speed (cm/s), swing time variability (%), and stride time variability (%) as a measure of high-level gait control [2]. The Dual Task effect (DTE, %) was calculated to evaluate the gait performance changes induced by the dual task with respect to a single task [3].

*Results:* Overall lower gait speed and higher stride time variability were noted in FGDs compared to healthy controls (for all, $p<0.001$). No significant Task×Group interactions were detected in any gait measure. The was a significant effect of group and Task×Group interaction for the dual-task effect on gait speed ($p <0.001$) but not for swing and stride time variability.

*Conclusions:* FGDs reported poorer gait performance and less automaticity and steadiness than healthy controls. However, gait performance but not automaticity and steadiness were affected by dual tasking, unlike different neurological diseases. Our findings shed light on higher-level gait control mechanisms in FGDs and suggest stride time and swing time variability as potential diagnostic biomarkers.

**References:**

[1] Gandolfi et al., 2021; Motor dual task with eyes closed improves postural control in patients with functional motor disorders: A posturographic study; Gait Posture.

[2] Geroin et al., 2018; Does dual-task training improve spatiotemporal gait parameters in Parkinson's disease?; Park Relat Disord.

[3] Gandolfi et al., 2023; Dual tasking affects gait performance but not automaticity in functional gait disorders: A new diagnostic biomarker Park Relat Disord.

**P26**

## Opinion, knowledge, and clinical experiences with functional neurological disorders among Italian psychiatrists: results from a national survey

*Angela Marotta*[1], M. Fiorio[1], A. Lasalvia[1], M.L. Nasi[2], E. Zalanda[3], G. Di Sciascio[4], C. Palumbo[4], D. Papola[1], C. Barbui[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of General Psychology, University of Padova, Padova, Italy
[3]Department of Mental Health, ASL Bari, Bari, Italy
[4]Department of Mental Health ASL TO3 & AOU San Luigi Gonzaga, Collegno, Torino, Italy

*Introduction:* Functional neurological disorder (FND) is characterized by motor, sensory, and cognitive symptoms that are incongruent with abnormalities due to a known organic cause [1]. A novel multidisciplinary approach to the diagnosis and treatment of FND has been recently proposed, with a growing body of evidence suggesting its efficacy [2]. Psychiatrists can play an essential role in managing FND, from establishing a diagnosis to developing tailored therapeutic plans for patients [3]. Thus, understanding their knowledge, opinion, and clinical approach to FND in light of the new approach to the illness is of utmost importance to highlight potential educational needs and improve patient care.

*Objective:* We surveyed Italian psychiatrists to explore their knowledge, opinion, and clinical experiences with FND.

*Methods:* Members of the Italian Society of Psychiatry (SIP) were invited via e-mail to complete an ad hoc 14-item web-based survey.

*Results:* 179 questionnaires were completed. “Conversion disorders” was the term most frequently used by Italian psychiatrists to refer to FND, thus conveying a psychological etiology of FND. Congruently with this view, many respondents stated that psychotherapy associated with pharmacological therapy was the most appropriate treatment for patients, while very few considered physiotherapy a useful approach to FND.

*Conclusions:* Our main findings suggest that Italian psychiatrists still have a psychogenetic conceptualization of FND. This could be due to poor knowledge about novel advances in the pathophysiology of these disorders. Professional education about novel approaches to FND would be an advantageous way to optimize psychiatrists’ management of FND and to enhance diagnosis, explanation, and management across health professionals, in line with a multidisciplinary approach to FND.

**References:**

[1] Hallett, 2018. Parkinsonism Relat Disord; 46 (Suppl 1): S80–S82.
[2] Gilmour et al., 2020. J Neurol; 267(7):2164-2172.
[3] Bègue I et al., 2021. Psychol Med; 51(12):1961-1963.

**P27**

## Diagnosis and care of functional neurological disorders across cultures: the Italian, Czechian, and Slovakian experience

*Angela Marotta*[1], M. Fiorio[1], I.A. Di Vico[1], M.L. Nasi[2], M. Tinazzi[1], L. Nováková[3], E. Růžička[3], T. Serranova[3]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of General Psychology, University of Padova, Padova, Italy
[3]Department of Neurology and Centre of Clinical Neuroscience, General University Hospital and First Faculty of Medicine, Charles University, Prague, Czech Republic

*Introduction:* Functional neurological disorder (FND) presents motor, sensory and cognitive symptoms that display clinical features incompatible with other neurologic conditions [1]. Novel approaches to the diagnosis and treatment of FND have been recently proposed, with improved efficacy in the management of this disabling condition [2]. Yet, culturally based differences in the adoption of the novel approach to FND still need to be established.

*Objective:* The current cross-cultural study tackles this issue by investigating the knowledge, opinion, and clinical experiences with FND among Italian, Czech, and Slovak neurologists.

*Methods:* Czech and Slovak neurologists completed a 14-item web-based survey investigating their approach to FND. The questionnaire was adapted from a previous one used by our group to survey Italian neurologists [3]. Results. 232 questionnaires were completed by Czech (n=172) and Slovak (n=60) neurologists. Due to the lack of significant differences, data from these countries were merged and compared with the responses of 490 Italian neurologists.

*Results:* Our main findings highlighted many similarities between Italian, Czech, and Slovak neurologists: the term “Functional neurological disorders” was used more frequently than other psychological-related terms (e.g., conversion disorder); congruently, respondents preferred explaining symptoms based on abnormal functioning of the nervous system than discussing mental illness, thus suggesting shared terminology and up-to-date conceptualization of FND. Yet, some differences stood out: Czech and Slovak neurologists were more likely to ask for additional neurological investigations (e.g., MRI), and to suggest physiotherapy as a treatment option for patients; more prone to provide educational intervention for patients and their relatives.

*Conclusions:* Despite the adoption of some new developments in the field of FND, further training is needed to improve knowledge of the diagnostic and therapeutic options for FND and to optimize patient management in different countries.

**References:**

[1] Hallett, 2018. Parkinsonism Relat Disord; 46 (Suppl 1):S80–S82.
[2] Gilmour et al., 2020. J Neurol; 267(7):2164-2172.
[3] Tinazzi et al., 2022. J Neurol; 269(5):2549-2559.

**P28**

## Relationship between bradykinesia and cognitive functions in patients with essential tremor

*Daniele Birreci*[1], G. Paparella[2], L. Angelini[1], A. Di Vita[1], R. Margiotta[1], A. Cannavacciuolo[2], D. Costa[1], M. De Riggi[1], M. Passaretti[1], D. Alunni Fegatelli[3], A. Berardelli[1,2], M. Bologna[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, IS, Italy
[3]Department of Public Health and Infectious Diseases, Sapienza, University of Rome, Rome, Italy

*Introduction:* Bradykinesia in essential tremor (ET) is one of the so-called 'soft signs' configuring the diagnosis of ET-plus [1-2-3]. Cognitive disturbances may also occur in ET with a higher prevalence than in the general population [1]. Though it has been demonstrated that soft signs often occur in combination, the relationship between bradykinesia and cognitive dysfunction in ET patients has never been explored [4].

*Aims:* To further investigate the association between bradykinesia, as objectively assessed with kinematic analysis, and cognitive functions in ET.

*Methods:* 45 ET patients (23 F, mean age: 66.48±13.69) underwent kinematic recordings of finger-tapping movements with an optoelectronic motion system. A comprehensive cognitive evaluation, including the assessment of executive and visuo-constructional functions, attention, and memory, was also performed on participants. Automatized algorithms were used for kinematic analysis, providing objective measurement of movement velocity and movement rhythm (expressed as coefficient of variation - CV, with higher values indicating a more irregular rhythm). Possible associations between kinematics and raw cognitive scores were assessed by using the Pearson correlation coefficient.

*Results:* We found a positive correlation between movement velocity and the Rey-Auditory Verbal Learning Test (RAVLT) immediate and delayed recall ($r=0.3$, $p=0.04$ and $r=0.35$, $p=0.019$, respectively). A negative association was found between CV and Forward Digit span scores ($r=-0.3$, $p=0.039$). Finally, CV values positively correlated with the Modified Card Sorting Test (MCST) errors ($r=0.43$, $p=0.024$). These results overall indicate that the lower the movement velocity and the more irregular the rhythm, the worse the performance on tests exploring memory and executive functions.

*Conclusions:* We here demonstrated a relationship between finger-tapping bradykinesia and memory and executive dysfunctions in ET. Our results are relevant for a better understanding of ET and ET-plus pathophysiology.

**References:**

[1] Bhatia KP, Bain P, Bajaj N, Elble RJ, Hallett M, Louis ED, Raethjen J, Stamelou M, Testa CM, Deuschl G; Tremor Task Force of the International Parkinson and Movement Disorder Society. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018 Jan;33(1):75-87. doi: 10.1002/mds.27121. Epub 2017 Nov 30. PMID: 29193359; PMCID: PMC6530552.
[2] Paparella G, Fasano A, Hallett M, Berardelli A, Bologna M. Emerging concepts on bradykinesia in non-parkinsonian conditions. Eur J Neurol. 2021 Jul;28(7):2403-2422. doi: 10.1111/ene.14851. Epub 2021 May 18. PMID: 33793037.
[3] Bologna M, Paparella G, Colella D, Cannavacciuolo A, Angelini L, Alunni-Fegatelli D, Guerra A, Berardelli A. Is there evidence of bradykinesia in essential tremor? Eur J Neurol. 2020 Aug;27(8):1501-1509. doi: 10.1111/ene.14312. Epub 2020 May 31. PMID: 32396976.
[4] Bologna M, Guerra A, Colella D, Cioffi E, Paparella G, Di Vita A, D'Antonio F, Trebbastoni A, Berardelli A. Bradykinesia in Alzheimer's disease and its neurophysiological substrates. Clin Neurophysiol. 2020 Apr;131(4):850-858. doi: 10.1016/j.clinph.2019.12.413. Epub 2020 Jan 27. PMID: 32066104.

**P29**

## Turning alterations in idiopathic REM sleep behaviour disorders

*Cinzia Zatti*[1], A. Pilotto[1], C. Hansen[2], A. Rizzardi[1], M. Catania[1], R. Romijnders[2], M.P. Pasolini[3], A. Galbiati[4], L. Ferini-Strambi[4], E. Schaeffer[2], D. Berg[2], W. Maetzler[2], A. Padovani[1,3]

[1]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Italy
[2]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany
[3]Department of Clinical and Experimental Sciences, Neurophysiology Unit, University of Brescia, Italy
[4]IRCCS San Raffaele Scientific Institute, Department of Clinical Neurosciences, Neurology-Sleep Disorders Centre, Milan, Italy

*Introduction:* State specific objective of study: Idiopathic REM sleep behaviour Disorder (iRBD) is a condition at higher risk of developing Parkinson's disease (PD) or other alpha-synculeinopathies. Aim of the study was to evaluate with Mobile health technology (MHT) subtle alterations of turning in iRBD subjects even in absence of parkinsonism at clinical examination.

*Methods:* The prospective study included consecutively individuals with PSG-confirmed iRBD, drug-naïve PD patients and healthy controls. Each individual underwent a multidimensional assessment including evaluation of motor and non-motor symptoms, cognitive status and comorbidity. All individuals were asked to perform Timed Up and Go test (TUG) both at normal and fast speed in clockwise and anti-clockwise supervised conditions using MHT. The turning parameters evaluated were mean, starting, middle and ending angular velocity and peak angular velocity of turning in different conditions.

*Results:* the study included 23 individuals with iRBDs, 61 drug-naïve PD patients and 80 controls. No iRBD showed a subthreshold parkinsonism at examination (MDS-UPDRS-III iRBD 2.26±2.01, PD 15.62±9.65). Angular velocity was reduced in all phases of turning (starting, middle, ending) with reduced mean and peak velocities in PD compared to controls in both normal and fast TUG ($p=<0.001$). iRBDs exhibited a reduced mean angular velocity compared to HC in both normal and fast conditions ($p=0.001$). iRBDs showed similar mean angular velocity in comparison to PD in normal TUG, but higher mean velocity in fast tests ($p=0.001$).

*Conclusion:* MHT assessment of turning identified subtle alterations in iRBDs, even in absence of parkinsonism at evaluation. Further longitudinal studies are warranted to evaluate the value of angular velocity in defining the risk of conversion and track the subtle motor progression in prodromal phases of PD.

**P30**

## Apraxia of speech in progressive supranuclear palsy: the use of video recordings to facilitate diagnosis

*Luisa Sambati*[1 2], L. Romano[2], F. Baschieri[1, 2], P. Guaraldi[1], G. Giannini[1,2], P. Cortelli [1,2], G. Calandra Buonaura[1,2]

[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[2]Dipartimento di Scienze Biomediche e Neuromotorie di Bologna, Bologna, Italy

*Objectives:* The aim of our study is to describe clinical characteristics of Apraxia of Speech (AOS) in a group of patients with probable Progressive Supranuclear Palsy (PSP), by viewing video recordings of the language assessment.

*Materials:* We administered the Apraxia of Speech Rating Scale 3.0 (ASRS 3.0) [1], while watching the video recording of the patients' performance at the Screening for Aphasia in NeuroDegeneration (SAND) and the patient's free description of a "typical day". Items 9, 10 and 11 of ASRS 3.0 were not used for the present study, as they were linked to the Alternate Motion Rate (AMR) and Sequential Motion Rate (SMR) tasks, not included in the original language assessment. Therefore, the maximum detectable score was 40 points instead of 52.

*Methods:* We retrospectively recruited 10 PSP patients from the Movement Disorder Clinic of the IRCCS Institute of the Neurological Sciences of Bologna. All participants had undergone full neuropsychological evaluation including language function assessment, we viewed each video by applying the protocol previously reported.

*Results:* No significant aphasic deficits were reported. Comprehension of Sentences and Reading were the only two compromised linguistic components. Two subjects presented clear signs of AOS while only one had no manifestation of AOS, the remaining showed mild signs. Six participants produced sound distortions, but only in one case they were frequent and pervasive, while five patients showed distorted sound substitutions. Two subjects presented a marked slow overall speech rate, while four manifested syllable segmentation within words and across words. Two subjects displayed a systematic tendency to lengthened vowel segments. Two patients showed false starts, indicating difficulty in articulating the first syllable of the word. No patient had clear signs of groping.

*Discussion:* In our study, video recordings proved to be extremely important to facilitate the differential diagnosis between AOS, dysarthria and aphasia, and may be useful to longitudinally monitor the evolution. We confirm that video recordings are a valid and useful resource in clinical practice [2].

*Conclusions:* This study points out that most of our sample of PSP patients had signs of AOS, albeit mild. It will be necessary to expand the current assessment protocol, adding AMR and SMR tasks. The present findings support the importance of integrating standard assessment protocols for these patients, to refine the diagnostic practice and be able to more effectively describe the linguistic profiles that better characterize PSP.

**References:**

[1] Wambaugh JL, Bailey DJ, Mauszycki SC, Bunker LD. Interrater Reliability and Concurrent Validity for the Apraxia of Speech Rating Scale 3.0: Application With Persons With Acquired Apraxia of Speech and Aphasia. Am J Speech Lang Pathol. 15 2019;28(2S):895–904.

[2] Sambati L, Baldelli L, Calandra Buonaura G, Capellari S, Giannini G, Scaglione CLM, et al. Observing movement disorders: best practice proposal in the use of video recording in clinical practice. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol. febbraio 2019;40(2):333–8.

**P31**

## Effects of immersive virtual reality rehabilitation program on motor and non-motor symptoms in patients with functional motor disorders

*Zoe Menaspà*[1], M. Gandolfi[1,2,3], A. Sandri[1], F. Bombieri[1], C. Geroin[4], D. Vidale[5], M. Pirini[5], M. Fiorio[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona, Verona, Italy
[4]Department of Surgery, Dentistry, Pediatrics and Gynecology, University of Verona, Verona, Italy
[5]Khymeia SRL, Padua, Italy

*Introduction:* Functional motor disorders (FMDs) are highly disabling neurological conditions manifesting with motor and non-motor symptoms. Rehabilitation is essential in the multi-disciplinary management of these patients to regain functional abilities, manage nonmotor symptoms and improve their quality of life. A future direction for research is to develop interventions for treating the pathophysiological features of FMDs [1-2]. Virtual Reality is a powerful tool that may simultaneously address attention, belief/expectations, and a sense of agency. To date, no RCT studies have been performed on patients with FMDs.

*Objective:* We evaluate the effects of an ad-hoc 5-day immersive VR rehabilitation treatment (VRT) versus a 5-day of conventional treatment (CT) on motor, nonmotor symptoms and the self-perception of change.

*Methods:* 13 patients with a definite diagnosis of FMDs were randomly assigned to the VRT (n=6) or CT (n=7). The ad-hoc VR rehabilitation consisted of graded exergames using 3D VR system (5 days/week, 1 week); CT included exercises without VR [3]. Patients were evaluated pre-treatment and after 5-day treatment by the Simplified Functional Movement Disorders Rating Scale (S-FMDRS) (primary outcome), the Multidimensional Fatigue Inventory (MFI), a Brief Pain Inventory (BPI), and a 7-point Clinical Global Impression for self-perception of change.

*Results:* The VR group reported more remarkable changes than the CT in the S-FMDRS (VR group: -10.5 [-16.5;-4.5]; CT group: 0 [-5;0]), in MFI total score (VR group: -22 [-38;-8]; CT group: -12 [-12;-2]), in MFI reduced motivation subscales (VR group: -7 [-8;1]; CT group: 0 [-0.5;0]), in MFI mental fatigue subscales (VR group: -5 [-7;-1]; CT group: 0 [-1.5;1.5]) and BPI interference (VR group: -19.5 [-22.75;-6.5]; CT group: 0 [-1;3]). No side effects were reported during the VR treatment.

*Conclusions:* VR treatment is a feasible alternative to in-clinic SIBT for reducing motor and non-motor symptom severity in patients with FMDs.

**References:**

[1] Perez, David L et al. “Decade of progress in motor functional neurological disorder: continuing the momentum.” Journal of neurology, neurosurgery, and psychiatry, jnnp-2020-323953. 15 Mar. 2021, doi:10.1136/jnnp-2020-323953.

[2] Gandolfi, Marialuisa, et al. “Motor dual task with eyes closed improves postural control in patients with functional motor disorders: A posturographic study.” Gait & posture vol. 88 (2021): 286-291. doi:10.1016/j.gaitpost.2021.06.011.

[3] Nielsen G, Stone J, Matthews A, et al. Physiotherapy for functional motor disorders: a consensus recommendation. J Neurol Neurosurg Psychiatry. 2015;86(10):1113-1119. doi:10.1136/jnnp-2014-309255.

**P32**

## Elderly onset functional movement disorders: an overview from the Italian Registry of Functional Motor Disorders

*Martina Petracca*[1], C. Geroin[2], S. Di Tella[3], A.R. Bentivoglio[1,4], A. Pilotto[5,6], F. Morgante[7,8], E. Marcuzzo[2], S. Cuoco[9], R. Ceravolo[10], S. Mazzucchi[10], A. Padovani[5], L.M. Romito[11], R. Eleopra[11], A. Nicoletti[12], C. Dallocchio[13], C. Arbasino1[3], F. Bono[14], G. Magro[14], B. Demartini[15], O. Gambini[15], N. Modugno[16], E. Olivola[16], L. Bonanni[17], A. Albanese[18], G. Ferrazzano[19], A. Tessitore[20], L. Lopiano[21], G. Calandra Buonaura[22,23], M. Esposito[24], A. Pisani[25,26], P. Manganotti[27], L. Tesolin[28], F. Teatini[28], G. Defazio[29], T. Ercoli[29], F. Stocchi[30], R. Erro[9], M. Zappia[1,2], M. Tinazzi[2]

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

[26]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[27]Clinical Neurology Unit, Department of Medical, Surgical and Health Services, University of Trieste, Trieste, Italy
[28]Functional Movement Disorders Outpt. Clinic, Clinical Neurology and Stroke Unit Dep., Central Country Hospital, Bolzano, Italy

[29]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[30]University and Institute of Research and Medical Care San Raffaele Roma, Rome, Italy

*Introduction:* Functional movement disorders (FMDs) are a frequent condition that affects patients with movement disorder. Generally described in young adults, their manifestation can be also associated to an elderly onset [1-2].

*Objective:* Aim of this study is to assess the prevalence and the clinical phenotype of elderly onset FMDs and to compare this sample to younger onset patients in order to investigate the possible risk factors.

*Methods:* We recruited patients with a clinically definite diagnosis of FMDs from the Italian Registry of Functional Motor Disorders. For each patient, we performed an extensive clinical assessment. For elderly onset, we set a chronological cut-off at 65 years or older. Multivariate regression models were implemented in order to estimate the adjusted odds ratio (OR; 95% confidence interval) of having an elderly onset FMDs related to socio-demographic and clinical characteristics.

*Results:* Out of 410 FMDs patients, 9% (n =34) had an elderly FMDs onset, with a mean age at onset of 70.9 years. They exhibited isolated FMD in 67.7%. The most frequent phenotype was tremor in 47.1%, followed by gait disorders, weakness, dystonia, jerks, parkinsonism and facial motor disorder. On multivariate regression analysis, elderly onset FMDs was more likely associated with comorbidities, in particular parkinsonism (OR 6.48, 95% CI 1.32–31.78, p= .021), cerebrovascular diseases (OR 4.64, 95% CI 1.15–18.68, p= .031), and hypertension (OR 5.15, 95% CI 2.12-12.49, p < .001). Elderly onset FMDs were also less likely to have fatigue as associated non-motor symptoms (OR 0.34, 95% CI 0.13-0.91, p = .031).

*Conclusions:* In line with literature data, the most frequent clinical phenotypes of elderly onset FMDs was tremor [1-2]. People with elderly onset FMDs may present with cerebrovascular and cardiovascular comorbidities and overlapping neurological conditions, i.e. parkinsonism [3]. This complexity unveils the frequent difficulty of FMDs diagnosis in elderly ages.

**References:**

[1] Batla A, Stamelou M, Edwards MJ, Pareés I, Saifee TA, Fox Z, et al. Functional movement disorders are not uncommon in the elderly. Mov Disord 2013;28(4):540–543.

[2] Chouksey A, Pandey S. Functional movement disorders in elderly. Tremor Other Hyperkinet Mov. 2019; 9. doi: 10.7916/tohm.v0.691.

[3] Tinazzi, M.; Geroin, C.; Erro, R.; Marcuzzo, E.; Cuoco, S.; Ceravolo, R.; Mazzucchi, S.; Pilotto, A.; Padovani, A.; Romito, L.M.; et al. Functional motor disorders associated with other neurological diseases: Beyond the boundaries of “organic” neurology. Eur. J. Neurol. 2021, 28, 1752–1758, doi:10.1111/ene.14674.

**P33**

## Idiopathic normal pressure hydrocephalus and parkinsonism: a positive shunt response with a negative tap test

*Giulia Giannini*[1,2], I. Jusue-Torres[3], P. Mantovani[4], L. Mazza[5], A. Pirina[4], N. Valsecchi[4], D. Milletti[6], L. Albini[7], S. Cevoli[1], S. Yasar[8,9], G. Palandri[4]

[1]Unit of Neurology, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[2]Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy
[3]Department of Neurological Surgery, Mayo Clinic, Rochester, MN, USA
[4]Unit of Neurosurgery, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[5]Dipartimento dell'Integrazione Geriatria, Ospedale Maggiore, AUSL Bologna, Bologna, Italy
[6]Unit of Rehabilitation Medicine, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[7]Unit of Neuroradiology, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[8]Division of Geriatric Medicine & Gerontology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
[9]Department of Neurology, Johns Hopkins School of Medicine, Baltimore, Maryland, USA

*Introduction:* Idiopathic Normal Pressure Hydrocephalus (iNPH) is a complex and often misdiagnosed syndrome, whose major challenge is to identify which patients will benefit from surgery. Recent studies revealed high rates of neurodegenerative disorders in iNPH patients, including Lewy body disease co-pathology, which could contribute to a specific iNPH clinical phenotype.

*Objective:* The aim of this study was to compare performances of iNPH patients with and without parkinsonism at initial evaluation, 72 hours after cerebrospinal fluid tap test (CSF TT) and 6 months after ventriculoperitoneal shunt (VPS) surgery.

*Methods:* This is an observational prospective study on iNPH patients who underwent VPS. Patients were classified as iNPH with (iNPH-P+) and without (iNPH-P-) parkinsonism. An extensive clinical evaluation, including motor and functional performances, was performed at baseline, 72 hours after CSF TT and six months after VPS surgery.

*Results:* A total of 64 iNPH patients were included, 12 patients were classified as iNPH-P+ and 52 as iNPH-P-. Overall, iNPH patients showed significant improvement in all clinical parameters after VPS. In respect to iNPH-P-, iNPH-P+ patients showed worse performances in the majority of variables at the three observation times. In the iNPH-P- group, motor and functional performances improved both at 72h post CSF TT and 6 months after VPS. In the iNPH-P+ group, the majority of motor and variables showed an improvement at 6 months after VPS, despite none of these parameters showed a significant response after CSF TT.
*Conclusions:* Despite the iNPH-P+ group did not show a significant response in motor and functional performances after CSF TT, a significant improvement in the majority of parameters was observed 6 months after VPS. This finding could positively impact the clinical practice, as an unsatisfying response to CSF TT in iNPH-P+ patients should not be taken as an exclusion criterion from VPS surgery.

**P34**

## Efficacy and safety of MRgFUS: a 4-years follow up following treatment

*Patrizia Sucapane*[1], G. Saporito[2], C. Marini[3], D. Cerone[1], T. Russo[1], F. Bruno[2], A. Catalucci[4], A. Splendiani[2], F. Pistoia[2]

[1]Department of Neurology, San Salvatore Hospital, L'Aquila, Italy
[2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
[3]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy
[4]Neuroradiology and Interventional Radiology, San Salvatore Hospital, L'Aquila, Italy

*Introduction:* MRgFUS is a useful and innovative tool in the treatment of medically refractory tremor. A few data are available on long-term outcomes of patients undergoing MRgFUS thalamotomy.

*Objectives:* We report the 4-year follow-up outcomes after MRgFUS thalamotomy.

*Methods:* Out of the 184 patients consecutively treated with MRgFUS at the San Salvatore Hospital of L'Aquila, 30 patients had a 4-years follow-up and were included in the study. Seven patients were later excluded as dead (n=4) or unavailable for control visits (n=3). The final sample consisted of twenty-three patients (mean age 65.3±8.5; mean disease duration 23.0±12.7 years) with ET (n=15; 65%) and PD-related tremor (n=8; 35%). Clinical Rating Scale for Tremor (CRST), MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Montreal Cognitive Assessment (MOCA) and Quality of life in Essential Tremor Questionnaire (QUEST) scores were assessed before and after the treatment at 6, 12, 24 and 48 months. A paired-samples T-test or Wilcoxon signed rank test was performed. After Bonferroni correction (0.05/7), a p value of 0.007 was considered statistically significant.

*Results:* At four years there was a significant improvement after thalamotomy in the motor domains, as reported by the CRST total score (from 34.8±8.5 to 17.2±10.6, p <001), Part A (from 13.5±4.9 to 6.9±3.4, p <001) and treated extremity score (from 5.4±1.8 to 2.2±1.8, p <001). Quality of life as measured by QUEST also improved (from 41.2±13.8 to 19.1±15.3, p <001). There were no significant changes between preoperative and postoperative scores for psychometric tests exploring global cognitive function. Scores of the MDS-UPDRS (from 64.2±17.0 to 52.1±11.8, p=0.094) and MDS-UPDRS-III (from 35.7±10.2 to 25.1±6.7, p=0.094) were improved following the treatment and the improvement was stable at the 4 years follow-up.

*Conclusions:* MRgFUS shows a stable safety and efficacy profile at 4 years after the treatment.

**P35**

## The effect of safinamide on axial symptoms in Parkinson's disease: a cross-sectional study

*Gaia Bonassi*[1], S. Mezzarobba[1], M. Putzolu[2], E. Ravizzotti[1], C. Cosentino[1], A. Botta[2], F. Di Biasio[2], S. Terranova[3], E. Pelosin[1,2], L. Avanzino[2,3]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[2]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[3]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy

*Introduction:* In Parkinson's disease (PD), dopaminergic therapy often has poor results with the "axial" symptoms. Disruptions in other neurotransmitter systems beyond the dopamine system, including the glutamatergic system, may underlie some of the axial symptoms in PD. As an example, left prefrontal glutamate levels evaluated with magnetic resonance imaging and spectroscopy were associated with difficulties in turning in bed [1]. A pilot study showed that a combination of memantine, an uncompetitive, partial antagonist of the open NMDA receptor, and L-dopa was associated with a slight, beneficial effect on axial impairment in advanced PD [2].

*Objective:* Exploring the effect of safinamide, a monoamine oxidase type-B inhibitor (MAOB-I) with anti-glutamatergic properties, on axial symptoms in PD patients, in comparison to other MAOB-I.

*Methods:* We enrolled 88 patients with PD receiving MAOB-I therapy for at least one year. We collected demographic and clinical characteristics and tests for balance and gait evaluation: the Short Physical performance battery (SPPB), the Timed up and go (TUG) test, and TUG under dual task, while executing a verbal fluency task. Continuous data were analyzed by a one-way Anova.

*Results:* In MAOB-I user cohort, approximately 29% (26 patients) were taking safinamide, 37% (33) rasagiline, and 33% (29) selegiline. As expected, according to the safinamide prescription's guidelines, these patients had longer disease duration ($p<0.001$), higher HY score ($p<0.001$) and higher MDS-UPDRS III score ($p<0.005$), compared to patients under rasagiline and selegiline. Safinamide patients showed higher MDS UPDRS IV score and mean LEDD with respect to patients under selegiline ($p<0.001$). SPPB, TUG and TUG dual task values were comparable between groups ($p$ always $> 0.05$).

*Conclusions:* This exploratory study supports the hypothesis that safinamide may impact on axial symptoms in PD. These data need further exploration with a prospective study on the effect of MAO-B inhibitors on gait and balance performance.

**References:**

[1] O'Gorman Tuura RL, Baumann CR, Baumann-Vogel H. Beyond Dopamine: GABA, Glutamate, and the Axial Symptoms of Parkinson Disease. Front Neurol. 2018 Sep 26;9:806. doi: 10.3389/fneur.2018.00806. PMID: 30319535; PMCID: PMC6168661.

[2] Moreau C, Delval A, Tiffreau V, Defebvre L, Dujardin K, Duhamel A, Petyt G, Hossein-Foucher C, Blum D, Sablonnière B, Schraen S, Allorge D, Destée A, Bordet R, Devos D. Memantine for axial signs in Parkinson's disease: a randomised, double-blind, placebo-controlled pilot study. J Neurol Neurosurg Psychiatry. 2013 May;84(5):552-5. doi: 10.1136/jnnp-2012-303182. Epub 2012 Oct 16. PMID: 23077087; PMCID: PMC3623038.

**P36**

## Predictors of long-term safinamide response in the multicenter Help Network

*Leandro Purin*[1], A. Pilotto[1], M. Bianchi[2], F. Pepe[3], D. Alimonti[4], F. Pisano[5], V. de Giuli[6], J.M. Melgari[7], A. Micheli[8], M.C. Rizzetti[9], S. Gipponi[1], E. Cottini[1], C. Zatti[1], T. Comunale[1], M. Catania[1], A. Lupini[1], B. Bigni[3], E. Magni[3], M. Sessa[4], M. Turla[5], B. Ferraro[7], A. Ciccone[10], A. Padovani[1]

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

*Background:* Several pharmacological strategies have been proposed for the treatment of motor fluctuations in Parkinson's disease (PD). Still, the long-term use of safinamide and other treatments in real-life scenario is theme of debate [1-2].

*Objective:* To evaluate the long-term impact of safinamide in Parkinson's disease complicated by motor fluctuations, in a large real life multicenter setting.

Methods: The Healthy East Lombardy Parkinson (HELP) network involve movement disorder outpatient clinic and rehabilitation centers adopting a shared digital platform to include motor variables and treatments of patients with motor fluctuations. PD patients with motor fluctuations who underwent safinamide treatment were selected and motor and non-motor assessment was evaluated at baseline and after long-term treatment.

*Results:* Seven-hundred-twenty-one patients were included in the network- of them, 313 presented motor fluctuations and 184 were treated with safinamide (Mean age 69 ± 8.9, mean disease duration 6.4 ± 4.6, mean UPDRS-III 21.0 ± 11.8 in ON, mean UPDRS-IV 2.9 ± 3.3). Middle/long- term follow-up data were available for 120 subjects (Mean follow-up duration 13.9 months). Safinamide was associated with significant improvement in motor and non-motor scores in most patients at 12 months, whereas we observed a slight increase in global motor severity and fluctuations increasing from 12 to 48 months. Better and longer response were associated with shorter onset of motor complication, independently from baseline age, sex, disease severity and LEDD.

*Conclusions:* Safinamide showed middle/long-term benefit for motor complications in Parkinson's disease. Further studies are needed in order to confirm the association between early fluctuations and longer treatment benefit.

**References:**

[1] Giossi R, Carrara F, Mazzari M, Lo Re F, Senatore M, Schicchi A, Corrù F, Fittipaldo VA, Pani A, Tramacere I, Elia AE, Scaglione F. Overall Efficacy and Safety of Safinamide in Parkinson's Disease: A Systematic Review and a Meta-analysis. Clin Drug Investig. 2021 Apr;41(4):321-339.
[2] Sharaf J, Williams KD, Tariq M, Acharekar MV, Guerrero Saldivia SE, Unnikrishnan S, Chavarria YY, Akindele AO, Jalkh AP, Eastmond AK, Shetty C, Rizvi SMHA, Mohammed L. The Efficacy of Safinamide in the Management of Parkinson's Disease: A Systematic Review. Cureus. 2022 Sep 13;14(9).

**P37**

## Neurological effects of probiotics in patients with Parkinson's disease and constipation

*Valentina Andreozzi*, R. Erro, M. Memoli, M. Di Filippo, G. Barbella, A. Silvestri, F. Fierro, M. Balestrieri, N. Ferrara, P. Barone, P. Iovino, M.T. Pellecchia

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

*Introduction:* Constipation is one of the most frequent non-motor symptoms of Parkinson's disease (PD). Previous research highlighted the association of constipation with disease duration and severity [1]. Furthermore, gut microbiota changes and brain-gut-axis (BGA) dysregulation are common in patients with PD, and these alterations are related with clinical manifestations [2, 3]. For this reason, probiotics, balancing the gut microbiota, are emerging as a potential therapeutic approach for PD patients.

*Objective:* To assess neurological and gastroenterological effects in PD patients with constipation after the administration of symbiotics (Enterolactis duo), with a focus on neuropsychological, cognitive and symptomatic impact.

*Methods:* This study enrolled patients with stable PD who met diagnostic criteria for functional constipation and/or irritable bowel syndrome with constipation according to Rome IV Criteria. Patients received a symbiotic treatment (Enterolactis duo, 4 sachets/day, containing the probiotic Lactobacillus casei and prebiotic inulin) for 12 weeks. The Montreal Cognitive Assessment (MoCA), Movement Disorder Society-Sponsored Revision of Unified Parkinson's Disease Rating Scale (MDS-UPDRS), SCales for Outcomes in PArkinson's disease - Autonomic Dysfunction (SCOPA-AUT), Toronto Alexithymia Scale (TAS-20), Reading the Mind in the Eyes Test (RMET), Parkinson Anxiety Scale (PAS), State-Trait Anxiety Inventory (STAI-Y), Beck Depression Inventory (BDI II), Hamilton depression rating scale (HAM-D) were collected pre- and post-intervention, in addition to a gastroenterological evaluation (PAC-SYM questionnaire, number of complete bowel movements per week, degree of defecation effort, Bristol stool Scale (BSS) and other items) before and after the treatment.

*Results:* 29 patients (16 women and 19 men) were consecutively enrolled. After treatment patients performed better in TAS-20 (p=0,011), SCOPA-AUT (p=0,004) and MDS-UPDRS part 1 score (p=0). PAS-A (p=0,091) and HAM-D (p=0,072) score show a trend towards significance. Gastroenterological scales also showed a significant improvement.

*Conclusions:* Probiotics treatment can effectively improve non motor features in PD patients, as well as improve constipation. Our data suggest that the addition of probiotics acting on the gut-brain-gut axis may be a useful therapeutic approach in PD.

**References:**

[1] Krogh K, Ostergaard K, Sabroe S, Laurberg S. Clinical aspects of bowel symptoms in Parkinson's disease. Acta Neurol Scand. 2008;117(1):60-64.

[2] Shen T, Yue Y, He T, Huang C, Qu B, Lv W, Lai HY. The Association Between the Gut Microbiota and Parkinson's Disease, a Meta-Analysis. Front Aging Neurosci. 2021 Feb 12;13:636545.

[3] Scheperjans F, Aho V, Pereira PA, et al. Gut microbiota are related to Parkinson's disease and clinical phenotype. Mov Disord. 2015;30(3):350-358.

**P38**

## The effect of cathodal transcranial direct current stimulation in the treatment of levodopa-induced dyskinesias in Parkinson's disease: a preliminary report

*Benedetta Angeloni*[1,2], R. Di Iorio[1], P. Sanginario[1,2], F. Bove[1], C. Piano[1,2], A.R. Bentivoglio[1,2], P. Calabresi[1,2]

[1]Università Cattolica del Sacro Cuore, Roma, Italy;
[2]IRCCS Policlinico A. Gemelli, Roma, Italy

*Introduction:* In Parkinson's disease (PD), levodopa is to date the most effective treatment for the management of motor symptoms. However, in a certain number of patients, prolonged treatment is associated with development of levodopa-induced dyskinesias (LIDs). In the pathophysiology of LIDs, aberrant synaptic plasticity seems to play a key role at different levels of brain system, including the primary motor cortex (M1). Non-invasive brain stimulation (NIBS) may restore normal functioning and ameliorate clinical deficits reversing these brain plasticity abnormalities. Based on these assumptions, our study aims to demonstrate the possible effect of transcranial direct current stimulation (tDCS) in the treatment of LIDs.

*Methods:* We administered cathodal bilateral tDCS over M1 of 8 PD patients with LIDs, selected according to similar age, disease duration, and levodopa equivalent daily dose (LEDD). Clinical and neurophysiological evaluation were performed before and after stimulation protocol at three different time points (3 days, 1 month and 3 months). Primary endpoint was reduction in LIDs severity measured by UDyRS. Secondary endpoint was improvement in depotentiation degree measured by MEP amplitude changes.

*Results:* tDCS over bilateral M1 induced a reduction in LIDs of 32% at 3 days, 9% at 1 month, and 9.8% at 3 months compared with baseline. In addition, a significant change in Depotentiation paradigm ($p=0.01$) was observed in post-tDCS recordings compared with baseline.

*Conclusion:* In conclusion, this preliminary report shows that, in PD patients with LIDs, cathodal bilateral tDCS over M1 induces a short-term improvement in LIDs severity associated with useful changes in synaptic plasticity.

**P39**

## Could trans-auricular vagus stimulation modulate STN activity in Parkinson's disease? Study design and pilot data by a sham-controlled intervention

*Gaia Anzini*[1], L. Saltarocchi[1], A. Magliozzi[1], F. Torrecillos[2], V. Di Lazzaro[1], M. Marano[1]

[1]Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[2]University of Oxford, UK

*Introduction:* Vagus nerve stimulation (VNS) is a valuable potential treatment for Parkinson's disease (PD). Our group successfully tested the non-invasive left VNS in PD: cervical VNS alleviated the subthalamic beta activity [1], while auricular VNS improved gait troubles [2].

*Objective:* Given the low experimental and clinical reliability of non-invasive cervical VNS, we want to investigate deep neurophysiological and clinical biomarkers of auricular VNS toward more robust continuous stimulation trials.

*Methods:* 15 PD patients with recording subthalamic deep brain stimulation devices (Percept, Medtronic) have been enrolled in a prospective interventional trial with non-invasive left ear auricular VNS. Data on med-OFF/stim-OFF neurophysiological and clinical (gait) parameters have been tested in a sham controlled cross over design of 4 trials of 120s of 20Hz left ear VNS with 60s intervals.

*Results:* 4 out of 15 patients completed both conditions in February 2023. There was a clear-cut modulation of beta band amplitude and stability over the contralateral right STN on 3 out of 4 subjects, only after the real stimulation condition, and prominent after 4 trials of VNS.

*Conclusions:* Preliminary results partially confirm what was observed with cervical VNS but showing a prominent contralateral effect. Gait parameters are currently under investigation, due to low numbers. If confirmed on a larger sample, our pilot results would help in design further robust trials for such a promising therapy [3].

**References:**

[1] Torrecillos F, Tan H, Brown P, Capone F, Ricciuti R, Di Lazzaro V, Marano M. Non-invasive vagus nerve stimulation modulates subthalamic beta activity in Parkinson's disease.Brain Stimul. 2022 Nov;15(6):1513-1516. doi: 10.1016/j.brs.2022.11.006. PMID: 36518556; PMCID: PMC7613925.
[2] Marano M, Anzini G, Musumeci G, Magliozzi A, Pozzilli V, Capone F, Di Lazzaro V. Transcutaneous Auricular Vagus Stimulation Improves Gait and Reaction Time in Parkinson's Disease. Mov Disord. 2022 Oct;37(10):2163-2164. doi: 10.1002/mds.29166. Epub 2022 Jul 21. PMID: 35861362; PMCID: PMC9796229.
[3] Sigurdsson HP, Hunter H, Alcock L, Wilson R, Pienaar I, Want E, Baker MR, Taylor JP, Rochester L, Yarnall AJ. Safety and tolerability of adjunct non-invasive vagus nerve stimulation in people with parkinson's: a study protocol. BMC Neurol. 2023 Feb 3;23(1):58. doi: 10.1186/s12883-023-03081-1. PMID: 36737716; PMCID: PMC9896761.

**P40**

## Glutamatergic overactivity in Parkinson's disease with fatigue: open label study on possible impact of safinamide

*Caterina Pauletti*[1], N. Locuratolo[1,2], D. Mannarelli[1], A. Maffucci[1], A. Petritis[1], E. Menini[1,3], F. Fattapposta[1]

[1]Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy
[2]National Centre for Disease Prevention and Health Promotion, National Institute of Health, Rome, Italy
[3]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Fatigue is a disabling a common non-motor symptom of Parkinson's disease (PD) and its pathophysiology is not yet fully elucidated [1-2].

*Objective:* To test the hypothesis that fatigue in PD may be related to high levels of extracellular glutamate associated with neuroinflammation, a pathological hallmark of PD, by verifying the impact of safinamide, a drug that targets both dopaminergic and glutamatergic systems, in reducing fatigue in fluctuating PD patients.

*Methods:* The validated version of FSS and PFS-16 were administered to 39 fluctuating PD patients with fatigue before and after a 24-week treatment period with safinamide 100mg as add-on therapy. An assessment of secondary variables such as depression, quality of life, motor and non-motor symptoms was conducted.

*Results:* After 24 weeks of treatment with safinamide, both FSS ($p<0,001$) and PFS16 ($p=0.02$) scores were significantly lower than at baseline. Moreover, 46,2% and 41% patients scored below the cut off for the presence of fatigue according to FSS and PFS, respectively (responders). At follow up, a significant difference emerged between responders and non-responders in BDI, PSQI (PSDI, mobility, ADL), and NMSS (total score, sleep/fatigue, apathy/mood, urinary). No difference emerged between groups in demographic or clinical characteristics.

*Conclusions:* Fatigue improved in fluctuating PD and more than 40% of patients were "fatigue-free" after 6-months treatment with safinamide, pointing to a possible role of glutamatergic overactivity in promoting this symptom. Moreover, patients without fatigue at follow up, displayed significant better scores in QOL domains, such as mobility or activities of daily living, although disease severity remained stable, supporting the hypothesis that fatigue is a primary manifestation of PD that could considerably affect QOL. PD-related fatigue is a complex phenomenon, and its pathogenesis is multifactorial [3], possibly involving also non-dopaminergic systems. Drugs that interact with multiple neurotransmission systems, such as safinamide, could be useful in reducing this symptom.

**References:**

[1] J.H. Friedman, R.G. Brown, C. Comella, C.E. Garber, L.B. Krupp, J.-S. Lou, L. Marsh, L. Nail, L. Shulman, C.B. Taylor, Fatigue in Parkinson's disease: A review, Movement Disorders. 22 (2007) 297–308. https://doi.org/10.1002/mds.21240

[2] B.M. Kluger, Fatigue in Parkinson's Disease, in: Int Rev Neurobiol, Academic Press Inc., 2017: pp. 743–768. https://doi.org/10.1016/bs.irn.2017.05.007

[3] G. Morris, M. Berk, P. Galecki, K. Walder, M. Maes, The Neuro-Immune Pathophysiology of Central and Peripheral Fatigue in Systemic Immune-Inflammatory and Neuro-Immune Diseases, Mol Neurobiol. 53 (2016) 1195–1219. https://doi.org/10.1007/s12035-015-9090-9

**P41**

## Anti-Tr/DNER Cerebellar Ataxia after Immune-checkpoint inhibitors therapy in a patient with a SCA2 family history

*Giovanni Merola*[1], P. Guaraldi[2], G. Giannini[1], G. Calandra Buonaura[1], T. Rossana[3], M. Longoni[3], P. Cortelli[1]

[1]Department of Biomedical and Neuromotor Sciences-DIBINEM, Alma Mater Studiorum University of Bologna, Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[3]Department of Neurology and Stroke Unit Cesena, Bufalini Hospital, AUSL Romagna, Cesena, Italy

*Introduction:* Anti-Tr/DNER Antibody-Associated Cerebellar Ataxia is a classical paraneoplastic neurological syndrome (PNS) associated with Hodgkin lymphoma (HL).

*Methods:* Describe a case of a paraneoplastic cerebellar ataxia associated with the use of Immune-checkpoint Inhibitors (ICI) that was initially misdiagnosed as being hereditary.

*Results:* A 39-year-old woman presented to the ER complaining with a one-week history of unstable walking and diplopia.
Her past medical history revealed a HL diagnosis at 30 years of age successfully treated with first-line chemotherapy that relapsed 5 years later. She didn't respond to second-line chemotherapy and joined an experimental protocol with ICI, stopped 6 months before the onset of neurological symptoms. Her mother was affected by spinocerebellar ataxia type 2 (SCA2).
At the first evaluation she presented with minor neurologic signs; brain MRI was normal, so she was discharged with a diagnosis of suspected SCA2.
In the next few days she noted worsening of symptoms, therefore she came to our attention.
A new brain MRI showed increased volume of the cerebellar cortex. Laboratory analysis showed mild CSF pleocytosis and serum anti-Tr/DNER positivity.
Total body FDG-PET/CT didn't show HL relapses, so we treated her with steroids and IVIg without benefit. Now she is being treated with Rituximab and is slowly getting better. Genetic testing proved negative.

*Conclusions:* This case highlights the importance of excluding acquired and treatable causes of cerebellar ataxia before thinking of familial degenerative forms.
Furthermore, it could represent the first described case of neurologic Delayed immune-related adverse event (nDIRE) of ICI therapy.

**P42**

## Digital telemedicine in functional motor disorders: preliminary data on the health outcomes from a randomized controlled trial

*Marialuisa Gandolfi*[1,2,3], Federico Schena[1], A. Sandri[1], Z. Menaspà[1], F. Bombieri[1], C. Geroin[4], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona,Verona, Italy
[4]Department of Surgery, Dentistry, Pediatrics, and Gynecology, University of Verona, Verona, Italy

*Introduction:* Functional motor disorders (FMDs) are highly disabling conditions associated with long-term disability, poor quality of life, and economic burden on health and social care [1-2]. While multidisciplinary 5-day rehabilitation programs have been shown to reduce motor and non-motor symptoms, long-term management and monitoring in FMDs remain unmet [3-4]. To date, no randomized controlled trials are evaluating the effectiveness of Digital telemedicine in the management of patients with FMD.

*Objective:* To report preliminary data to form a single-blind randomized-controlled trial (RCT) with 2-parallel arms to demonstrate the effectiveness of a 5-day intensive rehabilitation treatment followed by a digital telemedicine program on the motor, non-motor symptoms (pain, fatigue, anxiety, and depression), the self-perception of clinical change and Health-Related Quality of Life in patients with FMDs.

*Methods:* 51 FMD patients were randomly assigned to receive either a Digital Telemedicine program (n = 24) or a control program (n = 27). Digital Telemedicine Program consisted of an individualized intensive 5-day rehabilitation program (2 hours/day, five days/week, one week) by a qualified physiotherapist at the USD Parkinson's Disease and Movement Disorders Unit of Verona (Italy) followed by an individualized self-management program implemented with the Digital Telemedicine platform support (1 day/week with synchronous treatment; 2 days/week asynchronous, 24 weeks, with activity monitoring with wearable devices). The Control Program consisted of the same individualized intensive 5-day rehabilitation program (2 hours/day, five days/week, one week) of the Telemedicine Group followed by a home-based self-management plan (Treatment, as usual, one day, three days/week, 24 weeks) without any Digital Telemedicine platform support and wearable device. Patients were evaluated before treatment (T0), after treatment (T1), and at 3-month follow-up (T2).

*Results:* Overall, both groups showed a favorable trend over time with a progressive reduction in the severity of motor and non-motor complaints (fatigue, pain, anxiety, depression). The control group, however, at the 3-month follow-up (T2) reported a higher percentage of patients (15%) reporting a worse perception of their health status than the telemedicine group (6%).

*Conclusions:* This study provides novel preliminary evidence for a multidisciplinary digital telemedicine program's effect on patients with FMDs. Our preliminary data suggest that it may positively affect the patient's perceived health. The Brain Research Foundation Verona ONLUS supports this ongoing study.

**References:**

[1] Perez, D. L. et al. 2021. J Neurol Neurosurg Psychiatry 1–10.
[2] Tinazzi M et al. 2021. Front Neurol 12:786126.
[3] Gandolfi M, 2021. NeuroRehab 48:305–314.
[4] Nielsen G, et al 2017. J Neurol Neurosurg Psychiatry 88(6):484–490.

**P43**

## CSF tau levels predict long-term outcome of patients with idiopathic normal pressure hydrocephalus: a longitudinal retrospective study

*Jacopo Bissacco*, C. Simonetta, D. Mascioli, N.B. Mercuri, T. Schirinzi

Unit of Neurology, Department of Systems Medicine, Tor Vergata University of Rome, Rome, Italy

*Introduction:* Idiopathic normal pressure hydrocephalus (iNPH) is a neurodegenerative condition burdened by diagnostic uncertainty and challenging therapeutic options, including the shunt surgery [1]. Cerebrospinal fluid (CSF) biomarkers reflect brain neuropathology, facilitating the diagnosis and the prognostic predictions. iNPH is lacking a disease-specific CSF biomarker [2]; however, a panel of neurodegeneration-related CSF biomarkers might support patients stratification and the subsequent therapeutic strategies.

*Objectives:* To predict long-term clinical outcome of iNPH patients through a panel of neurodegeneration-related CSF biomarkers.

*Methods:* We conducted a single-centre retrospective study over an 8 year-long period, identifying 32 iNPH patients with CSF biomarkers (amyloid-β-42, phosphorylated-181-tau, total-tau). Nineteen patients had a long-term follow-up (5 years at least). The clinical assessment was conducted at baseline through the iNPH grading scale (INPHGS) [3] and the modified Ranking Scale (mRS) [4]. At follow-up patients were staged with the mRS and grouped in "poor outcome" (mRS≥5) and "positive outcome" (mRS<5).

*Results:* "Poor outcome" iNPH patients presented CSF total-tau levels higher than "positive outcome" group (mean±st.dev.:300.58±114.10pg/ml vs.175.69±94.57pg/ml, p=0.041), also in a model adjusted for age (p=0.037). There were no significant differences in the amyloid-β-42 (mean±st.dev.: 719.86 ± 354.16pg/ml vs. 618.64 ± 240.51pg/ml, p=0.717), and phosphorylated-181-tau (mean±st.dev.:42,48 ± 20,63pg/ml vs. 33,52 ± 26,73pg/ml, p=0.237) levels. Receiver operating characteristic analysis provided for CSF total-tau an area under the curve of 0.778 with the cut-off value of 202.5 pg/mL allowing distinguishing the clinical outcome with a sensitivity of 75% and a specificity of 72.7%. At baseline CSF t-tau levels directly correlated with iNPHGS cognitive subscore (Spearman Rho 0.508, p=0.026).

*Conclusions:* CSF levels of total-tau mirror brain neuronal loss [5]. Although nonspecific for iNPH pathology, CSF total-tau seems to support the identification of frailer iNPH patients. Higher total-tau levels could predict a long-term poor clinical outcome (severe disability or death) independently from the surgery, helping physicians in therapeutic management of iNPH patients.

**References:**

[1] Giordan E, Palandri G, Lanzino G, Murad MH, Elder BD. Outcomes and complications of different surgical treatments for idiopathic normal pressure hydrocephalus: A systematic review and meta-analysis. J Neurosurg. 2019;131(4):1024-1036. doi:10.3171/2018.5.JNS1875.

[2] Blennow K. Cerebrospinal Fluid Protein Biomarkers for Alzheimer's Disease. NeuroRx. 2004;1(2). doi:10.1602/neurorx.1.2.213.

[3] Kubo Y, Kazui H, Yoshida T, et al. Validation of grading scale for evaluating symptoms of idiopathic normal-pressure hydrocephalus. Dement Geriatr Cogn Disord. 2007;25(1). doi:10.1159/000111149.

[4] Banks JL, Marotta CA. Outcomes validity and reliability of the modified rankin scale: Implications for stroke clinical trials - A literature review and synthesis. Stroke. 2007;38(3). doi:10.1161/01.STR.0000258355.23810.c6.

[5] Migliorati K, Panciani PP, Pertichetti M, et al. P-Tau as prognostic marker in long term follow up for patients with shunted iNPH. Neurol Res. 2021;43(1):78-85. doi:10.1080/01616412.2020.1831300.

**P44**

## Reduced sensitivity to social pain in functional neurological disorders

*Angela Sandri*, M. Fiorio, M. Tinazzi

Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Functional Motor Disorders (FMDs) are common and disabling conditions impacting the patients' quality of life [1,2]. Nowadays, the symptoms are best explained according to the biopsychosocial framework, where predisposing, precipitating and perpetuating factors interact leading to symptoms' manifestation [3]. The social context contributes to the disorder, although it is unknown how patients respond in different social contexts. Investigating those reactions might help better understand the disorder.

*Objective:* To identify patterns of clinical variables as predictors of fall risk in PD patients through Machine Learning (ML) algorithms.

*Methods:* 31 FMDs patients (23 females, median years: 47 [41.50-50]) and 31 matched healthy subjects (24 females, median years: 43 [31-52]) underwent inclusion (I) and exclusion (E) conditions of the Cyberball game in counterbalanced order. Participants took part in a virtual ball-tossing game with two other participants. Out of 30 throws, they received 33% of them (I), or only two throws (6.7%) at the beginning of the game (E). Measures of fundamental needs and mood were collected after I and E games and 5 minutes after exclusion (R). R was the reference used to correct the two gaming conditions, calculating the corrected inclusion one (IR = I – R) and the corrected exclusion one (ER = E – R).

*Results:* 31 FMDs patients (23 females, median years: 47 [41.50-50]) and 31 matched healthy subjects (24 females, median years: 43 [31-52]) underwent inclusion (I) and exclusion (E) conditions of the Cyberball game in counterbalanced order. Participants took part in a virtual ball-tossing game with two other participants. Out of 30 throws, they received 33% of them (I), or only two throws (6.7%) at the beginning of the game (E). Measures of fundamental needs and mood were collected after I and E games and 5 minutes after exclusion (R). R was the reference used to correct the two gaming conditions, calculating the corrected inclusion one (IR = I – R) and the corrected exclusion one (ER = E – R).

*Conclusions:* The social context plays a fundamental role in predisposing and maintaining FMDs, but patients do not fully recognize a socially threatened situation. Such perception could be due to their altered expectations and beliefs [5,6].

**References:**

[1] Perez, D. L. et al. 2021. J Neurol Neurosurg Psychiatry 92, 668-677.
[2] Tinazzi, M. et al. 2021. Front Neurol 12, 786126.
[3] Voon, V. et al. 2016. J Neuropsychiatry Clin Neurosci 28, 168-190.
[4] Eisenberg, N. I. et al. 2003. Science 302, 290-292.
[5] Edwards, M. J. et al. 2012. Brain 135, 3495-3512.
[6] Fiorio, M. et al. 2022. Nature Rev Neurology 18, 624-635.

**P45**

## Reduced interoception abilities in patients with Restless Legs Syndrome

*Angela Sandri*[1], G.P. Mingolla[1], G. Camonita[1], M. Lippolis[2], M. Tinazzi[1], E. Antelmi[1]

[1]Neurology Unit, Parkinson Disease and Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]UOC Neurologia A, Department of Neurosciences, AOUI, Verona, Italy

*Introduction:* Restless legs syndrome (RLS) is a complex sensorimotor disorder occurring with a typical circadian fashion [1]. Association with additional features, like alexithymia and nocturnal compulsive behaviors further complicates the framework [2-4]. Some evidence suggests that alexithymia, impaired nocturnal sleep and eating disorders might share reduced interoception [5-7], a construct not yet investigated in RLS patients.

*Objective:* To assess interoception in RLS.

*Methods:* 25 RLS patients (mean age: 62.04 ± 16.70 years; 15 females) and 28 matched controls (mean age: 54.50 ± 14.47; 16 females) underwent the Heartbeat counting task (interoceptive accuracy, IAC) [8]. RLS symptoms' frequency, disturbance and duration, nocturnal behaviors, interoceptive awareness (IAW) [9], alexithymia, depressive and anxiety symptoms were also collected.

*Results:* RLS patients showed significant lower IAC ($p=0.0003$) and IAW ($p=0.012$) compared to controls, and reported more nocturnal eating behaviors ($p<0.001$). IAC positively correlated with IAW ($R=0.32$), and negatively correlated with age ($R=-0.58$). Nocturnal eating behaviors negatively correlated with IAC ($R=-0.44$) and IAW ($R=-0.50$).

*Conclusions:* RLS patients presented reduced interoceptive abilities correlating with higher nocturnal eating behaviors. Future studies are needed to explore the role of interception in RLS pathophysiology, also in relation to other sensorimotor aspects.

**References:**

[1] Manconi et al., 2021. Nat Rev Dis Primers; 7:80.
[2] Antelmi et al., 2014. Sleep Med; 15:168-172.
[3] Provini et al., 2010. Sleep Med; 11:218-220.
[4] Yilmaz et al., 2018. Neuropsychiatry Dis Treat; 14:2207-2214.
[5] Quadt et al., 2018. Ann NY Acad Sci; 1428:112-128.
[6] Ewing et al., 2017. Biol Psychol; 127:163-172.
[7] Mason et al., 2019. Eat Weight Disord; 24:307-312.
[8] Schandry, 1981. Psychophysiol; 18:483-488.
[9] Calì et al., 2015. Front Psychol; 6:1202.

**P46**

## Wearable devices for gait and posture monitoring in telemedicine in people with movement disorders and multiple sclerosis: a systematic review of literature

*Francesca Salaorni*, G. Bonardi, F. Schena, M. Tinazzi, M. Gandolfi

Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Movement disorders, Functional Motor Disorders (FMDs), and Multiple Sclerosis (MS) are highly disabling conditions characterized by gait and postural control impairments, along with other highly disabling motor and non-motor symptoms. Healthcare access and availability are becoming an issue for these patients that need continuous care, and the arrival of the Covid 19 pandemic has spurred telemedicine to be considered a valuable tool for them [1]. Telemedicine refers to the set of technologies and methods used to carry out remote diagnosis and treatment, and telerehabilitation is a part of it [1].
Physical therapy is considered a crucial element in managing these patients, and it can reduce functional disability and improve mobility; and is also an essential part of the treatment, mainly in FMDs [2].
Thanks to the increasing availability and usability of wearable technologies (such as inertial measurement sensors, accelerometers, smartwatches, and baropodometric insoles), by providing patients with such devices to perform specific rehabilitative exercises independently, physicians and physical therapists can manage more patients while maintaining continuity of care through telemonitoring and collecting essential clinical data to provide oversight and tailor therapy to the patient's needs [3].
However, to date, patients are not receiving the amount of evidence-based rehabilitation they need due to the lack of rehabilitation professionals, and the rehabilitation setting is inadequate for their long-term management and monitoring.

*Objective:* This review aims to evaluate the evidence of the use of wearable sensors in combination with telemedicine that can be used in a home-like environment to monitor the gait and balance performance in patients with movement disorders, FMDs, and MS. We would provide state-of-the-art on clinical population investigated, the type of devices used, and the aim set by clinicians in using such devices in the management of patients with movement disorders and MS.

*Methods:* The protocol of this systematic review was registered in the PROSPERO database (CRD42022355460). Literature research was conducted in PubMed, SCOPUS, COCHRANE LIBRARY, and SPORTDiscus databases considering only studies published in the last ten years and focused on adult patients affected by Movement Disorders, FMDs, and MS. All the studies had to consider any wearable devices used for monitoring gait and posture in the ecological setting combined with telemedicine. From 527 records obtained, after removing duplicates and according to the exclusion criteria, 426 were excluded. So, 27 studies were included.

*Results:* Among all records, 15(55,5%) studies were observational, 4(14,81%) pilot, 3(11,1%) clinical, 2(7.4%) evaluation, 1(3,7%) exploration, 1(3,7%) comparative and 1(3,7%) prospective. Of the 27 evaluated papers, 6(22,2%) were published from 2011 to 2014, 2(7.4%) in 2015, 3(11,1%) in 2016, 1(3.7%) in 2017, 6(22.2%) in 2018, and 9(33.3%) during the last four years. Indeed, 23(85,18%) studies evaluated patients in free-living conditions, while the remaining 4(14.82%) during specific tasks (i.e., Time-Up and Go Test). In particular, 22(81.48%) articles focused on body motion analysis in PD patients, 4(14.81%) on MS patients, and the remaining 1(3.7%) on Huntington patients. No studies in FMD patients were found. Only 4(14,81%) studies used two sensors, and the

remaining 23(85,19%) used only one sensor. The sensors used were mainly triaxial accelerometers (58.1%), followed by IMUs (29,03%), smart shoes and pressure insoles (6.45%), and smartwatches (3.22%). We recognized wearables relevant to patients and clinicians to provide accurate, objective, and real-time assessment of gait and activity in a real-world setting and their integration into telerehabilitation systems toward a digital rehabilitation transition. We highlighted the lack of studies on telemedicine programs using wearables, especially MS and FMD. These results encourage reflections to improve the home monitoring of these patients.

*Conclusions:* This review provides a comprehensive overview of the current technological solutions for PD, MS, and Huntington applications to monitor gait and balance in the ecological setting. Digital technology provides a means to objectively and remotely assess multiple different sides of movement disorders in a natural environment. Wearable devices can provide new insights into disability and progression to integrate the standard clinical assessments and enable deep clinical phenotyping of neurodegenerative diseases. Wearables may also enable more personalized treatment and improved clinical management. However, better validation of new digital outcomes and tools is needed. Moreover, appropriate digital and technological solutions hold enormous potential for improving the management of motor disorder patients, enhancing the QoL, and monitoring the effects and the outcomes of the therapy and rehabilitation during the disease progression.

**References:**

[1] Schneider RB, Biglan KM. The promise of telemedicine for chronic neurological disorders: the example of Parkinson's disease. Lancet Neurol. 2017;16(7):541-551. doi:10.1016/S1474-4422(17)30167-9.

[2] Truijen S, Abdullahi A, Bijsterbosch D, et al. Effect of home-based virtual reality training and telerehabilitation on balance in individuals with Parkinson's disease, multiple sclerosis, and stroke: a systematic review and meta-analysis. Neurol Sci. 2022;43(5):2995-3006. doi:10.1007/s10072-021-05855-2.

[3] Keogh A, Argent R, Anderson A, Caulfield B, Johnston W. Assessing the usability of wearable devices to measure gait and physical activity in chronic conditions: a systematic review. J Neuroeng Rehabil. 2021;18(1):1-17. doi:10.1186/s12984-021-00931-2.

**P47**

## Clinical and demographic characteristics of patients with functional neurologic disorders (FNDs): the experience of the University of Trieste

*Tiziana Maria Isabella Lombardo*, P. Caruso, S. Pavan, P. Manganotti

Neurology Unit, Department of Medical, Surgical and Health Sciences, Cattinara University Hospital, ASUGI, University of Trieste, Trieste, Italy

*Introduction:* Functional neurologic disorders (FNDs) are a common cause of disability and distress, especially in neurological practice.

*Objective:* Aim of the study is to report the clinical and demographic characteristics of FNDs patients that were evaluated in Neurological Clinic of Trieste during the last 7 years, considering the main neurological symptoms at disease onset.

*Methods:* We retrospectively collected data from consecutive patients who were referred to our centre, between January 1th 2016 and December 31th 2022, and who received a diagnose of FND.

*Results:* 75 patients were included. The majority of them (75%) were female and mean age at symptom onset was 43,41 yo. More than one-third (31%) had an upper educational level; 33% of them were working at the time of diagnosis, while 16% were still studying. Among all patients, 40% had psychiatric comorbidities: depression (44%), anxiety (26%) or both (12%), post-traumatic-stress-disorder (9%), and bipolar disorder (9%). In 44% of cases organic neurological co-pathologies were found (migraine, seizures, previous stroke). In half of the patients, symptoms at onset were characterized as pure motor weakness (24%), sensory-motor impairment (14,6%), pure sensory disturbances (6%), and pure speech impairment (9,3%). The other half presented with a combination of the symptoms above, associated, in small percentages, with instability (12%), impaired consciousness (7%), pain (7%) and visual disturbances (5%). Three main categories of FNDs were identified: stroke mimics (50,6%), movement disorders (29,4%) and PNES (20%). During the neurological examination, incoherence, variability, distractibility, and Hoover's sign were observed in almost half (49,3%) of the patients.

*Conclusions:* In this study, we describe the demographic and clinical characteristics of 75 consecutive patients with FNDs specifically referred to our centre between 2016 and 2022. Like previous studies, we found that women were clearly overrepresented. This series will contribute to better characterize FNDs.

**P48**

## Personality profiles in patients with functional motor disorders

*Cuoco Sofia*[1], R. Bisogno[1], R. Tedesco[2], V. Nisticò[2,3], C. Civilotti[4], O. Gambini[2,3,5], P. Barone[1], B. Demartini[2,3,5], R. Erro[1]

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

*Introduction:* Although psychological issues are not diagnostic of functional neurological disorders (FND), they have been often reported to occur in some patients with FND, especially those with functional epilepsy [1-2-3].
We used the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) to explore personality profiles in patients with functional motor disorder (FMD) and compare them to sex-, age- and education-matched healthy controls (HC).

*Methods:* We conducted Mann-Whitney test, to analyze the differences between 30 FMD and 16 HC on 10 clinical scales and 15 content scales of the MMPI-2. We conducted a factory analysis (FA) to explore whether specific factors within the clinical scales of the MMPI-2 could cluster in FMD.

*Results:* FMD patients presented significant higher score than HC in the clinical scales: Hypochondriasis, Depression, Hysteria, Psychopathic Deviate, Paranoia, Psychasthenia and Schizophrenia ($p<0.01$). FMD patients presented highest score than HC in the content scales: Anxiety, Obsessiveness, Depression, Family-Problems and difficulties at work ($p<0.01$).
In FMD sample, more than 50% of patients exceeded the proposed cut-off at the clinical scales for Hypochondriasis, Depression, Hysteria, Paranoia and about 45% of them exceed the cut-off at the content scales for Anxiety and Health-Concerns.
Using the clinical scales only, we identified three factors using the FA in FMD. The first factor, explaining 40.77% of the total variance, was composed by Depression, Psychopathic-Deviate, Paranoia, Psychasthenia, Schizophrenia and Social-Introversion and named "emotional-relational factor". The second one, named "psychosomatic factor", was composed by Hypochondriasis and Hysteria and explained 23.45% of the total variance. The third factor, named "reduced-initiative factor", was composed by Masculinity/Femininity and Hypomania and explained 14.70% of the total variance.

*Conclusions:* Patients with FMD show a strong tendency to somatization, depression, anxiety and interpersonal sensitivity. Personality profiles of these patients is mainly composed by three factors, with the emotional-relational factor seemingly being more influential than the psychosomatic one.

**References:**

[1] Cragar DE, Berry DT, Schmitt FA, Fakhoury TA. Cluster analysis of normal personality traits in patients with psychogenic nonepileptic seizures. Epilepsy Behav. 2005;6(4):593-600. doi:10.1016/j.yebeh.2005.03.007.
[2] Thompson AW, Hantke N, Phatak V, Chaytor N. The Personality Assessment Inventory as a tool for diagnosing psychogenic nonepileptic seizures. Epilepsia. 2010;51(1):161-164. doi:10.1111/j.1528-1167.2009.02151.x.
[3] Gale SD, Hill SW. Concurrent administration of the MMPI-2 and PAI in a sample of patients with epileptic or non-epileptic seizures: implications for an inpatient epilepsy monitoring unit. Epilepsy Behav. 2012;25(2):181-184. doi:10.1016/j.yebeh.2012.07.012.

**P49**

## Atypical neuropilar cerebellar immunochemistry staining in rapidly progressive cerebellar syndrome in woman with breast cancer

*Vincenzo D'Agostino*[1,2], A. Formenti[3], M. Di Stefano[3], P. Melzi[3], M. Vaccaro[3], E. Tagliabue[3], L. Airoldi[3], A. Tetto[3], M. Gastaldi[4], D. Franciotta[4], L. Lorusso[3]

[1]School of Medicine and Surgery and Milan Center for Neuroscience, University of Milan-Bicocca, Milan, Italy
[2]Department of Neurology, IRCCS San Gerardo dei Tintori Foundation, Monza, Italy
[3]Department of Neurology, San Leoopoldo Mandic Hospital, ASST Lecco, Merate, Italy
[4]Neuroimmunology Laboratory, IRCCS Mondino Foundation, Pavia, Italy

*Introduction:* Rapidly progressive cerebellar syndrome (RPCS) is frequently paraneoplastic in postmenopausal women with breast and ovarian cancer, associated with so-called high-risk for cancer antibodies [1]. This syndrome is a treatable condition but often with no full recovery [2].

*Case presentation:* A 67-years old woman was admitted to our Neurology Department for a ten days onset of nausea, vomit, sickness, weight loss (almost five kilograms in two weeks), marked gait instability, dysarthria, hypophonia, diplopia, dysphagia and limb and trunk ataxia, Modified Rankin Scale (mRS 4).

*Results:* The patient underwent several brain MRI scans, with nonspecific findings. Lumbar puncture was carried out showing elevated cerebrospinal fluid (CSF) protein concentration (48 mg/dl) and mild elevation of cell counts (27 cells/mm3), with glucose level in normal range (71 mg/dl). Cultural, virological exams and most common anti-cerebellar antibodies were all negative or nonspecific. PET total body scan and mammography detected a mammary lesion (BI-RADS 6) with axillary lymphadenopathy.
Biopsy with immunochemistry and biological profile found out estrogen receptor (ER) positive breast cancer. Using indirect immunofluorescent tissue based assay exploiting lightly fixed rat brain tissue, we detected on CSF an uncharacterized neuropilar staining involving the molecular layer of the cerebellum.
In the suspicion of paraneoplastic RPCS, the patient underwent five days of intravenous immunoglobulins treatment (twenty grams/day), according to patient's weight, then replaced by steroid with slow tapering. Surgery was excluded by the Breast Unit team, and nonsteroidal aromatase inhibitors (letrozole) treatment was started.
At 6 months follow-up, there was a little neurological improvement with persistence of dysarthria, and ataxic features, mRS 3.

*Discussion:* The features of immunochemistry staining resemble anti-Tr/Delta/Notch-like Epidermal growth factor-related Receptor (DNER) antibodies pattern. Our patient presented several clinical features in common with RPCS associated with these antibodies, usually lymphoma and solid tumors related [3], instead no breast cancer cases were still reported.

**References:**

[1] Francesc Graus, Alberto Vogrig, Sergio Muñiz-Castrillo et al. Updated Diagnostic Criteria for Paraneoplastic Neurologic Syndromes. Neurol Neuroimmunol Neuroinflamm 2021;8:e1014.
[2] Igor Gusmão Campana, Guilherme Diogo Silva, Anti-Tr/DNER Antibody–Associated Cerebellar Ataxia: a Systematic Review. The Cerebellum (2022) 21:1085–1091.
[3] Elise Peter, MSc, Le Duy Do, PhD, Salem Hannoun, PhD, Sergio Muñiz-Castrillo, et al. Cerebellar Ataxia With Anti-DNER Antibodies Outcomes and Immunologic Features. Neurol Neuroimmunol Neuroinflamm 2022;9:e200018.

**P50**

## Instrumental assessment of vestibular function, speech, balance and gait alterations in autosomal recessive spastic ataxia of Charlevoix-Saguenay: a case report

*Giacomo Argenziano*[1], F. Cavallieri[2], V. Fioravanti[2], A. Gessani[3], A. Castellucci[4], I. Campanini[5], A. Merlo[5], M. Menichetti[4], S. Grisanti[6], G. Toschi[2], M. Napoli[7], R. Pascarella[7], F. Valzania[2]

[1]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[4]Otolaryngology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5]LAM-Motion Analysis Laboratory, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[6]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[7]Neuroradiology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

*Introduction:* Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is an early-onset ataxia characterized by cerebellar dysfunction, early spasticity, and sensory-motor polyneuropathy due to mutations in the SACS gene (13q11). So far no studies have instrumentally assessed vestibular function, gait, balance, and speech alterations in these patients.

*Case presentation:* A 36 years-old woman with diagnosis of ARSACS came to our attention. Symptoms began at age two, with mild and progressive worsening over the years. She was found to harbor a homozygous mutation (c.12232 C>T, p.Arg4078Ter) in the SACS gene. Neurologic examination showed spastic-ataxic gait, dysarthric speech, four limbs ataxia, and spastic hypertonia with lower limbs' hyperreflexia.
Brain-MRI showed atrophy of the superior vermis and anterior lobes of the cerebellum. Electroneurography study showed a mixed sensory-motor polyneuropathy. Vestibular evaluation found gaze-evoked and rebound nystagmus on horizontal and vertical gaze, symmetrical bilateral vestibular impairment mostly involving the horizontal semicircular canals and slight impairment of VOR suppression. Perceptual speech assessment revealed mild ataxic dysarthria with scanning speech, pneumophonic incoordination, phonation on residual air, irregular articulatory breakdowns, consonant and vowel distortions, and a variable speech rate. Acoustic analysis showed slow speech, an alterated diadochokinetic (DDK) regularity and reduced rate, a significant reduction of the maximum phonation time and a higher standard deviation of the power spectral density. Balance, measured with eyes open/closed on a firm/soft surface, was impaired in all conditions. Sway amplitude and area increased with task difficulty until the inability to stand on the soft surface with closed eyes. The request for a cognitive task worsened balance, as well as the getting up, sitting down, and turning phases of the instrumented TUG test, but not walking.

*Conclusion:* We report a case of ARSACS with peculiar clinical-instrumental findings including vestibular disfunction, ataxic dysarthria, balance and gait specific alterations.

**P51**

## Effects of 3D immersive virtual reality on postural control in patients with functional motor disorders

*Marialuisa Gandolfi*[1,2,3], A. Sandri[1], Z. Menaspà[1], L. Avanzino[4,5], E. Pelosin[4,6], C. Geroin[7], D. Vidale[8], M. Pirini[8], M. Fiorio[1], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona, Verona, Italy
[4]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[5]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy
[6]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[7]Department of Surgery, Dentistry, Pediatrics and Gynecology, University of Verona, Verona, Italy
[8]Khymeia SRL, Padua, Italy

*Introduction:* Motor symptoms in functional motor disorders (FMDs) are disabling neurological conditions exhibiting involuntary learned altered movement patterns [1-3]. Developing interventions for treating the pathophysiological features of FMDs (altered focus of attention, sense of agency, and belief/expectations) is an unmet need [1]. Virtual reality (VR) can manipulate attentional focus and improve postural control by capitalizing simultaneously on patients' motivation.

*Objective:* To explore whether a 3D immersive VR environment can shape postural control in FMDs by manipulating attentional focus in FMDs.

*Methods:* This exploratory posturographic study involved 17 patients (mean age, 45.25 ±15.20 years) and 19 healthy controls (mean age, 41.58 ±16.58 years). Postural parameters were measured in the real environment (single real task), a virtual 3D room-like copy of the real room (single-task VR), a custom-made 3D city-like scene where subjects maintained visual fixation while disregarding distractors (VR visual dual-task) or counted them (VR visual-cognitive dual-task). The dual-task effect (DTE) was calculated for sway area, length of the center of pressure (CoP), and anteroposterior and mediolateral CoP displacement.

*Results:* Sway area and mediolateral CoP displacement were improved in patients compared to controls (all, $p < 0.049$) on the VR visual-cognitive dual-task, measured by a decrease in DTE. A reduction in sway area DTE on the VR visual-cognitive dual-task compared to the VR visual dual-task was observed in patients ($p=0.025$). No other significant effects were noted.

*Conclusions:* This study provides novel preliminary evidence for the effects of a 3D immersive VR environment combined with visual-cognitive dual-tasking in shaping postural control. Our findings may inform interventions for the rehabilitation of FMDs.

**References:**

[1] Perez, D. L. et al. 2021. J Neurol Neurosurg Psychiatry 1–10.
[2] Tinazzi, M. et al. 2021. Parkinsonism Relat Disord 91, 32–36.
[3] Gandolfi, M. et al. 2021. Gait Posture 88, 286–291.

**P52**

## Home-based education and rehabilitation program and caregiver support on motor and nonmotor symptoms and quality of life in patients with Parkinson's disease

*M. Gandolfi*[1,2,3], M. Tinazzi[1], C. Geroin[4], I.A. Di Vico[1], M. Riello[1], N. Smania[1,2,3]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona, Verona, Italy
[4]Department of Surgery, Dentistry, Pediatrics, and Gynecology, University of Verona, Verona, Italy

*Introduction:* Parkinson's disease (PD) is a progressive disabling condition affecting independence in activities of daily living with increased caregiver demands. Approximately 70% of patients suffer from severe gait and balance disturbances [1], and patients and family members are unprepared to cope with PD disability and progressive motor complications. Indeed, 65% of caregivers have a reduced level of knowledge about the disease and are unprepared for its management [2].

*Objective:* This observational study aimed to explore the effects of a home-based rehabilitation program and caregiver support on motor and nonmotor symptoms and quality of life in patients with Parkinson's Disease.

*Methods:* 200 patients with a clinical diagnosis of PD [3] attending the neurology unit's movement disorder outpatient service were consecutively enrolled (H&Y $\leq$4). Patients underwent ten individualized home-based treatment sessions (60 minutes, two days/week, five weeks) in the presence of the caregiver in collaboration with the Unione Parkinsoniani (Verona) and the Cooperativa Sociale di Solidarietà Promozione Lavoro (Verona). Twelve frontal lectures were performed on the disabling symptoms of PD. At the enrollment, we collected demographics and clinical data. Before (T0) and at the end of rehabilitation (T1), validated outcomes were collected to evaluate motor and nonmotor symptoms, gait and balance, and quality of life.

*Results:* A total of 190 patients (mean age 75.3±8.1); male (60%); mean disease duration: 8.7±6.6; H&Y=2.4±0.8) completed the study. 23.3% had camptocormia, 41.6% Pisa syndrome, and 21.1% anterocollo. After rehabilitation, there was a significant improvement in the freezing of gait, in the subitems of the UPDRS ADL and Motor scale, and in quality of life (for all, $p<0.001$). Gait and posturographic assessment (n=36) showed no significant improvements in gait speed and stride length. All patients enjoyed the rehabilitation activities and reported improvements in mobility.

*Conclusions:* Empowering the patient (and the caregiver) about their illness can contribute to the self-management of symptoms by administering exercises that the patient can perform independently at home. The Fondazione Cariverona supports this study (Rif. 2018.0209).

**References:**

[1] Ashburn, Stack, Ballinger, Fazakarley, & Fitton, 2008.
[2] Gultekin, Sarilar, Ekinci, Erturk, & Mirza, 2017.
[3] Postuma et al. 2015.

**P53**

## Feasibility study of a new extended reality system in Parkinson's disease

*Luigi Baratto*[1], E. Vallefuoco[2], A. Giglio[1], S. Perillo[1], N. Cuomo[1], C.V. Russo[1], P. Arpaia[2], G. De Michele[1], E. De Benedetto[2], A. De Rosa[1]

[1]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2] Department of Electrical Engineering and Information Technology, University of Naples Federico II, Naples, Italy

*Introduction:* Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Recent research has been indicating eXtended Reality (XR) as a promising tool for innovative and tailored therapeutic-rehabilitative intervention. XR refers to the application of immersive technologies that allow users to submerge in a virtual world or interact with a virtually extended world.

*Objectives:* Our aim was to assess the feasibility of a new XR system in PD patients.

*Patients and Methods:* We enrolled 22 PD patients (17M/5F; mean ± age SD 62.7±8.7 years) with MMSE >23. The experimenter started the game by the remote connection between the PC and the Hololens2 viewer applied to the subject's head. The patients performed the game session while sitting in a fixed position. The XR application was organized in two training sessions, and eight experimental game sessions (four for side) carried out respectively in "free" condition, during a simple cognitive task, during a contralateral motor task and during complex cognitive task. Then, System Usability Scale (SUS) and the User Experience Short Questionnaire (UEQ-S) were administered.

*Results:* The mean ± SD of the SUS score was 77.9±18.1 (SUS score > 70 suggests good usability). UEQ-S scores were high for both the pragmatic and the hedonic quality. We found no significant differences between the scores obtained by the more affected hand for all play levels nor between the more affected and the less affected side in all game sessions. Furthermore, there was not any significant relationship between the questionnaire scores, the game results, and the demographic and clinical data.

*Conclusions:* The usability, the acceptance and the tolerability were good, and the application was considered clear, interesting, and innovative by most of the patients. Our XR system could be considered a tool for use in research settings and in clinical practice.

**P54**

## Long-term effects of 24-week telemedicine program in patients with functional motor disorders: a prospective cohort study

*Angela Sandri*[1], M. Gandolfi[1,2,3], Z. Menaspà[1], F. Bombieri[1], V. Vandelli[4], M. Tinazzi[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Centre (CRRNC), University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, AOUI Verona, Verona, Italy
[4]Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic

*Introduction:* Motor symptoms in functional motor disorders (FMDs) are disabling neurological conditions manifesting involuntary but learned altered movement patterns [1,2]. They are associated with long-term disability, poor quality of life, and economic burden on health and social care [3]. Multidisciplinary 5-day rehabilitation programs reduce motor and non-motor symptoms, and a 12-week telemedicine program appears useful in providing support [4]. However, the telemedicine management of these patients through long-term monitoring is lacking.

*Objective:* To compare a 24-week telemedicine program against a 12-weeks telemedicine program after 5 days of rehabilitation on the motor, non-motor symptoms and quality of life in FMDs.

*Methods:* This prospective cohort study involves 52 consecutive FMDs patients who underwent a 5-day in-person rehabilitation program. The experimental group (n=26) underwent 12 sessions telemedicine program (1/7 days) followed by 12 sessions telemedicine program spread over 24 weeks (1/14 days). The control group underwent only 12 sessions telemedicine program (1/7 days). Validated measures of motor and non-motor symptoms such as fatigue and pain, quality of life, perception of change, anxiety, and depressive symptoms were recorded before (T0), after completion of rehabilitation (T1), at three months (T2), and nine months (T3).

*Results:* So far, 50 patients have completed all assessments and were included in the preliminary analyses. At the 9-month follow-up, only an effect of time was found in both groups for motor symptoms ($p<0.001$), physical fatigue ($p=0.015$), physical quality of life ($p=0.007$), and anxiety symptoms ($p=0.004$). Other variables were not significant.

*Conclusions:* Our preliminary results support the fundamental role of multidisciplinary management through telemedicine in the first critical months after diagnosis and a 5-day rehabilitation program. A 9-month telemedicine program consisting of multidisciplinary expert monitoring of patients with FMDs does not seem to impact patients' condition with respect to the usual three months telemedicine program [4].

**References:**

[1] Perez, D. L. et al. 2021. J Neurol Neurosurg Psychiatry 1–10.
[2] Tinazzi, M. et al. 2021. Parkinsonism Relat Disord 91, 32–36.
[3] Tinazzi, M. et al. 2021. Front Neurol 12, 786126.
[4] Gandolfi, M. et al. 2022. J Neurology 269, 5940-5953.

**P55**

## Integrating a functional calibration procedure and usability study towards the digitalization of upper limbs rehabilitation

*Francesca Salaorni*[2], C. Larini[1], S. Sciamanna[1], G. Ceruti[1], G. Recchia[1], M. Gandolfi[2], M. Tinazzi[2], F. Schena[2], A. Ravizza[3], P. Garofalo[4], M. Raggi[4]

[1]DigitalRehab Srl, Milan, Italy
[2]Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]USE-ME-D, Torino, Italy
[4]Turingsense Eu Lab, Forlì, Italy

*Introduction:* Neuro-motor rehabilitation has a primary relevance among healthcare services since it helps patients affected by acute or chronic conditions to optimize functional capabilities and maintain independence to achieve a good quality of life. When impairments occur, there is a need for effective rehabilitative therapies which medical devices can support. Among the available technologies, the combination of Virtual Reality using serious games and inertial measurement units (IMUs) results promising to maximize functional recovery: serious games merge engagement and rehabilitation purposes providing task-oriented activities in contextualized scenarios [1]. Moreover, IMUs provide for the gathering of kinematic parameters useful to monitor the therapy; thus, there is a need for accurate calibration procedures to reduce sources of errors, which depend on the measurement system itself and misalignments of sensor readings for underlying body segments. These latter are managed by Sensor-to-Segment (STS) calibration procedures, which estimate anatomical segment orientations. The validity and accuracy of the IMU-based system must be assessed through the comparison with the optoelectronic system.

*Objective:* This work focuses on the assessment of NiuRion. This digital rehabilitation device enables patients affected by neuromotor disorders or musculoskeletal conditions to perform rehabilitative sessions for upper limbs at home using a sensorized shirt interacting with software of serious games. Two main purposes have been identified: the integration of a functional STS calibration procedure to deal with the misalignment between sensor readings and underlying body segment, and the design of a usability study to assess the intuitiveness of the device as well as the adequateness of the user interface, from the perspective of both patients and therapists.

*Methods:* A. Integration of a model-based functional calibration procedure. An upper limb mechanical multibody model has been designed to implement and test the STS method proposed in [2]. Simulating the acquisition of five sensors arranged as in the Niurion mesh, the quaternions related to a static pose (Neutral pose) and a functional motion necessary for the calibration procedure were obtained. Sensors' readings have been exploited to estimate reference directions necessary to define the matrix which relates the sensors' reference frame to the anatomical one and to compute anatomical joint angles. The application of the calibration procedure has provided for the compensation of the STS misalignment, producing the expected anatomical joint angles.
B. Validation study protocol. The validation protocol has been designed to assess NiuRion as an effective measurement device after applying the STS calibration procedure. Thus, sensor data gathered from NiuRion during movements have been compared to the measurements simultaneously acquired by the Vicon system for 20 healthy subjects.
C. Usability study protocol. A usability test protocol has been designed according to [3] to examine the use scenario and identify errors. Since NiuRion is equipped with two executable interfaces, usability tests have been submitted separately to 15 medical professionals and 15 patients regarding questionnaires and received comments.

*Results:* A. Validation protocol results. Applying the STS calibration procedure has resulted in coherent outcomes for orientation and ROM values along the principal axis of functional movement. The comparison between calibrated data concerning optoelectronic system outcomes has shown significant correlations along the principal axis of movement, while differences in measurements have occurred on the other axis. Thus, the combination of effective strategies for the optimization of initialization and calibration procedures could demonstrate the device's reliability.
B. Usability protocol results. Usability test results have revealed a general willingness to use NiuRion, which has proven to be an easy-to-use and engaging tool for rehabilitation therapies.

*Conclusions:* Pursuing the purposes of assessing NiuRion from both a technical and a usability perspective, results have suggested it to be a promising digital rehabilitation device. Integrating the STS calibration procedure has been essential to estimate anatomical joint angles. From both the perspective of patients and therapists, NiuRion has proven to be an easy and engaging tool. Hence, results will lead to the further development of AuReha and could contribute to the digital transformation already in place.

**References:**

[1] E. e. a. Koutsiana, JMIR Serious Game, vol. 8, n. 4, 2020.
[2] G. Ligorio, E. Bergamini, et. al. IEEE Sensors Journal , vol. 15, 2020.
[3] British Standards Institution, «PD IEC/TR 62366-2:2016. BSI Standards Publication, 2016.

**P56**

## Telerehabilitation in people with Parkinson's disease: results of the "Ricominciare" study

*Maria Eleonora Leombruni*[1], R. Cima[1], M. Tamburini[1], F. Cenci[1], F.A. Barbini[1], A. Mantoan[2], S. Lai[2], S. Grilli[2], F. Sernissi[2], L. Ascari[2], M. Hibel[1], R. Izzo[1], P. Casoli[1], M.G. Ceravolo[1], M. Capecci[1]

[1]Dipartimento di Medicina Sperimentale e Clinica, Università Politecnica delle Marche, Ancona, Italy
[2]Camlin Italy Srl, Divisione Health, Parma, Italy

*Introduction:* Tele-rehabilitation is a viable option to manage progressive disabilities. ARC-Intellicare (ARC) is a mobile device with 5 inertial sensors, a tablet with an App and an extensive library of exercises for motor and respiratory rehabilitation with real-time feedback.

*Objective:* "Ricominciare" is a pilot single-center, prospective, pre- and post study aimed at verifying feasibility and safety of ARC, at home of people with mild moderate motor and respiratory disabilities also due to Parkinson's Disease (PD). Secondary objective is to monitor evolution of patients' functional condition after rehabilitation.

*Methods:* People with PD and indication to outpatient or home rehabilitation, who met at least one of the following criteria, were eligible: i) dyspnea (Barthel dyspnea ≤95), ii) difficulties in walking or iii) in dexterity, or iv) Walking Handicap Scale (Perry and Garrett '95) score ≤ 5. The study protocol included 45 minutes/day (5 days/week, for 4 weeks) of respiratory and motor rehabilitation at home through ARC. Primary outcome measures were: System Usability Scale, adherence, adverse events. Secondary measures were: modified Barthel index, Barthel-dyspnea index, 2MWT, Brief Fatigue inventory, Beck Depression or Anxiety Inventory, quality of life, UPDRS, King's Scale, and PD Sleep Disorders scale.

*Results:* Eighteen pwPD (age range [57-76], 5 women) were enrolled. 22% needed support to use the device. SUS score was stable at 71/100 (±14). Adherence to exercise prescriptions was over 77%. After treatment, the independence in ADL (mBI; z=-2.3;p=.03), dyspnea (BI-D; z=-2.3;p=.01) and meters at the 2MWT (z=-2.1;p=.03) improved. Fatigue (BFI; z=2.8;p=.005), pain (KS; z=-2.1; p=.03) and anxiety (BAI; z=2.8;p=.007) decreased, while the Health Status (z=2.8;p=.005) improved. UPDRS part II (z=3.0;p=.002) and part III (z=2.1;p=.04) improved. No severe AEs were reported.

*Conclusions:* ARC was found to be acceptable, usable and possibly effective to manage disabilities in pwPD.

**P57**

## Hospital based motor cognitive rehabilitation training. What after? An intervention aimed at patients support between admissions

*Anna Carollo*, C. Siri, G. Manoni, M. Canesi

Department of Parkinson's Disease and Movement Disorders Rehabilitation, Moriggia Pelascini Hospital, Gravedona, Italy

Rehabilitation therapies are recognized as part of the treatment of PD. Occupational, speech, and motor-cognitive therapy in specialized units demonstrated to be effective, but generally there is no follow up between admissions at hospital-based treatments.
The present intervention aimed at evaluating the adherence to the suggested training after dismission and to help patients coping with problems they experienced once back home.
Caregivers were involved for helping the understanding of patient's clinical status and needs; on the occasion, they were also offered a space to talk about their own feelings and coping strategies.
As the use of telemedicine has spread widely, teleconsultation was chosen as a valuable tool to broaden the hospital-based care to include home-based care.
A trained neuropsychologist enrolled 51 PD patients (age: 68.6±7.9; disease duration: 14.6±7.5; UPDRSIII on therapy: 33.8±11.6; M=35) who completed the multidisciplinary aerobic motor-cognitive rehabilitation training at our department. Patients were contacted by regular video or phone-calls once every 6-8 weeks after hospital discharge. A semi structured interview assessing their impression about cognition, mood and anxiety, adherence to speech and physical therapy training and their main problems (falls, dysphagia, ADL) was performed at each contact.
Results showed that 90% of the patients carries on with physical therapy at home (half of them at least 3 times a week) while 43% of the patients performs speech therapy exercises. Results are stable at each contact. No differences were found in clinical variables nor in cognition, mood and anxiety between patients who do and don't adhere to therapy.
Noteworthy, the intervention was useful in terms of clinical efficacy with thirteen patients helped to cope with difficulties regarding therapy or neuropsychiatric changes and the compliance was good as most of the patients and caregivers reported to benefit from the support and requested to continue with regular follow ups.

**P58**

## Rapido - one device two goals: rehabilitation and monitoring in patients with Parkinson's disease

*Nicoló Baldini*[1], E. Andrenelli[1], L. Pepa[2], L. Spalazzi[2], G. Bonardi[3], M. Tinazzi[3], M. Gandolfi[3], M. Capecci[1], M.G. Ceravolo[1], A. Antoniello[1], S. Valenti[1]

[1]Dipartimento di Medicina Sperimentale e Clinica, Università Politecnica delle Marche, Ancona, Italy
[2]Dipartimento di Ingegneria dell'Informazione, Università Politecnica delle Marche, Ancona, Italy
[3]Dipartimento di Neuroscienze, Biomedicina e Scienze del Movimento, Università di Verona, Verona, Italy

*Introduction:* Parkinson's disease (PD) is a chronic neurodegenerative disease resulting in progressive disability in activities of daily living (ADL) and social participation restrictions due to the evolution of both motor and non-motor symptoms. Rehabilitation has been demonstrated to reduce the progression of disability, but the access to specialized care is difficult. Remote continuous monitoring and tele-rehabilitation are viable options for the management of patients who require an ongoing, long-term approach, but few studies have investigated its effects [1-2]

*Objectives:* We aim to evaluate the acceptability and feasibility of an integrated telerehabilitation and telemonitoring system in patients with PD at any stage and further investigate the impact of the telerehabilitation and telemonitoring system on motor and non-motor function as well as on the quality of life and caregivers' burden.

*Methods:* This multicentre prospective interventional study tests the feasibility of continuous monitoring via smartwatch (24h/at least 5 days per week) and home-based training (3 times per week 45min/die) for 3 consecutive months by connecting via tablet to a web app. Aggregated information on daily motor activities, heart rate, stress levels and sleep details are recorded by the smartwatch. Outcome assessment is conducted at the beginning, at the end of the training (12-week) and after 6 months.

*Results:* The pilot testing on 5 patients showed that most subjects used the tablet correctly and efficiently, and the interaction with the healthcare professionals was satisfactory. In the long term, the physical activity level and the motor and non-motor symptoms remained stable.

*Conclusions:* We propose a system based on low-cost and widespread consumer devices that can improve the effectiveness, regularity, frequency and adherence to rehabilitation treatment in a monitored home environment.

**References:**

[1] Gandolfi M, et al.. Biomed Res Int. 2017;2017:7962826.
[2] Pepa L, et al..Expert Systems with Applications. 2020.

**P59**

## The evaluation of affective homeostasis in patients with functional neurological disorders

*Yvonne Radin*[2], M. Bulfon[2], A. Clarici[1,4], P. Caruso[3], M. Catalan[3], P. Manganotti[3]

[1]Department of Medical, Surgical and Health Sciences, Cattinara Hospital, University of Trieste, Trieste, Italy
[2]Department of Pediatrics, Institute for Maternal and Child Health Burlo Garofolo (IRCCS), Trieste, Italy
[3]Neurology Clinic, Department of Medical, Surgical and Health Sciences (UniTS), Trieste, Italy
[4]Centro Formazione e Ricerca in Psicoterapia a Orientamento Psicoanalitico, Trieste, Italy

*Introduction:* At the base of neurofunctional disorders, there is an alteration of attentional systems causing intermediate-level motor predictions to elicit movement errors and false attribution of agency [1]. Salient precision is erroneously assigned to sensorial inputs according to the activation of one of the seven basic emotional systems [2]. The symptom is interpreted by the patient as stemming from a particular body district. In the Freudian perspective [3], this is interpreted as a compromise formation in a conflict between cognitive and affective processes. In this model, in DNF, mental pain is disowned by the agent's consciousness, but it is still "felt" as a bodily symptom.

*Objective:* The objective is to explain the relationship between informational and neurobiological models and the psychoanalytic one, showing that such an intersection may help clinicians better understand functional symptoms.

*Methods:* The patient accepted psychological support after the functional diagnosis. Tests were administered before the course, at the end, and at follow-up two months later. Specifically, the tests used were the Affective Neuroscience Personality Scales [4], the SWAP-200 [5], and the Visual Analogue Scale [6].

*Results:* Functional symptoms are secondary to predictions, whereas agency is misguided by affective saliency. This misperception may yield a motivationally-driven intolerance of a specific content which is thus "highjacked" towards correlated body districts. Specific present-day life events may lead in patients with DNF to the re-emerging of abnormal automated adaptive solutions. Psychological support may help the patient to reconcile with the actual meaning expressed by the dysfunctional symptom.

*Conclusions:* An interdisciplinary (neurological and psychological) dialogue is advisable to share these implications with the long-term purpose of creating a clinical attitude to integrate the understanding of the (subjective) significance for the patient of these symptoms with the neurological (objective) definition of Functional Neurological Disorders.

**References:**

[1] Edwards et al., 2012. Brain; 135(11): 3495–3512.
[2] Panksepp, 1998.
[3] Freud, 1915. Vol 14(pp. 146–164).
[4] Davis et. al., 2003. Neuropsychoanalysis; 5(1): 57-69.
[5] Shelder et. al., 2007. Journal of Personality Assessment; 89, 41–55.
[6] Hayes et. al., 1921. Psychological Bulletin; 18, 98-99.

**P60**

## PSP-PFG cohort with unusual clinical features related to dopaminergic therapy

*Elena Benevento*, E. Del Prete, L. Tommasini, D. Frosini, R. Ceravolo

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

*Background:* The terms primary progressive freezing gait was previously used to define patients with isolated gait disorders causing gait freezing during the first 3 years. The most recently published MDS Criteria defines PSP-PGF as characterized by progressive gait disturbance with start hesitation and freezing of gait within 3 years after PSP related symptoms [1].

*Objective:* The aim of this study is to describe our PSP-PFG cohort, considering motor and non-motor presentation highlighting the presence of unusual response to dopaminergic treatment.

*Materials and methods:* In our study we included 9 PSP-PFG patients of the Movement Disorders Clinic at the Neurology Unit of Pisa University. All participants underwent systematic neurological examination at the first visit and in at least five years follow up. Neuropsychological evaluation was also performed. All patients performed 123I-FP-CIT SPECT and FDG- PET imaging and MRI imaging.

*Results:* Dopamine transporter imaging was abnormal in all patients, MRI excluded significant vascular lesions, FDG PET showed frontal or fronto-striatal hypometabolism. Neuropsychological evaluation showed executive and visuo spatial problems, without clear dementia. All patients started levodopa therapy soon after the diagnosis with a mean daily levodopa equivalent daily dose at 2 years follow up between 750-1000 mg. Two patients developed motor fluctuations after about 3 years from the introduction of levodopa with the need to split the daily therapeutic dose administration; three patients developed involuntary movements. Three patients showed dopaminoagonist-induced visual hallucinations, one patient developed impulse-control disorder.

*Conclusion:* In our cohort of PSP-PFG patients we found unusual clinical features related to dopaminergic therapy; further studies are needed to confirm these findings.

**References:**

[1] Höglinger GU, Respondek G, Stamelou M, et al.; Movement Disorder Society-endorsed PSP Study Group. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017;32(6):853–864.

**P61**

## Speech profile in different clinical PSP phenotypes: an acoustic-perceptual cohort study

*Giulia Di Rauso*[1,2], F. Cavallieri[3], A. Gessani[2], D. Fontanesi[1,2], S. Coniglio[1,2], V. Fioravanti[3], S. Contardi[4], E. Menozzi[5], S. Meletti[1,2], F. Antonelli[2], V. Rispoli[2], F. Valzania[3], C. Budriesi[1,2]

[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[3]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[4]IRCCS Istituto delle Scienze Neurologiche di Bologna, Neurologia e Rete Stroke Metropolitana, Ospedale Maggiore, Bologna, Italy
[5]Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK

*Introduction:* Progressive supranuclear palsy (PSP) is a neurodegenerative disease with pathologic hallmarks and different clinical presentations. Recently, the Movement Disorder Society (MDS) promoted a new classification; specific combinations of the core clinical features identify different phenotypes, including PSP with Richardson's syndrome (PSP-RS) and PSP with predominant parkinsonism (PSP-P). Since speech disorders are very common in PSP, they were included in the MDS-PSP criteria as a supportive clinical feature in the form of hypokinetic, spastic dysarthria. However, little is known about how dysarthria presents across the different PSP variants.

*Objective:* To evaluate the presence of differences in speech profile in a cohort of PSP-RS and PSP-P patients. Moreover, demographic and clinical variables were compared in these groups.

*Methods:* This prospective cohort study included patients with a clinical diagnosis of PSP according to the MDS-PSP criteria and admitted at the Neurology Department of the University Hospital of Modena or at the Neurology Unit of AUSL-IRCCS of Reggio Emilia. Each patient underwent to neurological evaluation and perceptual and acoustic analysis of speech. The clinical phenotype was determined according to the MDS-PSP criteria. Disease severity was rated using the Natural History and Neuroprotection in Parkinson plus syndromes–Parkinson plus scale (NNIPPS), including global score and sub-scores.

*Results:* Twenty-five patients were classified as PSP-RS while sixteen as PSP-P. These subgroups had homogeneous demographical and clinical characteristics, including disease severity quantified by the NNIPPS total score. No significant differences were found in all speech variables between the two groups. Only the NNIPPS oculomotor function sub-score significantly differed, being more impaired in PSP-RS patients.

*Conclusion:* The similar speech profile between the two different PSP subgroups examined are in keeping with the indication of the MDS-PSP criteria in considering dysarthria as a diagnostic supportive feature of PSP and not a distinguishing feature of the various phenotypes.

**P62**

## Parkinson and Gaucher in real life: results from the clinical practice of a panel of experts

*Massimo Marano*[1], C. Zizzo[2], M.C. Malaguti[3], F. Cavallieri[4], A.R. Bentivoglio[5], F. Spagnolo[6], F. Tamma[7], A. Pilotto[8], N. Modugno[9], T. Schirinzi[10], G. Mostile[11], M. Zibetti[12], M. Carecchio[13], R. Cilia[14], P. Sucapane[15], G. Arabia[16], R. Erro[17], G. Cossu[18], S. Ramat[19], M.G. Ceravolo[20], N. Tambasco[21], G. Fabbrini[22], M. Tinazzi[23], A. Tessitore[24], A.B. Di Fonzo[25]

[1]Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[2]IRIB CNR, Palermo, Italy
[3]Ospedale S. Chiara, Trento, Italy
[4]Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Italy
[5]Università Cattolica del Sacro Cuore, Roma, Italy
[6]Ospedale A. Perrino, Brindisi, Italy
[7]Ospedale "F. Miulli", Acquaviva delle Fonti, Bari, Italy
[8]Università di Brescia, Italy
[9]IRCCS INM Neuromed, Pozzilli, Isernia, Italy
[10]Università di Roma "Tor Vergata", Rome,Italy
[11]Università di Catania, Catania, Italy
[12]Università di Torino, Torino, Italy
[13]Università di Padova, Padova, Italy
[14]Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
[15]Ospedale San Salvatore, L'Aquila, Italy
[16]Università Magna Graecia, Catanzaro, Italy
[17]Università di Salerno, Baronissi, Salerno, Italy
[18]Ospedale Brotzu, Cagliari, Italy
[19]Università di Firenze, Firenze, Italy
[20]Università Politecnica Delle Marche, Ancona, Italy
[21]Ospedale e Università di Perugia, Perugia, Italy
[22]Università di Roma “La Sapienza”, Roma, Italy
[23]Università di Verona, Verona, Italy
[24]Università della Campania "Luigi Vanvitelli", Napoli, Italy
[25]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

*Introduction:* GBA mutation represents the most important genetic risk factor for Parkinson’s disease (PD). Homozygous or compound heterozygous mutations cause Gaucher’s disease (GD) – the most common recessive lysosomal storage disorder [1]. Incidence of GD among PD is unclear, such as the role of the mutation in the PD pathogenesis in patients with or without GD.

*Objectives:* Investigate the experience of an Italian group of 24 PD experts on screening patients using Dried Blood Spot tests (DBSt) and a criteria list for identifying GBA and GD-PD.

*Methods:* Participants were equipped with a suspicion index of neurological (PD or LBD cases with pain, RBD, neuropsychiatric issues, dysautonomia, early fluctuations) and general (organomegaly, fractures/bone pain, hematological issues) criteria. Participants obtained and tested DBSt for CGase activity, substrate (LysoGB1) accumulation and GBA status as for GD routine [2].
*Results:* 336 patients were screened (age 33–93). 63/336 (18.7%) had a heterozygous GBA mutation: 7 L444P (11%), 11 N370S (17.5%), 19 E326K or T369M (30%), 26 (41%) other rarer variants. Mean GCase activity and LysoGB1were 4.64 nMol/h/ml and 5.08 ng/ml. Two patients had compound heterozygous mutations (T369M/N370S, E326K/C342F) and a LysoGB1 over the reference. Intriguingly, 8/63 presented abnormal LysoGB1 despite having normal GCase activity and

heterozygous mutations. The large part of centers screened PD (>75%), but also LBD (<25%) cases. The role of neurological criteria on selecting cases was largely over the 50%, while the use of general criteria was frequently of 50% or lower. The most relevant criteria for identify GBA-PD cases were considered early fluctuations/psychiatric symptoms and hematological issues.

*Conclusions:* Large genotype-phenotype studies on GBA PD are already available [3], however there is still the unmet need to identifying GBA-PD. Here we provide early evidence of the use of a suspicion index in selecting GBA-PD cases, but a further prospective study is warranted.

**References:**

[1] Riboldi GM, Di Fonzo AB. GBA, Gaucher Disease, and Parkinson's Disease: From Genetic to Clinic to New Therapeutic Approaches. Cells. 2019 Apr 19;8(4):364. doi: 10.3390/cells8040364.

[2] Zizzo C, Ruggeri I, Colomba P, et al. Hemochromatosis Mimicked Gaucher Disease: Role of Hyperferritinemia in Evaluation of a Clinical Case. Biology (Basel). 2022 Jun 15;11(6):914.

[3] Petrucci S, Ginevrino M, Trezzi I, et al.; ITA-GENE-PD Study Group. GBA-Related Parkinson's Disease: Dissection of Genotype-Phenotype Correlates in a Large Italian Cohort. Mov Disord. 2020 Nov;35(11):2106-2111. doi: 10.1002/mds.28195.

**P63**

## Gait analysis between a cohort of Alzheimer's disease, Lewy Body Dementia, Parkinson disease and healty control group a cross sectional study with wearable devices

*Marcello Catania*[1], A. Pilotto[1], A. Rizzardi[1], C. Zatti[1], A. Benussi[1], S. Caratozzolo[1], A. Lupini[1], C. Tirloni[1], A. Galli[1], C. Hansen[2], W. Maetzler[2], A. Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Study of Brescia, Brescia, Italy
[2]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany

*Background:* The application of wearable motion sensors is currently in continuous expansion in the field of motion disorders. Numerous studies demonstrate the usefulness and need for an objective assessment, using tools capable of quantifying the movement, walking and balance of patients, which have so far been assessed using the indirect measurement of international assessment scales.
To date there is still no application of these devices in the panorama of degenerative disorders, considering movement disorders, gait alteration as a possible marker, in this case, a digital marker to evaluate the patient suffering from cognitive impairment.

*Objective:* To investigate the performance differences of standard motion tasks detected with wearable motion sensors between healthy subjects and patients with Alzheimer's disease and Lewy body dementia.
Comparison of sensory measurements in the two groups of patients affected by cognitive impairment (AD or DLB) in tests characterized by dual tasking tasks (motor and cognitive).

*Methods:* A cohort of 140 subjects, divided into 19 patients diagnosed with AD, 20 DLB, 21 patients diagnosed with PD and 80 Healty Controls were selected among the patients belonging to the outpatient clinic designated for patients with movement disorders or for patients with neurocognitive decline at the Neurological Clinic of the U.O. Neurology II of the Civil Hospitals of Brescia and tested in an ambulatory settings whit Reha Gait (Magdeburg, DE) wearable sensor.

*Results:* From the comparison analysis of the data collected using wearable motion sensors we find out significant differences emerged between the various measurements: several significant differences were found between the cohort of healthy subjects and patients with cognitive impairment, both in patients with dementia with Lewy bodies and in patients with Alzheimer's disease. The comparison between the group of AD and DLB patients did not reveal significant differences between the motor and cognitive dual tasks considering the average values of the various gait parameters recorded by the wearable sensors, but analyzing the COST compared to the Straight Walking fast significant differences emerged in the cognitive task, particularly in the Number of Steps ($p = 0.017$), Step Time and derived measures ($p < 0.05$).

*Conclusions:* Wearable movement sensors are able to demonstrate a statistically significant difference in gait between healthy subjects of the same age, sex, education and patients affected by either AD, DLB and PD. Furthermore, from the analysis of the data it emerges that subjects affected by AD also show significant differences compared to healthy controls in terms of gait alterations. These alterations are comparable to those presented by patients with DLB, with respect to which statistically significant differences in the cognitive Dual task (Serial Subtraction) can be appreciated.

**P64**

## The impact of psychotherapy in functional neurological disorder: an insight into neurobiological systems

*Stefania Pavan*[1], Y. Radin[2], P. Caruso[1], A. Clarici[3,4], M. Bulfon[2], T. Lombardo[1], P. Manganotti[1]

[1]Neurology Unit, Department of Medical, Surgical and Health Sciences, Cattinara University Hospital, ASUGI, University of Trieste, Trieste, Italy
[2]Department of Pediatrics, Institute for Maternal and Child Health Burlo Garofolo (IRCCS), Trieste, Italy
[3]Department of Medical, Surgical and Health Sciences, Cattinara Hospital, University of Trieste, Trieste, (UniTS), Italy

*Introduction:* Functional neurological disorders (DNF) are conditions in which the primary pathophysiological processes is the dysfunction of sensory processing, motor or thought output, or both. Limbic influences on awareness and control of sensory, motor and behavioral functions are thought to contribute directly to the generation of DNF symptoms [1].
Assess a definitive diagnosis through positive symptoms found in clinical evaluation is the first step in managing DNF. Afterwards it is important to define a tailor-made multimodal therapeutic approach, where psychotherapy can play an important role.

*Objective:* To evaluate the impact of a cycle of psychotherapy over time in subjects affected by functional neurological disorder.

*Methods:* Sixteen subjects diagnosed with DNF were enrolled on a voluntary basis (2 males and 14 females). Subjects were given a cycle of 10 weekly psychological interviews. Before starting the interview cycle (T0), patients were administered two tests: SHEDLER-Westen Assessment Procedure (SWAP), a personality assessment instrument [2], and Affective Neuroscience Personality Scale (ANPS), to measure behavioral traits related to 6 affective neurobiological systems (play, seek, care, fear, anger, and sadness) [3]. The tests were then repeated at the end of the psychotherapeutic cycle (T1) and after two months (T2).

*Results:* Comparing the performance on the ANPS test before the start of the interviews (T0) and at the end of the process (T1), a significant difference emerges for the sadness system. This difference zeroes when comparing the performance at T0 with the follow-up (T2). Likewise, a significant difference emerges on the SWAP test at T0 and at T1 as regards the narcissistic factor. This difference is zeroed again by comparing the performances before the psychological cycle and after two months from the end of the same.

*Conclusions:* These data seem to bring out the need to establish a specialist clinic for DNF patients periodically followed by psychotherapists adequately trained in the neuroscientific field.

**References:**

[1] Hallett M, Aybek S, Dworetzky BA, McWhirter L, Staab JP, Stone J. Functional neurological disorder: new subtypes and shared mechanisms. Lancet Neurol. 2022; 21 (6): 537-550.
[2] Shedler J, Westen D. The Shedler-Westen Assessment Procedure (SWAP): making personality diagnosis clinically meaningful. J Pers Assess. 2007; 89 (1): 41-55.
[3] Davis K.L., Panksepp J, & Normansell L. The Affective Neuroscience Personality Scales: Normative data and implications. Neuropsychoanalysis. 2003; 5, 57–69.

**P65**

## Hemichorea-hemiballismus as an unusual presentation of diabetes mellitus – A case report

*Maria Vizziello*[1], G. Oggioni[2], M. Secchi[2], C. Rosci[2], M. Zardoni[2], C. Manfredi[2], T. Bocci[2,3], A. Priori[2,3], A. Bertini[1]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Clinical Neurology Unit, ASST Santi Paolo & Carlo and Department of Health Sciences, University of Milan, Milan, Italy
[3]Aldo Ravelli Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy

*Introduction:* Hyperglycemia-induced hemichorea-hemiballismus syndrome (HHHS) is a rare, potentially severe but reversible cause of chorea. It usually develops in patients already known to be diabetic, but it can also rarely be the first presentation of diabetes [1].
Brain magnetic resonance imaging (MRI) often shows typical findings and is crucial in differentiating HHHS from vascular chorea.
Since treatment of the underlying metabolic alteration plus symptomatic therapy usually reverse symptoms, it is important to consider HHHS as a cause of acute-onset chorea.

*Objective:* To describe the clinical and neuroradiological findings in a patient with HHHS.

*Methods:* A patient with recent history of uncontrolled diabetes and acute onset of hemichorea underwent neurological examination, routine blood and urine analysis, and brain MRI.

*Results:* A 78-year-old woman was admitted to our hospital complaining of 6 days of choreic movements affecting her left upper and lower extremity. She had been diagnosed with type 2 diabetes two weeks before, but despite therapy she reported poor control of blood glucose values.
Blood tests showed blood glucose level of 357 mg/dL and serum osmolality of 301 mOsm/kg. Her venous pH was 7.39, and bicarbonate 29 mmol/L. Glycosylated hemoglobin (HbA1c) was 138 mmol/mol. Brain MRI revealed a high intensity signal on T1-weighted images in both lentiform nuclei, more evident on the right side.
Abnormal limb movements persisted even after normalization of the blood glucose levels, so symptomatic attempt with haloperidol was started.
At a 6-months-follow up visit after hospital discharge, movements were no more noticeable.

*Conclusions:* Nonketotic hyperglycemia is an unusual, potentially easily-treatable cause of chorea-ballismus. Early recognition is crucial in order to start a prompt management and prevent further complications. HHHS should always be suspected in new-onset chorea/hemichorea, even in patients with no history of diabetes. The prognosis is excellent in most of the cases.

**References:**

[1] Bhagwat NM, Joshi AS, Rao G, Varthakavi PK. Uncontrolled hyperglycaemia: a reversible cause of hemichorea-hemiballismus. BMJ Case Rep. 2013 Sep 6;2013:bcr2013010229. doi: 10.1136/bcr-2013-010229. PMID: 24014327; PMCID: PMC3794112.

**P66**

## The use of an Instagram filter for postural tremor assessment

*Cristiano Sorrentino*, M. Russo, M. T. Pellecchia, M. Picillo, P. Barone, R. Erro

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

*Introduction:* The assessment of tremor is currently performed by means of validated scales which require patients to be evaluated in person, but there is the need for remote tremor telemonitoring.

*Objective:* The aim of this study is to evaluate an Instagram filter as a complementary tool for postural tremor assessment.

*Methods:* We asked patients to take a video of a printed Archimedes' spiral using an Instagram filter (i.e., Slit-scan), which overlaps single video frames into one picture. The photographed spirals (p-spirals) were then scored using the identical system used to score the classic Archimedes' spirals drawn by the patients themselves (d-spirals), according to TETRAS. A blinded author evaluated the level of agreement between the p-spirals and the d-spirals of the 21 patients with the most common action tremor syndromes (Essential tremor, Essential tremor plus and dystonic tremor).

*Results:* Using the Spearman test, a significant correlation was found between p-spirals and d-spirals scores ($\rho=0.444$, $p\leq0.003$), and between the p-spirals scores and the mean of the items assessing postural tremor (i.e., outstretched- and wing-beating- positions) ($\rho=0.535$, $p\leq0.010$). Severity of kinetic tremor and of the total TETRAS did not correlate with p-spirals scores.

*Conclusions:* The use of slit-scan could represent a useful tool for measuring postural tremor in addition the classic Archimedes' spirals drawing. Its use might be useful in distinguishing the various components of action tremor and their response to therapeutic treatment. Larger studies are needed to validate this Instagram filter as a tool to be used in clinical practice.

**P67**

## Atypical sonographic findings in a young man with parkinsonism in Machado-Joseph disease

*Maria Luisa Usai*[1], R. Meloni[1], C. Frau[2], P. Chessa[1], V. Floris[1], C. Bagella[3], A. Mura[3], P. Solla[2], C.F. Bagella[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Unit of Neurology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
[3]Unit of Nuclear Medicine, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

*Introduction:* Machado-Joseph disease (MJD), also known as spinocerebellar ataxia type 3 (SCA3), is an autosomal dominantly inherited cerebellar ataxia caused by CAG trinucleotide repeat expansions in the coding regions of ATXN3 gene [1]. Few studies have performed transcranial sonography (TSC) in SCA 3 patients and found hyperechogenicity of Substantia Nigra (SN) associated with a larger width of third ventricle and lenticular nucleus hyperechogenicity compared to healthy controls [2-3]. The disease is characterized by phenotype variability and several subtypes have been defined [4] that could be related to the atypical echofeatures found in our young patient.

*Objective:* Case report.

*Methods:* We studied the case of a 27 years old African man with a 3-years history of gradually progressive slowness of movements and balance difficulty, with referred negative family history for neurological diseases. He underwent full neurological examination and genetic analysis on peripheral blood sample using PCR and capillary electrophoresis.

*Results:* Neurological examination revealed marked bradykinesia (mainly on the left) and gait ataxia, moderate gaze-evoked horizontal nystagmus and generalized hyperreflexia, without tremor, hypertonia or rigidity. Poor response to L-dopa therapy.
Brain MRI showed cerebellar vermian atrophy with ventricular enlargement.
123I-FP-CIT SPECT revealed a moderate bilateral reduction of dopamine presynaptic transporter levels.
TCS showed third ventricular enlargement and right lenticular nucleus hyperechogenicity. There was no evidence of SN hyperechogenicity.
Genetic analysis demonstrated pathogenetic CAG repeat expansion (67 repeats) in the coding region of ATXN3 gene.

*Conclusions:* In agreement with previous studies, MJD should be considered in the differential diagnosis of PD-like symptoms. The enlargement of third ventricle but the absence of SN hyperechogenicity found in our patient may suggest the presence of different pathophysiologic substrates correlated to a possible distinctive phenotype, that deserves to be investigated. Furthermore, given the fact that lenticular nucleus hyperechogenicity is associated with dystonia [5], follow-up is indicated regarding a possible development of this symptom.

**References:**

[1] Schöls L, Bauer P, Schmidt T, Schulte T, Riess O. Autosomal dominant cerebellar ataxias: clinical features, genetics, and pathogenesis. Lancet Neurol. 2004 May
[2] Postert T, Eyding J, Berg D, Przuntek H, Becker G, Finger M, Schöls L. Transcranial sonography in spinocerebellar ataxia type 3. J Neural Transm Suppl. 2004
[3] Pedroso JL, Bor-Seng-Shu E, Felício AC, Braga-Neto P, Teixeira MJ, Barsottini OG. Transcranial sonography findings in spinocerebellar ataxia type 3 (Machado-Joseph disease): a cross-sectional study. Neurosci Lett. 2011 Oct 24

[4] Fowler HL. Machado-Joseph-Azorean disease. A ten-year study. Arch Neurol. 1984 Sep
[5] Naumann, M., Becker, G., Toyka, K. V., Supprian, T., and Reiners, K. (1996). Lenticular nucleus lesion in idiopathic dystonia detected by transcranial sonography

**P68**

## Should patients with atypical presentation of parkinsonism be tested for lysosomal storage diseases?

*Giulia Grigioni*[1], A. Govoni[1], L. Caremani[1], F. Piattellini[1,2], S. Valente[1,2], S. Mombelli[1,2], D. Greco[1,2], A. Caciotti[3], F. Feo[3], A. Morrone[2,3], S. Ramat[1]

[1]Parkinson Unit, Department of NeuroMuscular–Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[2]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[3]Laboratory of Molecular Biology of Neurometabolic Diseases, Neuroscience Department, Meyer Children's Hospital, IRCCS, Florence, Italy

*Introduction:* The correlation between lysosomal storage diseases (LSDs) and neurodegenerative disorders has become increasingly evident, in particular the association between mutations of GBA gene, which encodes the lysosomal β-glucosidase, and Parkinson's disease (PD) has been reported.

*Objective:* To present the case of a patient with parkinsonism enrolled in a study (acronym Lysolate). This research project is funded by Tuscany Region.

*Methods:* The Lysolate study investigates the presence of late onset LSDs in patients with undefined neurodegenerative symptoms with or without multiorgan involvement. Patients enrolled in the study were analysed using a Next Generation Sequencing (NGS) panel including more than 65 genes involved in LSDs.

*Results:* We present the case of a woman who suffered from mood disorder characterized by phobias and anxiety from a young age, whose symptoms worsened at the age of 70 to include obsessive-compulsive behaviours. She developed clear extrapyramidal signs, hallucinations, seizures and a rapid and progressive cognitive decline, which leaded to muteness, a bedridden condition and finally to death at the age of 80. She also suffered from high blood pressure, diabetes, thrombocytopenia, glaucoma, cataract, right retinal melanoma and Horton's arteritis. Brain MRI showed cerebral atrophy with enlargement of cerebrospinal fluid spaces and white matter alterations. SPET brain DaTscan highlighted a severe degeneration of the nigrostriatal system. The NGS analysis showed that she was heterozygous for the known pathogenic c.662A>G p.(Tyr221Cys) variant in the CLN6 gene, previously associated with Neuronal ceroid lipofuscinosis [1].

*Conclusions:* Clinical data are consistent with a possible diagnosis of ceroid lipofuscinoses 6 related to mutations in the CLN6 gene. Unfortunately, the mis-identification of the second disease causing variant in the CLN6 gene didn't allow a definitive diagnosis. However, these data confirm that patients with an atypical presentation of parkinsonism should undergo a detailed genetic analysis, including screening for genes causing LSDs.

**References:**

[1] Cannelli N, Garavaglia B, Simonati A, Aiello C, Barzaghi C, Pezzini F, Cilio MR, Biancheri R, Morbin M, Dalla Bernardina B, Granata T, Tessa A, Invernizzi F, Pessagno A, Boldrini R, Zibordi F, Grazian L, Claps D, Carrozzo R, Mole SE, Nardocci N, Santorelli FM. Variant late infantile ceroid lipofuscinoses associated with novel mutations in CLN6. Biochem Biophys Res Commun. 2009 Feb 20;379(4):892-7.

**P69**

## The relationship between total electrical energy delivered (teed) and post-DBS cognitive function in patients with Parkinson's disease: a preliminary analysis

*Francesca Mameli*[1], E. Zirone[1], R. Ferrucci[2], S. Marceglia[3], M. Prenassi[3], L. Borellini[1], F. Cogiamanian[1], M.T. Molisso[1], R. Girlando[1], E. Pirola[1], M. Locatelli[1], S. Barbieri[1], A. Priori[3], F. Ruggiero[1]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2]University of Milan, Milan, Italy
[3]University of Trieste, Trieste, Italy

*Introduction:* Bilateral deep brain stimulation (DBS) of the subthalamic nucleus (DBS-STN) is the current treatment option for advanced Parkinson's disease (PD) that is unresponsive to drug therapy. While the motor benefits of surgery are well established, the consensus on the long-term neuropsychological outcome remains debated.

*Objective:* We examined the cognitive outcome in PD, 6 months after bilateral deep DBS-STN and the possible effect of the amount of total electrical energy delivered (TEED) on neuropsychological changes.

*Methods:* 21 patients with PD (10 female, mean [±SD] age 59 ± 7.07 years) were included in this study. Cognitive functions were assessed in all patients with MoCA) [1], phonemic [2] and semantic verbal fluency tasks [3] before (T0) and 6 months after surgery (T1). At T1, we recorded stimulation parameters, to estimate TEED to STN [4].

*Results:* One-way repeated measures ANOVAs showed a significant main effect of 'Time' on phonemic fluency ($F[2.40] = 10.39$; $p < 0.001$; $\eta 2=0.34$) and semantic fluency ($F[2.40]=11.21$; $p < 0.001$; $\eta 2=0.33$). Bonferroni-corrected post-hoc tests showed that phonemic and semantic verbal fluency worsened at T1 (phonemic fluency T0 vs T1: mean ± SD=42.38 ± 10.85 vs. 36.33 ± 10.80; $p=0.001$; semantic fluency T0 vs T1: mean ± SD=48.14 ± 8.36 vs. 40.86 ± 9.41; $p<0.001$). There was no significant main effect on MoCA test ($p=0.362$). TEED did not differ significantly between the left and right STN at T1 ($p=0.601$). We found no significant correlations between cognitive performance and TEED left ($p>0.05$), TEED right ($p>0.05$), or TEED laterality ($p>0.05$).

*Discussion:* Chronic stimulation has been suggested as the underlying mechanism, but we found no correlation with TEED. It is possible that other effects may underlie the etiology of the cognitive sequelae in STN-DBS. More systematic studies of the prevalence of verbal fluency deficits after DBS are needed to better understand the complex nature of the neuropsychological outcome.

**References:**

[1] Santangelo et al. (2015) Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36(4), 585-591.
[2] Carlesimo et al. (1996) The Mental deterioration battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. Eur Neurol, 36:378–384.
[3] Costa et al. (2014). Standardization and normative data obtained in the Italian population for a new verbal fluency instrument, the phonemic/semantic alternate fluency test. Neurological Sciences, 35(3), 365-372.
[4] Mameli et al. (2022) Energy Delivered by Subthalamic Deep Brain Stimulation for Parkinson Disease Correlates With Depressive Personality Trait Shift. Neuromodulation, S1094-7159(22)00024-1.

**P70**

## Motor outcomes and possible predictive factors for directional deep brain stimulation

*Leonardo Rigon*[1], F. Bove[1], D. Genovese[1], P. Sanginario[1], A.R. Bentivoglio[1,2], P. Calabresi[1,2], C. Piano[1]

[1]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[2]Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy

*Background:* Deep Brain Stimulation (DBS) is a well-established therapeutic approach for patients with advanced Parkinson's disease [1-2]. Directional stimulation (DS) extended the therapeutic window by increasing the side effects threshold and minimizing the impact of suboptimal lead placement as compared to conventional stimulation (CS) [3], although its superiority in motor outcomes is still debated.

*Objective:* We aimed to assess possible predictive factors for DS use and its motor outcomes as compared to CS.

*Methods:* Patients with DBS implant compatible with DS with at least six-months follow-up were included. Subjects were divided into two subgroups (DS vs CS), according to the stimulation settings at the latest follow-up. Motor outcomes were compared between the two groups. Predictive factors for the use of DS were evaluated.

*Results:* A total of 42 patients were included. At the latest follow-up, DS and CS subgroups showed the same population (21 subjects each). DS seemed to achieve better, although not significantly superior, motor outcomes, in particular in the stimulation-induced improvement of the Unified Parkinson's Disease Rating Scale (UPDRS) III in off-medication state (DS 31% vs CS 24%, p=0,9) and in the reduction of the Levodopa Equivalent Daily Dose (LEDD) (DS 47% vs CS 40%, p=0,6). Among those considered at baseline (demographic variables, disease duration, motor phenotype, Hoehn & Yahr stage, LEDD, motor impairment, axial symptoms, improvement after levodopa challenge), no clear predictive factor for DS use was highlighted.

*Conclusions:* In our study DS seemed to achieve better motor outcomes as compared to CS, although such trend resulted not statistically significant, possibly due to the limited sample size and short follow-up period. Similarly, no clinical feature at baseline correlated with DS use. Larger study samples and longer follow-up periods are needed to elucidate whether DS, along with the renown milder side effects3,4, achieves better motor outcomes as compared to CS.

**References:**

[1] Weaver FM, Follett K, Stern M, et al. Bilateral deep brain stimulation vs best medical therapy for patients with advanced Parkinson disease: a randomized controlled trial. JAMA. 2009;301(1):63-73. doi:10.1001/jama.2008.929.
[2] Kleiner-Fisman G, Herzog J, Fisman DN, et al. Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. Mov Disord. 2006;21 Suppl 14:S290-S304. doi:10.1002/mds.20962.
[3] Dembek TA, Reker P, Visser-Vandewalle V, et al. Directional DBS increases side-effect thresholds-A prospective, double-blind trial. Mov Disord. 2017;32(10):1380-1388. doi:10.1002/mds.27093.
[4] Reker P, Dembek TA, Becker J, Visser-Vandewalle V, Timmermann L. Directional deep brain stimulation: A case of avoiding dysarthria with bipolar directional current steering. Parkinsonism Relat Disord. 2016;31:156-158. doi:10.1016/j.parkreldis.2016.08.007.

**P71**

## STN DBS in Parkinson's disease camptocormia

*Elena Caputo*[1], F. Tamma[1], M. Egidi[2], S. Tagliente[1], G. Casaceli[2], P. Mancino[1], A. Fasano[3]

[1]UOC Neurologia/Stroke Unit, Osp. Gen. Reg. "F. Miulli", Acquaviva delle Fonti, Bari, Italy
[2]UOC Neurochirurgia, ASST Santi Paolo e Carlo, Milano, Italy
[3]Division of Neurology, University of Toronto, Ontario, Canada

*Introduction:* DBS effects on camptocormia are still poorly clarified, a consense on the best target (GPi vs STN) is still lacking [1-2]. We describe a case of severe camptocormia in an advanced PD, treated with STN DBS.

*Case report:* A 73 yo male patient with a 15-years history of PD, developed motor fluctuations after 10 years of disease, and eventually severe camptocormia and Pisa syndrome appeared. His mobility and independance were heavily compromised by extreme anterior bending of spine (video segment 1), which resolved only when supine, while did not respond to suspension of pramipexole and only minimally to levodopa increase up to 2000 mg a day. Dorso-lumbar MR did not reveal myopathy. Cognition was notably intact, there were no comorbidities.
After discussing pros and cons with the patient and his caregiver, bilateral STN electrodes were implanted on December 6th, 2022. Stimulation was switched on after réglage on January 9th, 2023. A moderate reduction of camptocormia was achieved after 30 days of stimulation (video segment 2), along with good control of motor fluctuations.

*Discussion:* Lacking scientific and clinical data for clearcut inclusion criteria for DBS procedures in PD patients with postural deformities, including target choice, we think that each contribute, even a single case report may add on general knowledge on this topic.
Our case shows that STN DBS may improve parkinsonian truncal deformities, providing these symptoms have a recent onset and are not due to myopathy, as stated in literature.
Moreover advanced age is not an absolute contraindication for STN DBS in subjects with severe camptocormia not responding to other therapeutic options, providing other comorbidities are absent, and strong motivation along with comprehension of risk/benefit ratio are respected [3]. A longer follow up is needed to confirm the long term effect of STN DBS in our patient.

**References:**

[1] Spindler et al., 2022. Neurosurg Rew; 45: 3083-3092.
[2] Lizarraga et al., 2019. Mov Dis Clin Pract; 6 (8): 627-638.
[3] Margraf et al., 2016. J Park Dis; 6 (3): 485-501.

**P72**

## The impact of dysphagia in Parkinson's disease patients treated with levodopa/carbidopa intestinal gel

*Domiziana Rinaldi*[1,2], G. Imbalzano[3,4], S. Galli[1], E. Bianchini[1], C. Ledda[3,4], L. De Carolis[1], M. Zibetti[3,4], L. Lopiano[3,4], F.E. Pontieri[1,2], C.A. Artusi[3,4]

[1]Dipartimento di Neuroscienze, Salute Mentale e Organi di Senso, Sapienza Università di Roma, Rome, Italy
[2]Fondazione Santa Lucia, IRCCS, Rome, Italy
[3]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[4]SC Neurologia 2U, AOU City of Health and Science, Turin, Italy

*Background:* Dysphagia is a common feature in advanced phases of Parkinson's disease (PD), representing a significant risk factor for aspiration pneumonia, which is the first cause of death in PD. The impact of dysphagia in advanced PD patients treated with levodopa-carbidopa intestinal gel (LCIG) has been poorly investigated.

*Methods:* We retrospectively evaluated data from 95 consecutive PD patients treated with LCIG in two Italian movement disorder centers. Kaplan-Meier survival analysis and log-rank test were used to compare the survival between patients developing dysphagia (LCIG-Dys) or not (LCIG-NDys). A Cox regression was used to estimate the influence of age, disease duration, Hoehn and Yahr (H&Y) at LCIG implantation, and presence of dysphagia on mortality. We used univariate and multivariate regression analysis to estimate the association between dysphagia and age, disease duration, H&Y, hallucinations, and dementia at last evaluation.

*Results:* The survival analysis showed a significant higher mortality in LCIG-Dys vs. LCIG-NDys group. Dysphagia was the only variable significantly associated with mortality (95%CI 2.780–20.609; $p< 0.001$). Univariate analyses showed a significant correlation between dysphagia and dementia (OR: 0.387; p: 0.033), hallucinations (OR: 0.283; p: 0.009), and H&Y score (OR: 2.680; $p< 0.001$). In the multivariate analysis, only the H&Y stage survived (OR: 2.357; p: 0.003).

*Conclusions:* Dysphagia significantly increased the risk of death in our cohort of LCIG-treated patients, independently from the presence of dementia and hallucinations. These findings confirm the management of this symptom as a priority in the advanced PD stages, especially in people treated with LCIG.

**P73**

## Neuropsychological alterations secondary to symptomatic edema after subthalamic nucleus deep brain stimulation surgery for Parkinson's disease: a case series

*Giulia Di Rauso*[1], S. De Ieso[2,3], F. Cavallieri[2], D. Beltrami[2,3], A. Marti[2,3], M. Napoli[4], R. Pascarella[4], A. Feletti[5,6], V. Fioravanti[2], G. Toschi[2], V. Rispoli[7], F. Antonelli[7], A. Puzzolante[6], G. Pavesi[5,6], F. Gasparini[2,3], F. Valzania[2]

[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[2]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3]Clinical Neuropsychology, Cognitive Disorders and Dyslexia Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[4]Neuroradiology Unit, Radiology Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5]Neurosurgery Unit, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy
[6]Neurosurgery Unit, Azienda Ospedaliero-Universitaria di Modena, Ospedale Civile di Baggiovara, Modena, Italy
[7]Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

*Introduction:* Severe non-infectious or hemorrhagic brain edema surrounding the electrode represents a rare complication of subthalamic nucleus deep brain stimulation (STN-DBS) surgery.

*Objective:* To report three patients with advanced Parkinson's disease (PD) who developed symptomatic brain edema after STN-DBS surgery treated with intravenous steroids with a specific profile of reversible cognitive alterations.

*Methods:* Patients were systematically evaluated with a deep neuropsychological and behavioural assessment before the surgery (baseline), as they became symptomatic for the post-surgery edema and few more times in follow-up.

*Case description:* The first PD patient was a 63-years-old woman without previous cognitive deficits or emotional-behavioural alterations who underwent bilateral STN-DBS surgery, complicated by delayed-onset bilateral frontal subcortical edema manifested with difficulties in language production and spatial-temporal disorientation. Subsequent neuropsychological assessment detected left unilateral spatial neglect related to personal and peripersonal space, executive deficits and complete anosognosia. Three weeks after surgery, the CT scan showed complete resolution of brain edema with resolution of cognitive alterations. Second patient was a 55-years-old male with baseline slight executive and visuo-spatial deficits. Five days after surgery he developed confusion, spatial-temporal disorientation with severe cerebral edema. Neuropsychological reassessment showed severe worsening of cognitive performances, particularly left unilateral spatial neglect and inhibitory control deficits. Six weeks later neuropsychological assessment revealed a cognitive and psychological improvement with complete resolution four months after surgery. The third patient was a 60 years-old woman who underwent bilateral STN-DBS with normal baseline cognitive performances. 7 days after surgery the patient complaint new onset procedural difficulties and brain CT-scan revealed left middle-upper frontal edema. Neuropsychological evaluation documented executive and visuospatial deficits. After 6-months, neuropsychological evaluation was repeated and resulted superimposable to the pre-operative one.

*Conclusion:* In all patients we observed the resolution of cognitive deficits within six months after surgery with the corresponding reabsorption of edema at brain CT scans.

**P74**

## Peri-lead idiopathic delayed-onset bilateral edema after implantation of deep brain stimulation in a GBA mutation carrier: a case report

*Pietro Antenucci*[1], A. Gozzi[1], F. Morgante[2], C. Sorbera[3], M.A. Cavallo[4], M. Sensi[5]

[1]Department of Neurosciences and Rehabilitation, University of Ferrara, Cona, Ferrara, Italy
[2]Motor Control and Movement Disorders Group, Institute of Molecular and Clinical Sciences, St George's University of London, London, UK
[3]Neurorehabilitation Unit IRCCS Centro Neurolesi "Bonino Pulejo," Messina, Italy
[4]Neurosurgery Unit, Ferrara University Hospital, Department of Morphology Surgery and Experimental Medicine, Ferrara, Italy
[5]Department of Neuroscience and Rehabilitation, Azienda Ospedaliero-Universitaria S. Anna, Ferrara, Italy

Peri-lead idiopathic delayed-onset edema (IDE) is a self-limiting edema along a single intracranial lead, occurring ≥ 72 h after surgery in the absence of trauma that could rarely complicated deep brain stimulation (DBS) implantation for Parkinson's disease (PD) treatment [1]. No risk factors for IDE predisposition have been identified and switching-off the stimulation has been proposed as the safest managing options for IDE [1-2]. We report the case of a 39-year-old male carrying a GBA genetic mutation (G202R) with an early onset of tremor dominant PD who underwent the DBS intervention and a few days later developed symptomatic and bilateral synchronous edema along the leads. Due to the presence of severe parkinsonism, stimulation was switched on the 16th day after implantation once measured normal impedance values even though the edema was still present, with a satisfactory improvement on motor symptoms. According to the literature, G202R mutations have been associated with a subtype of Gaucher Disease [3] characterized by nonimmune hydrops with abnormal nonimmune interstitial fluid collections [4]. Regarding the absolute rare incidence of bilateral and synchronous IDE, we assumed a possible correlation between genotype variants of GBA mutation and the predisposition to the occurrence of IDE [5-6-7].

**References:**

[1]. de Cuba, et al. Idiopathic delayed-onset edema surrounding deep brain stimulation leads: Insights from a case series and systematic literature review. (2016).
[2]. Hooper, S. & Cameron, T. Neurotoxicity screening test for deep brain stimulation leads. J Biomater Sci Polym Ed 18, 1309–1320 (2007).
[3]. Grace, M. E., et al. Identification and expression of acid beta-glucosidase mutations causing severe type 1 and neurologic type 2 Gaucher disease in non-Jewish patients (1997)
[4]. Al ‐ Kouatly, H. B. et al. Lysosomal storage disease spectrum in nonimmune hydrops fetalis: a retrospective case control study. Prenat Diagn 40, 738–745 (2020).
[5]. Giraldo, P. & Andrade-Campos, M. Novel Management and Screening Approaches for Haematological Complications of Gaucher's Disease. J Blood Med Volume 12, 1045–1056 (2021).
[6]. Vitner, E. B., et al. Contribution of brain inflammation to neuronal cell death in neuronopathic forms of Gaucher's disease. (2012)
[7]. Pal, G. et al. Parkinson Disease and Subthalamic Nucleus Deep Brain Stimulation: Cognitive Effects in GBA Mutation Carriers. (2022).

**P75**

## One year of brain sensing: a real life experience on the use of brain sense DBS technology in clinical practice

*Massimo Marano*[1], A. Magliozzi[1], G. Anzini[1], D. Mei[2], D. Marruzzo[2], F.R. Barbieri[2], V. Di Lazzaro[1], R. Ricciuti[2]

[1]Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[2]UO Neurochirurgia, Ospedale Belcolle, Viterbo, Italy

*Introduction:* In recent years deep brain stimulation (DBS) surgery for patients with Parkinson's disease (PD) made substantial technological advancements: first with the availability of directional stimulation (DS) leads, then with the use of local field potential (LFP) in clinical practice. The latter is under current investigation for its clinical utility and for its future application in adaptative DBS [1].

*Objectives:* Analyzing the use of directional brain sense technology (Percept IPG, SenSight leads, Medtronic) [2] in clinical practice through a retrospective analysis of PD patients' medical records collected since April 2022.

*Methods:* Data on disease and therapy, reconstructed lead positioning (SureTune4, Medtronic), and stimulation were collected for 10 STN DBS PD patients out of 14. LFPs amplitude was evaluated through a qualitative methodology (0-3 score) such as the impact of sensing on programming, chronic stimulation, troubleshooting, and event reporting.

*Results:* Mean patient age was 57.3±5.3 (8 males). Follow-up duration was 6.5±3 months. LEDD before surgery vs last follow-up visit was 1158±316 mgs vs 320±209 mgs. The most prevalent STN lead location was centro-medial (45%). 70% of leads were on DS due to mood (50%), motor control (40%), speech (20%) and sensory complaints (10%). Current intensity ranged from 1.6 to 3.5 for ring stimulation (30%) and from 0.7 to 3.1 for directional contact (70%), mean pulse width was 65±12 μs and frequency 130±20 Hz. There was a significant interaction between the LFP amplitude and the stimulating contact ($p<0.05$). The monitored frequency was 18.8±4.7 Hz. Sensing was judged of high relevance (score 3) in 50% programming, in 30% of long-term management/troubleshooting (40% if event reporting was adopted).

*Conclusions:* This study provides real-life insights on new DBS technologies. The use of brain sensing in clinical practice is still questioned, but of uttermost importance toward the application of the closing loop stimulation [3].

**References:**

[1] Feldmann LK, Neumann WJ, Krause P, Lofredi R, Schneider GH, Kühn AA. Subthalamic beta band suppression reflects effective neuromodulation in chronic recordings. Eur J Neurol. 2021 Jul;28(7):2372-2377.
[2] Jimenez-Shahed J. Device profile of the percept PC deep brain stimulation system for the treatment of Parkinson's disease and related disorders. Expert Rev Med Devices. 2021 Apr;18(4):319-332.
[3] Nakajima A, Shimo Y, Fuse A, Tokugawa J, Hishii M, Iwamuro H, Umemura A, Hattori N. Case Report: Chronic Adaptive Deep Brain Stimulation Personalizing Therapy Based on Parkinsonian State. Front Hum Neurosci. 2021 Aug 13;15:702961.

**P76**

## Longitudinal multicentric study on the impact of GBA variants on the clinical outcome of Parkinson's Disease patients with deep brain stimulation

*Micol Avenali*[1,2], R. Zangaglia[2], G. Cuconato[3], I. Palmieri[2], A. Albanese[4], C.A. Artusi[5], M. Bozzali[5], F. Cavallieri[6], R. Cilia[7], A. Cocco[4], R. Eleopra[7], A. Imarisio[3], G. Imbalzano[5], C. Ledda[5], L. Lopiano[5], M.C. Malaguti[8], F. Mameli[9], P. Mitrotti[1], F. Spagnolo[10], C. Tassorelli[1,2], F. Valentino[2], F. Valzania[6], A. Di Fonzo[9], C. Pacchetti[2], E.M. Valente[2,3]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Molecular Medicine, University of Pavia, Pavia, Italy
[4]IRCCS Humanitas Research Hospital, Milan, Italy
[5]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Torino, Italy
[6]Azienda USL-IRCCS Reggio Emilia, Reggio Emilia, Italy
[7]IRCCS Besta Neurological Institute, Milan, Italy
[8]Neurology Unit, ASPP, Trento, Italy
[9]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[10]Antonio Perrino's Hospital, Brindisi, Italy

*Introduction:* GBA mutations are a well-known genetic risk factor for PD. We investigated the impact of GBA variants on the long-term outcome of deep brain stimulation (DBS) in a large cohort of Italian PD subjects who underwent DBS-surgery.

*Methods:* We retrospectively analysed clinical data from a multicentric Italian cohort of DBS-PD patients upon stratification for the presence/absence of GBA variants. Motor and non-motor features were recorded before surgery and after 1, 3 and 5 years.

*Results:* We recruited 294 DBS-PD patients, of whom 63 (22%) carried GBA variants (severe=29, mild=14, risk=12, unknown=8). In GBA-PD, mean age at onset was 44.1 ±1.1yrs, mean disease duration 9.0±0.5 yrs and age at DBS implant was 53.5±1.1. At pre-DBS evaluation, GBA-PD had earlier age at onset and shorter disease duration than non-mutated PD (NM-PD) but showed similar clinical features except dyskinesias (more prevalent in GBA-PD). At 3 to 5 years post-DBS, both groups showed motor improvement with satisfactory control of fluctuations and dyskinesias; all non-motor symptoms were also comparable except for cognitive scores, which worsened significantly faster in GBA-PD than NM-PD, already at 3 years from DBS. However a diagnosis of dementia were performed only in 25.81 % of GBA-PD after 5 years of follow-up. Analysis on GBA-PD stratified by mutation type are ongoing.

*Conclusions:* This is the first report addressing the impact of GBA variants on DBS clinical outcomes in a large well-characterized Italian PD cohort with a relatively long follow-up. Our data, although preliminary, suggest that GBA-PD patients benefit from DBS as much as NM-PD, as the frequency of motor complications is similar between the two groups. Cognitive performance, although progressively worsening in both groups, shows a more rapid deterioration in GBA-PD, however only a small percentage of them developed dementia after 5 years from DBS surgery.

**P77**

## Long-term safety and efficacy of frameless subthalamic deep brain stimulation in Parkinson's disease

*Danilo Genovese*[1,2], F. Bove[1,3], L. Rigon[3], T. Tufo[4], A. Izzo[4], P. Calabresi[1,3], A.R. Bentivoglio[1,3], C. Piano[1,3]

[1]Neurology Unit, IRCCS Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]The Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, Department of Neurology, NYU Langone Health, New York, NY, USA
[3]Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy
[4]Neurosurgery Unit, IRCCS Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

*Background:* Bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) is standard of care for Parkinson's disease (PD) patients and a correct lead placement is crucial to obtain good clinical outcomes for DBS surgery. The procedure can be performed through the use of a stereotactic frame, whose use is consolidated, or alternatively using a frameless system. Evidence demonstrating the comparable targeting accuracy of frameless technique, along with the advantages for patients and clinicians, is solid, but data reporting long-term clinical outcomes for PD patients are still lacking.

*Objectives:* The study aims to assess the clinical safety and efficacy of frameless bilateral STN-DBS in PD patients at 5 years from the surgery.

*Methods:* Consecutive PD patients undergoing bilateral STN-DBS with a frameless system were included in this single-center retrospective study. Clinical features, including the Unified Parkinson's Disease Rating Scale (UPDRS) in its total motor score and axial subscores, and pharmacological regimen were assessed at baseline, 1 year, 3 years and 5 years after surgery. The adverse events related to procedure, stimulation or to the presence of the hardware were systematically collected.

*Results:* No complications occurred during surgery and perioperative phase, and no unexpected serious adverse event occurred during the entire follow-up period. After 5 years from the surgery there was sustained motor efficacy of STN stimulation: STN-DBS significantly improved the off-stim UPDRS III score at 5 years by 37.6 % ($P < 0.001$), while the dopaminergic medications remained significantly reduced versus baseline ($P = 0.036$).

*Conclusions:* Our data support the use of frameless system for DBS, as a safe and well-tolerated technique, with long-term clinical benefits comparable with the data available in the frame-based literature.

**P78**

## Deep brain stimulation for medically refractory tremor in Wilson's disease: a single case and review of the literature

*Alfonso Giordano*[1], R. De Micco[1], M. Sensi[2], A. Gozzi[2], M.A. Cavallo[3], M. Cirillo[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]Department of Neuroscience and Rehabilitation, Azienda Ospedaliera-Universitaria S. Anna, Ferrara, Italy
[3]Neurosurgery, S. Anna University Hospital, Ferrara, Italy

A 41-years-old woman was referred to our outpatient clinic for a five year slowly progressive onset of speech impairment and tremor involving the arms and head. She had previously received a genetically confirmed diagnosis of Wilson's disease (WD) at the age of three years. At the admission neurological examination showed: a) action and postural tremor of the upper limbs (left more than right); its amplitude increased with a longer duration of posture (i.e wing-beating tremor); b) horizontal head tremor (i.e. "no-no"); c) voice tremor (video 1). Brain T2-MRI showed the typical "face of the giant panda sign" ( i.e. normal intensity of red nuclei and lateral portions of substantia nigra pars reticulata with high signal intensity of tegmentum and hypointensity of the superior colliculus) with no other evidence of basal ganglia structural changes.

Because of first line (primidone and propranolol) and second line (topiramate, pregabalin, clonazepam) therapy agents for tremor were unsuccessful, a surgical approach was proposed; the patient underwent to Deep Brain Stimulation (DBS) of ventral intermediate (Vim) thalamic nucleus. High stimulation output led to a significant reduction of her tremor amplitude of both arms and head; speech impairment remained stable and no potential DBS-related side effects were reported.

Vim has emerged as the most effective and established target for medically refractory tremor in patients with essential tremor (ET) [1]. Even though the pathophysiology of tremor is different between WD and ET our experience and published evidence support the potential role of Vim DBS as an effective and safe approach in carefully selected WD patients, although the presence of structural changes in the basal ganglia may limit the therapeutic success of the surgical procedure [2].

**References:**

[1] Krack P, Volkmann J, Tinkhauser G, Deuschl G. Deep Brain Stimulation in Movement Disorders: From Experimental Surgery to Evidence-Based Therapy. Mov Disord. 2019.
[2] Hedera P. Treatment of Wilson's disease motor complications with deep brain stimulation. Ann N Y Acad Sci. 2014.

**P79**

## Can rheumatoid arteritis be a risk factor for stroke during deep brain stimulation surgery? A case report with literature review

*Tiziana Benzi Markushi*[1], R. Marchese[2], L. Avanzino[2,3], F. Di Biasio[1]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy
[2]IRCCS Policlinico San Martino, Genoa, Italy
[3]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy

*Introduction:* Deep brain stimulation (DBS) is an increasingly therapeutic option for people with Parkinson disease (PD), but little is known about the outcomes in patients with PD and rheumatoid arthritis (AR).

*Case report:* We present the case of a 54 years-old woman with 9-years history of PD, started with tremor on the right side. For several years she presented good response to treatment. She had an aunt with PD, but genetic testing was referred as negative. She had not risk factors for cerebrovascular disease, except AR treated with methotrexate. During the surgery, after the implantation of the second electrode on the right (less affected side on the left), she presented abnormal involuntary movement of the right arm, initially interpreted as seizure. The TC scan showed a possible ischemic thalamic lesion, later confirmed by brain MRI, that revealed a vascular lesion on the postero-medial thalamic left side. Despite everything she obtained good results from DBS.

*Discussion:* although several studies have extensively analyzed hemorrhagic complications during DBS [1-2] few reports describe subcortical ischemic adverse events [3-4]. It is well established that AR increases the risk of cerebrovascular disease [5-6], but little is known about the role that AR and disease-modifying anti-rheumatic drugs could have on the PD patients during and after DBS. It has been reported that the use of specific treatments for AR may be a risk factor for infections after DBS [7]. Although other possible etiologies need to be considered, including physical disruption or compression of small artery branches, trauma-induced vasospasm, or electrically induced atraumatic vasoconstriction, in our case, given the absence of cerebrovascular risk factors, the most probable cause of stroke was the co-existence of AR rather than the procedures during DBS. Larger samples of patients and studies are needed to understand if DBS is a safe treatment in patients with PD and AR.

**References:**

[1] Sansur CA, Frysinger RC, Pouratian N, et al. Incidence of symptomatic hemorrhage after stereotactic electrode placement. J Neurosurg, 2007.
[2] Zrinzo L, Foltynie T, Limousin P, Hariz MI. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. J Neurosurg, 2012.
[3] Novak KE, Nenonene EK, Bernstein LP, Vergenz S, et al. Two cases of ischemia associated with subthalamic nucleus stimulator implantation for advanced Parkinson's disease. Mov Disord, 2006.
[4] Downes AE, Pezeshkian P, Behnke E, et al. Acute Ischemic Stroke During Deep Brain Stimulation Surgery of Globus Pallidus Internus: Report of 5 Cases. Oper Neurosurg, 2016.
[5] Zhang Q, Liao Y, Liu Z, Dai Y, Li Y, Li Y, Tang Y. Interleukin-17 and ischaemic stroke. Immunology, 2021.
[6] Maiuolo J, Muscoli C, Gliozzi M, et al. Endothelial Dysfunction and Extra-Articular Neurological Manifestations in Rheumatoid Arthritis. Biomolecules. 2021.
[7] Oses M, Ordás CM, Feliz C, et al. Disease-modifying anti-rheumatic drugs as a risk factor for delayed DBS implant infection. Parkinsonism Relat Disord, 2018.

**P80**

## A patient with limb apraxia and myoclonic tremor. Two possible culprits: venous drainage anomaly or cortico-basal syndrome?

*Francescantonio Cammarota*[1,2], F. Valentino[1], A. Pichiecchio[2,3], C. Asteggiano[3], R. Zangaglia[1], G. Vaghi[2], M. Todisco[4], C. Pacchetti[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Advanced Imaging and Radiomics Center, IRCCS Mondino Foundation, Pavia, Italy
[4]Traslational Neurophisiology Research Unit, IRCCS Mondino Foundation, Pavia, Italy

*Introduction:* Unilateral apraxia is often evocative of corticobasal syndrome (CBS). It is a neurodegenerative disorder that poses a significant diagnostic challenge given the wide variety of presentations: from early behavioral or cognitive impairment to classic asymmetric akinetic-rigid motor syndrome and apraxia.

*Objective:* In the present work, we describe the case of a 78-year-old female with a three-year history of myoclonic tremor and left arm apraxia not responsive to L-dopa and biperiden.

*Methods:* The patient was admitted to our department for clinical-diagnostic assessment.

*Results:* Clinical and neurophysiological evaluations were performed. Left hand tremor presented an irregular and high frequency myoclonic pattern at the electromyographic examination. Left hand ideomotor apraxia was confirmed at a neuropsychological assessment, and it was associated with a mild cognitive impairment with short-term memory and executive functions involvement. Single-photon emission computerized tomography (SPECT) with DaTscan showed a bilateral reduction of putaminal uptake, predominantly on the left. Surprisingly, brain MRI highlighted a venous drainage anomaly in the right posterolateral thalamic area, associated with potential paramagnetic deposits in the putamen and substantia nigra bilaterally and fronto-parietal cortical sulci enlargement. The patient was discharged at home with the indication to start clonazepam for the myoclonic tremor, which was only partially effective. Five months later, she underwent a Positron Emission Tomography (PET), which showed moderate bilateral FDG hypofixation in the sensorimotor cortex, predominant on the right.

*Conclusions:* Asymmetric presentation of myoclonic tremor and apraxia can pose a diagnostic challenge. In our case, SPECT radiological features showed reduced basal ganglia uptake while MRI detected a venous anomaly, which only partially fitted the clinical picture. Based on the clinical presentation, evocative of cortico-basal syndrome, a PET was performed and was diagnosed as cortico-basal degeneration. The clinical presentation should guide the choice of the right diagnostic test.

**P81**

## Personality traits and psychological characteristics in functional movements disorders

*Antonina Luca*, T. Lo Castro, G. Mostile, G. Donzuso, C.E. Cicero, C. Terravecchia, A. Nicoletti, M. Zappia

Department of Medical, Surgical Sciences and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy

*Introduction:* Psychological characteristics of patients with Functional Movement Disorders (FMD) are still unclear.

*Objectives:* Aim of the study was to assess personality traits and psychological characteristics of patients with FMD.

*Methods:* Patients affected by clinically definite FMDs were enrolled and compared to patients affected by Organic Weakness (OW). Personality was assessed with the administration of the Rorschach according to Exner's comprehensive system and the Structured Clinical Interview for Personality Disorders (SCID-II). The presence of alexithymia was assessed with the Toronto Alexithymia Scale (TAS-20). Self-reported general psychological features were assessed with the Symptom Checklist-90 (SCL-90), total score and sub-items: somatization, obsessive-compulsive, interpersonal sensibility, depression, anxiety, anger-hostility, phobic-ideation, paranoid ideation, psychoticism, sleep disorders.

*Results:* Thirty-one patients affected by FMD (27 women; mean age 40.2±15.5 years) and 24 patients affected by OW (18 women; mean age 35.8±16.3 years) were enrolled. In the FMD group, the predominant symptom was weakness, variously associated with other movement symptoms. The OW group was represented by patients with multiple sclerosis (n.19), post-ischemic stroke weakness (n. 4) and amyotrophic lateral sclerosis (n.1). At the Rorschach test, the avoidant type of coping was significantly more frequent among patients with FMD than OW. Moreover, patients with FDM presented a significantly higher frequency of "popular" responses and "Human" responses than patients with OW. At the SCID-II no significant differences were recorded. At univariate analysis, patients with FMD presented significantly higher SCL-90 (both global score sub-items) and TAS-20 scores than patients with OW. However, at multivariate analysis, only the association between FMD and SCL-90 somatization was confirmed (OR 11.3;95%CI 1.90-67.23; p-value 0.008).

*Conclusions:* FMD presented an avoidant copying stile and a markedly conformist personality. Moreover, a strong association between FMD and SCL-90 somatization was found.

**P82**

## Essential tremor worsening after SARS-CoV-2 infection: a second case report

*Davide Costa*[1], L. Angelini[1], M. Passaretti[1], D. Birreci[1], D. Colella[1], A. Cannavacciuolo[2], G. Paparella[2], A. Berardelli[2], M. Bologna[1,2]

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

*Introduction:* Worsening of pre-existing neurological symptoms and/or the development of new neurological diseases are both possible consequences of SARS-CoV-2 infection. In essential tremor (ET) only one case report documented so far ET worsening due to SARS-CoV-2 infection [1].

*Aim:* To describe clinical and kinematic features of tremor, as well as non-motor symptoms, in a case of ET after SARS-CoV-2 infection.

*Methods:* As a routine assessment, we collected clinical and kinematic data of tremor, as well as cognitive and psychiatric data by means of clinical scales in a 63-year-old patient with ET (T0) [2]. One month after the assessment, the patient suffered from a SARS-CoV-2 infection. Two months after infection (T1) the patient was evaluated as in T0. Moreover, at T1 the patient underwent blood laboratory examinations and a cerebral MRI scan.

*Results:* Compared to T0, at T1 we found an increase in the Fahn-Tolosa-Marin Tremor Rating Scale score (T0 vs T1: 27 vs. 41). As compared to T0, kinematic analysis of tremor at T1 revealed an increase in postural tremor amplitude of upper limbs (average percent variation + 45%) and head (average percent variation +284%). No variations in postural tremor frequency nor in rest and kinetic tremor features were observed. Cognitive and psychiatric symptoms did not change. Finally, blood laboratory exams and cerebral MRI did not show significant abnormalities.

*Conclusion:* We report a second case of tremor worsening in a patient with ET after SARS-CoV-2 infection. This novel observation suggests that ET worsening after SARS-CoV-2 infection may be more frequent than reported so far. Tremor worsening may be due to neuroinflammation processes induced by the virus and the involvement of brain areas with a key role in ET pathophysiology, i.e., the cerebello-thalamic network [3-4]. A longer follow-up and the dosage of neuroinflammation biomarkers may be useful to better define the causal role of SARS-CoV-2 infection in ET worsening.

**References:**

[1] Passaretti M, De Biase A, Paparella G, Angelini L, Cannavacciuolo A, Colella D, Berardelli A, Bologna M. Worsening of Essential Tremor After SARS-CoV-2 Infection. Cerebellum. 2023 Feb;22(1):155-158. doi: 10.1007/s12311-022-01366-8. Epub 2022 Jan 6. PMID: 34989982; PMCID: PMC8732967.
[2] Angelini L, Paparella G, De Biase A, Maraone A, Panfili M, Berardelli I, Cannavacciuolo A, Di Vita A, Margiotta R, Fabbrini G, Berardelli A, Bologna M. Longitudinal study of clinical and neurophysiological features in essential tremor. Eur J Neurol. 2023 Mar;30(3):631-640. doi: 10.1111/ene.15650. Epub 2022 Dec 11. PMID: 36437695.
[3] Vanderheiden A, Klein RS. Neuroinflammation and COVID-19. Curr Opin Neurobiol. 2022 Oct;76:102608. doi: 10.1016/j.conb.2022.102608. Epub 2022 Jun 29. PMID: 35863101; PMCID: PMC9239981.
[4] Pietracupa S, Bologna M, Tommasin S, Berardelli A, Pantano P. The Contribution of Neuroimaging to the Understanding of Essential Tremor Pathophysiology: a Systematic Review. Cerebellum. 2022 Dec;21(6):1029-1051. doi: 10.1007/s12311-021-01335-7. Epub 2021 Oct 16. PMID: 34657271.

**P83**

## Primary familial brain calcification due to a novel mutation in SLC20A2 gene: a case report

*Sara Pompanin*[1], F.M. Farina[1], T. Scaravilli[1], M. Petrella[2], E. Cracco[3], R. Quatrale[1]

**[1]Neurology Unit, Ospedale dell'Angelo, Mestre, Italy**
**[2]Pediatric Unit, Ospedale dell'Angelo, Mestre, Italy**
**[3]Medical Nuclear Unit, Ospedale dell'Angelo, Mestre, Italy**

*Introduction:* Primary familial brain calcification (PFBC) is a neurodegenerative disorder characterized by extensive intracranial calcium deposition. Patients mostly present with parkinsonism and cognitive impairment. Pathogenic variants in six genes (SLC20A2, PDGFB, PDGFRB, XPR1, MYORG, JAM2) have been associated with PFBC, but genotype-phenotype correlations have not been established [1]. We report the case of a PFBC patient with a novel heterozygous SLC20A2 mutation presenting with postural tremor.

*Case report:* A 69-year-old man was followed for bilateral arms tremor beginning 10 years earlier. He had a positive family history (tremor and epilepsy in two siblings, tremor and psychiatric disorder in his mother). His first neurological consult at age 62 found bilateral axisymmetric postural and kinetic hands tremor. In the suspect of essential tremor, different pharmacological therapies (propranolol, primidone, valproate) were started unsuccessfully. Levodopa/benserazide 100mg/25mg bid was prescribed with minor improvement. He underwent brain CT and MRI that revealed bilateral calcifications in the cerebellum, thalami and basal ganglia. DAT-scan showed mildly diminished right striatal binding. Serum biochemical parameters of bone and mineral metabolism were unremarkable. Follow-up evaluations documented persistent mild hands tremor with dystonic component on the left side, anticholinergic therapy was added (trihexyphenidyl 4mg daily). At 68 y.o. patient begin to complain craving for sweet food, insomnia and nocturnal hyperactivity. Cognitive evaluation revealed attentive deficits and behavioural disinhibition (MMSE 29/30). Episodic tongue protrusion during stress was described. Right hand rest tremor appeared without bradykinesia or rigidity. Genetic test identified the c.410G>A, p.(Trp137Ter) heterozygous variant of SLC20A2 gene. This is a novel mutation, yet not described on GnomAD database (https://gnomad.broadinstitute.org/), that gives rise to a stop codon and is considered pathogenic by many prediction programs. The patient's sons refused to be tested.

*Conclusions:* For patients classified as having essential tremor-plus phenotype, PFBC must be considered in the differential diagnosis, especially this novel SLC20A2 variant.

**References:**

[1] Balck A, Schaake S, Kuhnke NS et al. A. Genotype-Phenotype Relations in Primary Familial Brain Calcification: Systematic MDSGene Review. Mov Disord. 2021 Nov;36(11):2468-2480.

**P84**

## Botulinum neurotoxin in FXTAS-related tremor: a "successful" case report

*Angelo Tiziano Cimmino*[1], P. Sanginario[1], A.R. Bentivoglio[1,2], P. Calabresi[1,2], M. Petracca[2], G. Di Lazzaro[2]

[1]Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy
[2]UOC Neurologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

*Introduction:* Fragile-X-associated tremor/ataxia syndrome (FXTAS) is a X-linked neurodegenerative disease due to the premutation in the FMR1 gene [1], manifesting as late-onset ataxia associated with postural-kinetic tremor and cognitive decline. In this condition, tremor commonly represents a disabling and unsatisfactorily-treated symptom.

*Objective:* We report the case of a FXTAS-affected man with disabling tremor, who experienced a significant benefit from botulinum neurotoxin (BoNT) injection treatment.

*Methods:* A 59-year-old man came to our attention for a 10-years-lasting hand tremor. The tremor, mainly during voluntary movements, began in the right hand and progressively extended to the left hand and the lower limbs. The neurological examination revealed a moderate, right-prevailing, kinetic tremor of the hands, accompanied by rest and postural components, with subtle right-hand clumsiness. The brain MRI showed a cerebello-pontine atrophy with T2-FLAIR hyperintensity of both the middle cerebellar peduncles and the splenium of corpus callosum. Genetic testing was performed and revealed an expansion of the CGG-trinucleotide FMR1 gene sequence with 106 triplets.
The patient did not tolerate oral propranolol therapy due to bradycardia. Hence, an attempt with BoNT was made with a single session of incobotulinum toxin type A injection (diluted in 2cc of 0.9% sodium chloride solution) in the right flexor digitorum superficialis muscle (30 units) and right extensor digitorum muscle (10 units).
A pre-injection and post-injection evaluations with wrist-worn accelerometry were performed by using a wrist triaxial accelerometer and recording tremor in rest, postural and kinetic conditions.

*Results:* About two weeks after the injection, the patient reported a subjectively significant reduction of the tremor. The post-injection accelerometric assessment demonstrated a great decrease in the amplitude of the tremor. The beneficial effect lasted about 5 months.

*Conclusions:* BoNT injection typically constitutes a therapeutic second-line-option in tremor syndromes refractory to pharmacological agents [2-3]. Our case suggests the possibility of its broader application in the symptomatic treatment of FXTAS-related tremor.

**References:**
[1] Hagerman P. Fragile X-associated tremor/ataxia syndrome (FXTAS): pathology and mechanisms. Acta Neuropathol. 2013;126(1):1-19. doi:10.1007/s00401-013-1138-1.
[2] Mittal SO, Lenka A, Jankovic J. Botulinum toxin for the treatment of tremor. Parkinsonism Relat Disord. 2019;63:31-41. doi:10.1016/j.parkreldis.2019.01.023.
[3] Mittal SO, Pandey S. Botulinum toxin for the treatment of tremor. J Neurol Sci. 2022;435:120203. doi:10.1016/j.jns.2022.120203.

**P85**

## Can a single lung metastasis without solid lesion induce an opsoclonus-myoclonus syndrome, related to antiMa2 antibodies?

*Salvatore Panetta*[1], M. Mainardi[2], L. Avanzino[1,3], F. Di Biasio[2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy
[2]IRCCS Policlinico San Martino, Genoa, Italy
[3]Section of Human Physiology, Department of Experimental Medicine, University of Genoa, Genoa, Italy

*Introduction:* Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder characterized by involuntary, arhythmic, multidirectional saccades with horizontal, vertical and torsional components [1-2]. Although the pathophysiology of OMS remains unknown, several evidence suggests that the disorder results from an autoimmune process, due to the presence of onconeural antibodies, causing limbic, diencephalic or brainstem dysfunction. We describe the peculiar case of OMS induced by a single lymph node metastasis of a lung adenocarcinoma without lung solid lesion with anti-Ma2 antibodies.

*Case report:* A 57-years-old woman came to our attention for a 4 months history of subjective dizziness and a referred visual impairment. Her neurological examination showed rapid, involuntary, multidirectional eye movements. We performed a cerebrospinal fluid analysis that showed a mild inflammatory pattern with the presence of cells (2.6 cells/mm3) and proteins (0.33 g/l). Biological paraneoplastic investigations showed positive anti-Ma2 antibodies both in the serum and CSF. The brain MRI revealed bilateral hyperintensity of the parahippocampal gyrus in T2/FLAIR sequences. The 18F-FDG PET scans of body showed an abnormal enhancement of a subcarinal lymphadenopathy. Finally, an endobronchial ultrasound guided biopsy demonstrated metastasis of a lung adenocarcinoma with EGFR exon 18 mutation, BRAF V600E, PDL-1 75-80%, but not the presence of solid lesions. The patient was treated with intravenous immunoglobulin and tumor-specific therapy (Dabrafenib+Trametinib), without significative improvement. She presented a neurological progression with persistent opsoclonus and ataxia.

*Discussion:* With our case we aim to underline that even just a single lymph node metastasis of a lung adenocarcinoma can be so aggressive to trigger an autoimmune process; this process can start with an apparently simple phenomenology to become later “the start point” of an encephalitis. The antibody positivity could have an important influence on the prognosis and treatment response, but so far, no sufficient data are available to distinguish the different antibodies positivity and the outcome or the treatment response.

**References:**

[1] Oh, Sun-Young, Ji-Soo Kim, and Marianne Dieterich. Update on opsoclonus–myoclonus syndrome in adults. Journal of Neurology 266.6 (2019): 1541-1548.
[2] Klaas JP, Ahlskog JE, Pittock SJ, Matsumoto JY, Aksamit AJ, Bartleson JD et al (2012) Adult-onset opsoclonus-myoclonus syndrome. Arch Neurol 69(12):1598–1607.

**P86**

## Movement disorders in emergency: a single-center study in a third level hospital

*Lorenzo Bresciani*, P. Santurelli, G. Bonato, M. Carecchio

Padua University Hospital

*Background:* Limited data are available in the literature on movement disorders in the emergency department (ED) and in inpatients outside the neurology ward.

*Objective:* To describe the frequency and type of movement disorders (MD) in an ED and among inpatients outside the neurology ward in a third-level hospital.

*Materials and Methods:* Patients seen at the Padua University Hospital in the first six months of 2022 who presented with a MD requiring urgent neurological evaluation were included. Movement disorders were differentiated into hyperkinetic (tremor, chorea, myoclonus, dystonia, ataxia, restless legs syndrome) and hypokinetic (parkinsonism, gait disturbances). Type of onset was distinguished into acute (within 28 days) or chronic (> 28 days). Chi-Square test and Fisher Exact test were used for statistical analysis; was considered significant.

*Results and Conclusion:* Patients were divided in two groups: 1) subjects evaluated in the ED; 2) inpatients admitted in departments outside the Neurology ward. Among 2433 patients who accessed the ED requiring a neurological consultation, 34 (1.39%) had a movement disorder. Among 1039 neurological consultations required in the second group, 68 (6.3%) were for movement disorders. In the ED, hypokinetic MD (24/34, 70.6%) were more frequent than hyperkinetic MD (10/34, 29.4%) and were associated with a chronic and an acute onset ($p < 0.05$), respectively. Among inpatients, hyperkinetic MD were more frequent in under 65 (11/27, 40.7%) compared to over-65 patients (1/29, 3.4%) and were associated with acute onset ($p < 0.05$). Patients in intensive care units (ICU) tend to present hyperkinetic disorders with an acute onset (7/38, 18.4%) compared to patients from other units (1/30, 3.3%) (p 0.055).
Parkinsonism was the most frequently observed MD in both groups; Parkinson's disease in poor therapeutic control was MD seen more frequently. Other common causes of MD were drug-induced disorders (5 patients) and metabolic abnormalities (6 patients).

**P87**

## Clinical, genetic and neuroradiological characterization of an Italian PFBC cohort

*Silvia Andretta*[1], G. Bonato[1], P. Santurelli[1], L. Bresciani[1], F. Baroni[1], C. Bertolin[2], A. Antonini[1], L. Salviati[2], M. Carecchio[1]

[1]Movement Disorder Unit, Neurology Clinic, Neuroscience Department, University of Padova, Padova, Italy
[2]Clinical Genetics Unit, Department of Women and Children's Health, University of Padova, Padova, Italy

*Introduction:* Primary familial brain calcification (PFBC) is a neurodegenerative disorder caused by mutations in seven genes (SLC20A2, PDGFRB, PDGFB, XPR1, MYORG, JAM2, CMPK2).

*Objective:* To describe the clinical, neuroradiological and genetic analysis of a cohort of PFBC patients.

*Methods:* PFBC patients seen at the movement disorders clinic of Padova University (2018-2022) were included. Clinical phenotypes, neuropsychological profiles, CT scans (calculating total calcification score, TCS), DaTSCAN features, genetic analyses are presented.

*Results:* Among 51 patients (mean age at onset 52±14years) 45 were symptomatic (88%). 73% presented at least one movement disorder: parkinsonism (76% with a positive DaTSCAN), tremor (49%), dystonia (25%), cerebellar signs (20%). Anxiety, depression and headache were the most commonly reported non-motor symptoms. 42% had MCI and 9% dementia, with visuospatial functions, language and executive functions being the most involved domains. There was no difference between groups in age at onset, disease duration and clinical phenotype. 10 patients carried mutations in SCL20A2, 3 in PDGFB, 1 in PDGFRB, 1 in XPR1, 2 in JAM2 (monoallelic mutation), 6 in MYORG (6 biallallelic, 1 monoallelic), 21 tested negative.
We observed 3 symptomatic monoallelic MYORG and JAM2 mutation carriers. Bilateral lenticular calcification were observed in 100% of patients, followed by dentate nuclei (63%), thalami (51%), caudate nuclei (49%), white matter (WM, 41%). Symptomatic and asymptomatic subjects showed no difference in TCS, without correlation between TCS and age at onset, age at CT scan and disease duration, with the exception for age at CT scan and TCS in SLC20A2 patients.
MYORG and SLC20A2 patients showed higher TCS score than the indeterminate genetic group, whereas MYORG patients had a higher score at DN, thalami and WM than the indeterminate genetic group.

*Conclusions:* Our study confirms that no clear correlation between genotype and clinical-radiological phenotype exists in PFBC patients.

**P88**

## Comparing clinical ratings and 3D kinematic measurements for tremor assessment. A pilot study

*Roberta Terranova*[1*], G. Mostile[1,2*], C. Terravecchia[1], F. Contrafatto[1], C.E. Cicero[1], G. Donzuso[1], M. Zappia[1], A. Nicoletti[1]

[*]*These Authors have contributed equally to this work and share first authorship*

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

*Background:* Clinical rating is the current gold standard for the evaluation of tremor. In neurologic examination, tremor of a body segment is expressed as displacement in centimeters in an ordinal scale [1]. Objective tremor quantification is often performed with inertial sensors, which indirectly estimate tremor in the frequency domain of either linear acceleration or angular velocity signals [2]. However, objective displacement in position units is rarely measured in both clinical and research practice.

*Objectives:* The aim of this study was to assess arms tremor as measure in position units and to compare it with clinical rating scales.

*Methods:* A kinematic analysis of movement was performed in patients with action tremor affecting upper limbs using six infrared HD digital cameras (BTS SMART-DX, Milan, Italy) and a refractive marker positioned in the third phalanx of each II finger. Tremor was recorded in forward outstretched position and measured as the 95° percentile of the linear displacement in the three axes (x, y and z). A linear regression analysis was run to understand the relationship between measured hand displacements and the score of TETRAS rating scale item for outstretched limb position (FO-TETRAS).

*Results:* N = 15 patients were enrolled (N = 6 ET; N = 6 ET-plus; N = 3 dystonic tremor) and N = 90 observations were obtained (left and right for each movement axis). Measured displacements were significantly associated with clinical estimations, accounting for 22.7 % of the variation in FO-TETRAS score ($F = 25.79$, $p < 0.001$; $R2 = 0.227$). One mm increment in tremor displacement leads to an increase of 0.4 point (95% CI: 0.23 to 0.54) in FO-TETRAS score. Overall, lower displacement values (max measured displacement = 6 mm) were found as compared to clinical ratings (max FO-TETRAS score = 2.5, corresponding by definition to a tremor amplitude between 3 and 5 cm).

*Conclusion:* Estimated point-to-point displacement significantly correlated with clinical ratings. However, kinematic tremor measurement showed smaller displacement values than clinical ratings. This should be considered when comparing wearable devices measurements of tremor.

**References:**

[1] Elble R, Comella C, Fahn S, Hallett M, Jankovic J, Juncos JL, Lewitt P, Lyons K, Ondo W, Pahwa R, Sethi K, Stover N, Tarsy D, Testa C, Tintner R, Watts R, Zesiewicz T. Reliability of a new scale for essential tremor. Mov Disord. 2012 Oct;27(12):1567-9. doi: 10.1002/mds.25162. Epub 2012 Oct 2. PMID: 23032792; PMCID: PMC4157921.

[2] Elble, R. J., & McNames, J. (2016). Using portable transducers to measure tremor severity. In Tremor and Other Hyperkinetic Movements (Vol. 2016). Center for Digital Research and Scholarship. https://doi.org/10.7916/D8DR2VCC.

**P89**

## Different effects of supra-nuclear and sub-nuclear vascular lesions on clinical and imaging findings in a case of vascular parkinsonism

*Simone Valente*[1,2], F. Piattellini[1,2], S. Mombelli[1,2], D. Greco[1,2], G. Grigioni[2], L. Caremani[2], A. Govoni[2], A. Lombardo[1,3], M.T.R. De Cristofaro[3], A. Bianchi[4], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Department of NeuroMuscular-Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[3]Nuclear Medicine Unit, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy
[4]Department of Neuroradiology, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

*Introduction:* Vascular parkinsonism is a form of atypical parkinsonism due to vascular lesions in the basal ganglia or in the nigrostriatal pathway. The most common clinical features are postural instability, gait impairment, absence of tremor, lower limbs rigidity and lack of response to L-dopa therapy. Ioflupane-SPET usually shows a preserved or mildly reduced only degree of striatal radiotracer uptake.

*Objective:* We present the case of an 87-years old woman with a diagnosis of extrapyramidal disorder and the complete absence of radiotracer uptake in the left striatum in Ioflupane-SPET due to a sub-nuclear vascular lesion.

*Methods:* Since the beginning of her clinical history, the patient underwent neurological examination, MRI and SPET studies.

*Results:* The patient has been suffering from hypercholesterolemia and hypertension and had a transitory ischemic attack, so she has been regularly taking cardiovascular secondary prevention treatment. At the age of 82 years, she started to have postural instability, gait impairment, mild rigidity and bradykinesia in her right limbs and signs of mild cognitive impairment. L-dopa therapy was then started without significant clinical benefit. CT scan showed diffuse vascular leukoencephalopathy. Ioflupane-SPET revealed markedly reduced uptake in the left striatum, which appeared to correlate with slightly right-predominant motor signs, while normal FP-CIT uptake was present in the right striatum. A brain MRI was then performed which showed chronic vascular leukoencephalopathy and a left subnuclear lacunar infarct. At the last follow-up visit in January 2023, despite stopping levodopa therapy, her neurological signs and symptoms remained stable, suggesting a probable form of vascular parkinsonism.

*Conclusion:* This is an explicative example of how supra and sub-nuclear vascular lesions may cause different symptoms and Ioflupane-SPET findings. In particular, subnuclear vascular lesions may provoke the loss of dopaminergic neuronal terminals resembling that of the neurodegenerative disorders such as Parkinson’s disease.

**P90**

## Adult-onset KMT2B-related dystonia

*Edoardo Monfrini*[1,2], A. Ciolfi[3], F. Cavallieri[4,5], M. Ferilli[3], P. Soliveri[6,7], L. Pedace[8], R. Erro[9], F. Del Sorbo[6,7], F. Valzania[4], V. Fioravanti[4], G. Cossu[10], M. Pellegrini[11], L. Salviati[12], F. Invernizzi[13], V. Oppo[10], D. Murgia[10], B. Giometto[11], M. Picillo[9], B. Garavaglia[13], F. Morgante[14,15], M. Tartaglia[3], M. Carecchio[16,17], A.B. Di Fonzo[2]

[1]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[3]Genetics and Rare Diseases Research Division, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy
[4]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Reggio Emilia, Italy
[6]Parkinson Institute, ASST G. Pini-CTO, Milan, Italy
[7]Fondazione Grigioni per il Morbo di Parkinson, Milan, Italy
[8]Department of Onco-Hematology, Cell Therapy, Gene Therapy and Hemopoietic Transplant, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy
[9]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi (SA), Italy
[10]Department of Neuroscience, Brotzu Hospital, Cagliari, Italy
[11]Neurology Unit, Trento Hospital, Azienda Provinciale per i Servizi Sanitari (APSS) di Trento, Trento, Italy
[12]Clinical Genetics Unit, Department of Woman and Child Health, University of Padua, Padua, Italy
[13]Medical Genetics and Neurogenetics Unit, Fondazione IRCCS Istituto Neurologico C. Besta, Milan, Italy
[14]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's, University of London, London, UK
[15]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy
[16]Parkinson Disease and Movement Disorders Unit, Department of Neuroscience, University of Padua, Padua, Italy
[17]Study Center for Neurodegeneration (CESNE), University of Padua, Padua, Italy

*Introduction:* KMT2B-related dystonia (DYT-KMT2B, also known as DYT28) is an autosomal dominant neurological disorder characterized by varying combinations of generalized dystonia, psychomotor developmental delay, mild-to-moderate intellectual disability, and short stature. Disease onset occurs typically before ten years of age [1-3].

We report the clinical and genetic findings of a series of subjects affected by adult-onset dystonia, hearing loss, or intellectual disability carrying rare heterozygous KMT2B variants.

Twelve cases from five unrelated families carrying four rare KMT2B missense variants predicted to impact protein function are described. Seven affected subjects presented with adult-onset focal or segmental dystonia, three developed isolated progressive hearing loss, and one displayed intellectual disability and short stature. Genome-wide DNA methylation profiling allowed to discriminate these adult-onset dystonia cases from controls and early-onset DYT-KMT2B patients [4].

These findings document the relevance of KMT2B variants as a potential genetic determinant of adult-onset dystonia and prompt to further characterize KMT2B carriers investigating non-dystonic features.

**References:**

[1] Carecchio M, Invernizzi F, Gonzàlez-Latapi P, et al. Frequency and phenotypic spectrum of KMT2B dystonia in childhood: A single-center cohort study. Movement Disorders. 2019;34(10):1516-1527. doi:10.1002/mds.27771.

[2] Zech M, Boesch S, Maier EM, et al. Haploinsufficiency of KMT2B, Encoding the Lysine-Specific Histone Methyltransferase 2B, Results in Early-Onset Generalized Dystonia. Am J Hum Genet. 2016;99(6):1377-1387. doi:10.1016/j.ajhg.2016.10.010.

[3] Meyer E, Carss KJ, Rankin J, et al. Mutations in the histone methyltransferase gene KMT2B cause complex early-onset dystonia. Nat Genet. 2017;49(2):223-237. doi:10.1038/ng.3740.

[4] Ciolfi A, Foroutan A, Capuano A, et al. Childhood-onset dystonia-causing KMT2B variants result in a distinctive genomic hypermethylation profile. Clinical epigenetics. 2021;13(1):157. doi:10.1186/s13148-021-01145-y.

## P91

### Idiopathic cervical dystonia and autonomic nervous system: expanding the non-motor symptoms list?

*Fabiana Colucci*[1], M. Sensi[2], J.G. Capone[2], E. Sette[2], M. Pugliatti[1], I. Casetta[1], V. Tugnoli[2]

[1]Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy
[2]Department of Neuroscience and Rehabilitation, Azienda Ospedaliero-Universitaria S. Anna, Ferrara, Italy

*Background:* Non-motor symptoms in idiopathic cervical dystonia(ICD) [1] (e.g. neuropsychiatric symptoms, sleep disturbances, fatigue, cognitive impairment, sexual dysfunction, sensory abnormalities) have been widely reported. The autonomic nervous system (ANS) involvement is still poorly understood [2-3].

*Objects:* To investigate ANS functions by clinical and neurophysiological assessment in idiopathic cervical dystonia.

*Methods:* 20 ICD patients and 20 controls were enrolled to investigate ortosympathetic and parasympathetic functions by clinical and neurophysiological assessment. The Composite-Autonomic-System-Scale-31/COMPASS-31 was used to clinically assess the ANS functions. The laser doppler flowmetry quantitative spectral analysis, recorded from the indexes skin, was used to measure at rest, after parasympathetic (six deep breathing) and sympathetic (isometric handgrip and mental arithmetic calculation) activation, the power of high-frequency and low-frequency oscillations and the low-frequency/high-frequency ratio.

*Results:* ICD patients featured more often autonomic symptoms at COMPASS-31($p<0.05$, 86%), mainly orthostatic intolerance (35%) and gastrointestinal manifestation (55%) compared to controls. At rest, lower high-frequency powerband was detected among cases, statistically significant in the subgroup of age³60-year-old ($p<0.05$;11.25 right and 10.2 left; 71% right, 86% left). The latter group showed lower low-frequency/high-frequency ratio than in the same age control subgroup at rest ($p<0.05$;0,64 right and 0,29 left; 86% right and left) and after mental calculation ($p<0.05$;1,18 right, 1,25 left;100% right, 86% left). Cases showed lower ratio during handgrip than controls ($p<0.05$;1,64;80%), and a similar increase of the low-frequency oscillatory component was observed in both groups. By contrast, high-frequency component remained unchanged among cases and decreased in controls. No differences between the two groups were detected during deep breathing, featuring a significant increase in high-frequency oscillations.

*Conclusion:* The present study detected ANS dysfunction in ICD patients at clinical and neurophysiologic levels. Abnormal parasympathetic-sympathetic interaction might be hypothesised. Low gamma-aminobutyric acid (GABA) concentration in ICD1 might contribute to ANS dysfunction. Indeed, in rats, injection of GABA-agonist increased sympathetic nerve activity [4-5]; in humans, low GABA levels lead to abnormal vagal efference [6].

**References:**

[1] Stamelou M, Edwards MJ, Hallett M, Bhatia KP. The non-motor syndrome of primary dystonia: clinical and pathophysiological implications. Brain. 2012 Jun;135(Pt 6):1668-81. doi: 10.1093/brain/awr224.
[2] Tiple D, Strano S, Colosimo C, Fabbrini G, Calcagnini G, Prencipe M, Berardelli A. Autonomic cardiovascular function and baroreflex sensitivity in patients with cervical dystonia receiving treatment with botulinum toxin type A. J Neurol. 2008 Jun;255(6):843-7. doi: 10.1007/s00415-008-0753-6.
[3] Hentschel F, Dressler D, Abele M, Paus S. Impaired heart rate variability in cervical dystonia is associated to depression. J Neural Transm (Vienna). 2017 Feb;124(2):245-251. doi: 10.1007/s00702-016-1639-x.

[4] Osborne PG, Kurosawa M. Perfusion of the preoptic area with muscimol or prostaglandin E2 stimulates cardiovascular function in anesthetized rats. J Auton Nerv Syst. 1994 Mar;46(3):199-205. doi: 10.1016/0165-1838(94)90037-x.
[5] Tanaka M, McKinley MJ, McAllen RM. Roles of two preoptic cell groups in tonic and febrile control of rat tail sympathetic fibers. Am J Physiol Regul Integr Comp Physiol. 2009 Apr;296(4): R1248-57. doi: 10.1152/ajpregu.91010.2008.
[6] McMenamin CA, Travagli RA, Browning KN. Inhibitory neurotransmission regulates vagal efferent activity and gastric motility. Exp Biol Med (Maywood). 2016 Jun;241(12):1343-50. doi: 10.1177/1535370216654228.

**P92**

## Seed-based functional connectivity changes and cervical motion analysis alterations in patients with cervical dystonia

*Elisabetta Sarasso*[1,5], D. Emedoli[6], A. Gardoni[1], L. Zenere[1], S. Iannaccone[6], S. Amadio[4], U. Del Carro[4], M. Filippi[1,2,3,4,5], F. Agosta[1,2,5]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[3]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[4]Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy
[5]Vita-Salute San Raffaele University, Milan, Italy
[6]Department of Rehabilitation and Functional Recovery, IRCCS San Raffaele Scientific Institute, Milan, Italy

*Introduction:* Evaluating neck movement quality and studying the brain mechanisms underlying cervical dystonia (CD) are fundamental to plan the best treatment options.

*Objective:* To assess kinematic and resting-state functional connectivity (FC) characteristics in patients with CD relative to healthy controls.

*Methods:* Electromagnetic sensors were used to obtain spatio-temporal parameters of neck movements in CD patients and healthy controls during three tasks: repeated cervical movements, target reaching and joint position error. Mean and maximal cervical movements amplitude was measured, both with eyes open and closed. Movement quality parameters during target reaching were obtained. Joint position error parameters were registered with both eyes open and closed. The precise dystonic position was also calculated. All participants underwent resting-state functional MRI (RS-fMRI). A seed-based FC analysis with supplementary motor area (SMA) as region of interest was performed. Correlations between motion analysis parameters and FC data were assessed.

*Results:* Seventeen CD patients and 14 age- and sex-matched healthy controls were recruited. CD patients relative to controls showed reduced mean and maximal range of motion (ROM) in rotation both towards and against dystonia pattern and reduced total ROM in rotation both with eyes open and closed. Moreover, CD patients had less severe dystonia pattern with eyes open relative to eyes closed. The RS-fMRI analysis showed reduced FC in CD patients between SMA and bilateral occipital and cerebellar areas compared to controls. A reduced FC within the visuo-motor network correlated with a lower cervical ROM in rotation both with eyes open and closed and with a worse cervical movement quality during target reaching.

*Conclusions:* A FC alteration in the visuo-motor network may represent the neural basis of cervical motor control deficits in CD patients. Electromagnetic sensors and RS-fMRI might be promising tools to monitor CD and to assess the efficacy of rehabilitative interventions.

**P93**

## The role of the somatosensory system in cervical dystonic patients: a study with high-frequency oscillation and short-latency afferent inhibition

*Alessandro Cruciani*[1,2], A. Magliozzi[1,2], J. Lanzone[3], G. Anzini[1,2], V. Di Lazzaro[1,2], M. Marano[1,2]

[1]Department of Medicine, Research Unit of Neurology, Neurophysiology and Neurobiology, Università Campus Bio-Medico di Roma, Rome, Italy
[2]Fondazione Policlinico Universitario Campus Bio-Medico, Operative Research Unit of Neurology, Rome, Italy
[3]Neurorehabilitation Department, IRCCS Istituti Clinici Scientifici Salvatore Maugeri di Milano, Milan, Italy

*Introduction:* In the past few decades, researcher and clinicians have focused their attention on the sensory system's contribution to the pathogenesis of focal dystonia [1]. It is well known that patients suffering from cervical dystonia complain of sensory symptoms, such as pain in the neck or forearm, even before the clinical disease onset [2]. Moreover, other clinical evidence supports the idea that sensory abnormalities contribute to focal dystonia pathogenesis come from the sensory tricks phenomenon that is well described in particular in cervical dystonia [3]. Non-invasive brain stimulation (NIBS) and in particular High-frequency oscillation (HFOs) and short-latency intracortical inhibition (SAI) are two reliable neurophysiological parameters that give us the opportunity to study in vivo the status of the somatosensory system and the sensorimotor integration [4-5]. Thus, with the present study, we aim to investigate the role of the somatosensory system and sensorimotor integration in patients with cervical dystonia with the study of HFOs and SAI.

*Objective:* To investigate the role of the somatosensory system in Dystonia pathogenesis.

*Methods:* We consecutive enrolled 5 right -handed healty subjects (Mean age 45 ± 1,2) and 5 right-handed patients with cervical dystonia (Mean age 46 ± 12, mean TWSRS 15.8 ± 6.5) from movement disorders clinic of the Fondazione Campus Bio-Medico di Roma. Neurophysiological assessment includes bilateral registration of short-latency afferent inhibition (SAI) values and somatosensory evoked potentials (SEPs) elicited from the median nerve of the dominant hand. Then we applied a digital 400–800 Hz bandpass butterworth filter to extract HFOs from SEPs signal. Data were compared trought independent sample t-test or Mann-Whitney U test according to their distribution (Shapiro-Wilk test).

*Results:* Comparison between controls and dystonic patients shown no statistical differences in terms of SAI values in the dominant hemisphere ($p = 0,343$) and non-dominant hemisphere ($p = 0,343$). There was a statistically significant difference in terms of HFOs total area under the curve ($p = 0,03$) between patients and controls, reflecting higher values of early HFOs. Nonetheless, this difference does not reach a statistically significant difference ($p = 0,08$). No differences were found in the late HFOs area under the curve ($p = 0,144$).

*Conclusions:* Our study found that patient with cervical dystonia has HFOs values significantly higher than healthy controls, especially in the early component – i.e. the thalamo-cortical part - but without differences in terms of SAI. Accordingly, those evidence suggest that in dystonic patients there is a selective alteration of the somatosensory pathway rather than an implication of their integration with the motor cortex. Inoue et co-workers have tried to assess HFOs in cervical dystonia patients, found opposite results consisting in a significant decrement in the late HFOs [6]. Those results are not contrasting with our findings, but instead reinforce the concept that in cervical dystonia there is an impairment in the sensory input signaling and processing that in neurophysiology studies could led

to an alteration of the late or early HFOs components. Those preliminary data are part of a more extend study that also comprehend a second neurophysiological assessment after 30 days of treatment with Onabotolinum toxin A (Botox) in order to evaluate the central effects of the toxin and a biomarker to predict patients' degree of improvement with Botox.

**References:**

[1] Conte, A., Defazio, G., Hallett, M., Fabbrini, G. & Berardelli, A. The role of sensory information in the pathophysiology of focal dystonias. Nat. Rev. Neurol. 15, 224–233 (2019).
[2] Relja, M. & Miletić, V. When movement disorders hurt: Addressing pain in hyperkinetic disorders. Parkinsonism Relat. Disord. 44, 110–113 (2017).
[3] Ramos, V. F. M. L., Karp, B. I. & Hallett, M. Tricks in dystonia: ordering the complexity. J. Neurol. Neurosurg. Psychiatry 85, 987–993 (2014).
[4] Cruciani, A., Lanzone, J., Musumeci, G., Di Lazzaro, V. & Marano, M. Focal vibrations enhance somatosensory facilitation in healthy subjects: A pilot study on Equistasi® and high-frequency oscillations. Front. Neurol. 13, 1052989 (2022).
[5] Tokimura, H. et al. Short latency inhibition of human hand motor cortex by somatosensory input from the hand. J. Physiol. 523, 503–513 (2000).
[6] Inoue, K. et al. Disinhibition of the somatosensory cortex in cervical dystonia—decreased amplitudes of high-frequency oscillations. Clin. Neurophysiol. 115, 1624–1630 (2004).

**P94**

## Blepharoplasty yes or no? A single-center study on the influence of blepharoplasty on treatment with botulinum toxin injections

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

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

*Background:* Blepharospasm (BS) is a focal dystonia that can be treated with botulinum toxin (BoNT) injections [1-2]. However, some poor responder patients resort to upper eyelid surgery (blepharoplasty) in order to improve their symptoms.

*Objectives:* To compare the responses to the BoNT injections of both groups of patients (Blepharoplasty YES/NO), in order to clarify if the surgery may improve the response to BoNT.

*Methods:* We collected data of 60 BS patients [3], and we divided them into two groups – blepharoplasty YES (8) and NO (52). Patients who underwent to surgery were operated on at least 3 years before this assessment. Then, we compared their demographic – age, sex – and clinical data – age at onset, disease duration, duration of the treatment with BoNT.
Therefore, we assessed the level of disability trough the Blepharospasm Disability Index (BSDI) [4] and the severity of BS trough Jancovic Rating Scale (JRS) [5] in two times - before the BoNT injections and after 4 weeks. Finally, we compared the differences between their scores (post BoNT – pre BoNT).

*Results:* Groups did not present any significative differences in terms of demographic and clinical data. BSDI and JRS differences of scores were significantly higher in non-operated patients. Therefore, improvement after BoNT was higher in non-operated patients.

*Conclusions:* Blepharoplasty does not provide a long term benefit in patients with BS since they present severe dystonia and few years after surgery response to BoNT injections is poor.

**References:**

[1] Trinchillo et al. The impact of the reclusion on patients with blepharospasm during the COVID19 pandemic Clin Neur and Nerurosurg (2022) doi: 10.1016/j.clineuro.2022.107363.
[2] G. Defazio et al. Blepharospasm 40 years later Mov. Disord., Vol. 32 (No. 4) (2017), p. 2017, 10.1002/mds.26934.
[3] G. Defazio et al.Diagnostic criteria for blepharospasm: A multicenter international study Park. Relat. Disord., 91 (2021), pp. 109-114, 10.1016/j.parkreldis.2021.09.004.
[4] Goertelmeyer S et al. The Blepharospasm Disability Index (BSDI) for the assessment of functional health in focal dystonia. Clin Neurophysiol 2002;113(Suppl 1):S77-S78.
[5] Jankovic J et al. A toxin for cranial-cervical dystonia: a double-blind, placebo-controlled study. Neurology 1987;37:616-623. 9.

**P95**

## A novel variant in ANO3 presenting with autosomal dominant combined dystonia in an Italian family

*Marco Percetti*[1,2,3], G. Sacilotto[1], M. Zini[1], F. Cogiamanian[4], E. Orunesu[5], B. Garavaglia[6], G. Pezzoli[1,7], I.U. Isaias[1,8]

[1]Parkinson Institute Milan, ASST G. Pini-CTO, Milano, Italy
[2]School of Medicine and Surgery and Milan Center for Neuroscience, University of Milano-Bicocca, Milano, Italy
[3]Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[4]Neurophysiopathology Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy
[5]Nuclear Medicine Department, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy
[6]Medical genetics and Neurogenetics Unit, National Neurological Institute Carlo Besta, Milano, Italy
[7]Fondazione Grigioni per il Morbo di Parkinson, Milano, Italy
[8]University Hospital of Würzburg, Würzburg, Germany

*Introduction:* Mutations in DYT-ANO3 are a rare cause of autosomal dominant isolated or combined dystonia, mainly presenting in the adulthood.

*Objective:* To describe the phenotype of an Italian family affected by autosomal dominant combined dystonia carrying a novel variant in ANO3.

*Methods:* Clinical and genetic data were collected. A next-generation sequencing (NGS) panel including 59 genes associated with dystonia was performed. All identified variants were validated by Sanger sequencing.

*Results:* A 21-year-old girl presented with a 10-year history of postural and rest tremor of her right hand, which worsened after orthopedic surgery. After two years she developed painful dystonic movements in her right arm, which impeded her writing and eating. The tremor then spread to her lower limbs, interfering with walking. Mild bradykinesia and rigidity in the right arm were observed. The patient suffers psychomotor delay, dyslexia, dysgraphia, and dyscalculia. A therapeutic attempt with topiramate, carbamazepine, propranolol, clonazepam, and levodopa were ineffective. Brain CT and MRI were normal. SPECT with FP-CIT excluded loss of striatal dopaminergic innervation. EMG documented dystonic tremor in the lower limbs during orthostatism. Family history was significative for psychomotor delay and postural tremor in the father and two sisters with an autosomal dominant pattern. A novel heterozygous variant in ANO3, c.17G>T p.G6V, was identified in the case index, in three affected and two asymptomatic relatives, showing incomplete penetrance. The variant was classified as likely pathogenic according to the latest ACMG criteria.

*Conclusions:* We described the phenotype associated with a novel variant in ANO3 and demonstrated the utility of NGS analysis in the differential diagnosis of combined dystonic syndromes with tremor and early-onset parkinsonism.

**P96**

## Validation of a guideline for the diagnosis of cervical dystonia

*Tommaso Ercoli*[1], G. Defazio[1,2], D. Belvisi[3,4], C. Comella[5], M. Hallett[6], H.A. Jinnah[7], P. Cimino[1], A. Latorre[8], M.M. Mascia[2], L. Rocchi[1,2], A.F. Gigante[9], A. Berardelli[3,4]

[1]Department of Medical Sciences and Public Health, Institute of Neurology, University of Cagliari, Cagliari, Italy
[2]Institute of Neurology, Azienda Ospedaliero Universitaria di Cagliari, Monserrato, Cagliari, Italy
[3]IRCCS Neuromed, Pozzilli, IS, Italy
[4]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[5]Rush University Medical Center, New Philadelphia, OH, USA
[6]Human Motor Control Section, NINDS, NIH, Bethesda, MD, USA
[7]Department of Neurology and Human Genetics, Emory University, Atlanta, GA, USA
[8]Department of Clinical and Movement Neurosciences UCL Queen Square Institute of Neurology, University College London, London, UK
[9]Section of Neurology, San Paolo Hospital, Bari, Italy

*Introduction:* Cervical dystonia (CD) is the most frequent form of focal dystonia. Due to the lack of a diagnostic test, CD diagnosis is based on clinical examination, and it is therefore open to bias [1, 2].

*Objective:* This study aims to provide practical guidance for clinicians in confirming or refuting suspected CD.

*Method:* Participants were video-recorded according to a standardized protocol assessing 6 main clinical features possibly contributing to CD diagnosis: presence of repetitive, patterned head/neck movements/postures inducing head/neck deviation from neutral position (item 1); sensory trick (item 2); and red flags related to conditions mimicking dystonia that should be absent in dystonia (items 3 to 6). To estimate sensitivity and specificity, the gold standard was CD diagnosis reviewed at each site by independent senior neurologists.

*Results:* The validation sample included 43 idiopathic CD patients and 41 control subjects (12 normal subjects, 6 patients with isolated head tremor, 4 with chorea, 6 with tics, 4 with head ptosis due to myasthenia or amyotrophic lateral sclerosis, 7 with orthopedic/rheumatologic neck diseases, and 2 with ocular torticollis). The best combination of sensitivity and specificity was observed considering all the items omitting the item related to capability to voluntarily suppress spasms. Indeed, the final algorithm yielded a sensitivity of 96.1% and a specificity of 81%.

*Conclusions:* An accurate diagnosis of CD can be achieved if, in addition to the core motor features, we also consider some clinical features related to dystonia mimics that should be absent in dystonia. The diagnostic algorithm without the item “ability to voluntarily suppress spasms” was sensitive and specific enough to be proposed as a guideline for presumptive diagnosis of CD, though it needs to be further expanded and validated in a larger sample.

**References:**

[1] Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: A consensus update. 2013 Movement Disorders 28:863–873.
[2] Romano M, Bagnato S, Altavista MC, et al. Diagnostic and therapeutic recommendations in adult dystonia: a joint document by the Italian Society of Neurology, the Italian Academy for the Study of Parkinson’s Disease and Movement Disorders, and the Italian Network on Botulinum Toxin. 2022 Neurol Sci.

**P97**

## Cortico-subcortical white matter bundles alterations in cervical dystonia and blepharospasm

*Maria Ilenia De Bartolo*[1], C. Giannì[1,2], C. Piervincenzi[2], D. Belvisi[1,2], S. Tommasin[2], G. Ferrazzano[2], N. Petsas[2], G. Leodori[1,2], N. Fantoni[2], A. Conte[1,2], A. Berardelli[1,2], P. Pantano[1,2]

[1]IRCCS Neuromed, Pozzilli (IS)
[2]Dipartimento di Neuroscienze Umane, Sapienza Università di Roma, Roma, Italy

It is now thought that dystonia is due to an involvement of a network including basal ganglia, cerebellum, thalamus, and sensorimotor cortices [1–3]. In line with this hypothesis, several studies have found abnormalities in the basal ganglia thalamo-cortical circuit in patients with dystonia [1,4–8]. We aimed to investigate in cervical dystonia (CD) and blepharospasm (BSP) possible microstructural changes of white matter (WM) bundles connecting pre-defined subcortical and cortical regions involved in the network underlying the pathophysiology of focal dystonia and possible correlations between WM microstructural damage and clinical features of dystonic patients. Thirty-five patients (17 with CD and 18 with BSP) and 17 healthy subjects underwent MRI, including diffusion tensor imaging (DTI). Probabilistic tractography (BedpostX) was performed to reconstruct WM tracts connecting globus pallidus, putamen, and thalamus, with primary motor, primary sensory, and supplementary motor cortices. WM tract integrity was evaluated by deriving their DTI metrics. Significant differences in mean, radial and axial diffusivity between CD and HS, and between BSP and HS were found in the majority of the reconstructed WM tracts, while no differences were found between the two groups of patients. We also found a significant correlation between the extent of WM damage and the clinical severity in patients with blepharospasm, but not in patients with CD. The observation of abnormalities in DTI metrics of specific WM tracts suggests a diffuse and extensive loss of WM integrity as a common feature of CD and BSP, converging to the increasing evidence of microstructural damage of several brain regions belonging to specific circuits, i.e., the basal ganglia-thalamo-cortical circuit, thus likely reflecting a common pathophysiological mechanism of focal dystonia.

**References:**

[1] Conte, A.; Defazio, G.; Hallett, M.; Fabbrini, G.; Berardelli, A. The Role of Sensory Information in the Pathophysiology of Focal Dystonias. Nat Rev Neurol 2019, 15, 224–233, doi:10.1038/s41582-019-0137-9.

[2] Conte, A.; Rocchi, L.; Latorre, A.; Belvisi, D.; Rothwell, J.C.; Berardelli, A. Ten-Year Reflections on the Neurophysiological Abnormalities of Focal Dystonias in Humans. Mov Disord 2019, 34, 1616–1628, doi:10.1002/mds.27859.

[3] Quartarone, A.; Hallett, M. Emerging Concepts in the Physiological Basis of Dystonia. Mov Disord 2013, 28, 958–967, doi:10.1002/mds.25532.

[4] Giannì, C.; Pasqua, G.; Ferrazzano, G.; Tommasin, S.; De Bartolo, M.I.; Petsas, N.; Belvisi, D.; Conte, A.; Berardelli, A.; Pantano, P. Focal Dystonia: Functional Connectivity Changes in Cerebellar-Basal Ganglia-Cortical Circuit and Preserved Global Functional Architecture. Neurology 2022, 98, e1499–e1509, doi:10.1212/WNL.0000000000200022.

[5] Brodoehl, S.; Wagner, F.; Prell, T.; Klingner, C.; Witte, O.W.; Günther, A. Cause or Effect: Altered Brain and Network Activity in Cervical Dystonia Is Partially Normalized by Botulinum Toxin Treatment. Neuroimage Clin 2019, 22, 101792, doi:10.1016/j.nicl.2019.101792.

[6] Norris, S.A.; Morris, A.E.; Campbell, M.C.; Karimi, M.; Adeyemo, B.; Paniello, R.C.; Snyder, A.Z.; Petersen, S.E.; Mink, J.W.; Perlmutter, J.S. Regional, Not Global, Functional Connectivity Contributes to Isolated Focal Dystonia. Neurology 2020, 95, e2246–e2258, doi:10.1212/WNL.0000000000010791.

[7] Pan, P.; Wei, S.; Ou, Y.; Jiang, W.; Li, W.; Lei, Y.; Liu, F.; Guo, W.; Luo, S. Reduced Global-Brain Functional Connectivity and Its Relationship With Symptomatic Severity in Cervical Dystonia. Front Neurol 2019, 10, 1358, doi:10.3389/fneur.2019.01358.

[8] Tomić, A.; Agosta, F.; Sarasso, E.; Svetel, M.; Kresojević, N.; Fontana, A.; Canu, E.; Petrović, I.; Kostić, V.S.; Filippi, M. Brain Structural Changes in Focal Dystonia-What About Task Specificity? A Multimodal MRI Study. Mov Disord 2021, 36, 196–205, doi:10.1002/mds.28304.

**P98**

## Myoclonic dystonia with DYT1 gene mutation

*Giorgio Belluscio*[1,2], F. Valentino[1], G. Cosentino[2,3], S. Gana[4], R. Zangaglia[1], C. Pacchetti[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Translational Neurophysiology Research Unit, IRCCS Mondino Foundation, Pavia, Italy
[4]Neurogenetics Research Center, IRCCS Mondino Foundation, Pavia, Italy

*Introduction:* DYT1 gene mutations lead to early-onset dystonia that typically begins with twisting of an arm or leg and subsequent generalization. Anyway, it has emerged that the phenotype associated with the DYT1 mutation can be variable.

*Objective:* In the present work, we describe the case of a 54 years old man who presented an early onset (7-8 years old) of unilateral tremor of the right hand, spreading to the contralateral one during the following 4-5 years, and progressively worsening over time. Abnormal and painful muscular contractions of both hands were associated to tremor.

*Methods:* Clinical and neurophysiological evaluations were performed. Previously conducted neuroimaging studies (brain MRI, CT scan) were negative for pathological findings.

*Results:* The patient had an unremarkable history for perinatal or central nervous system insults. Family history revealed similar symptoms in the patient's father and father's uncle with juvenile onset. At the age of 43 he first came for evaluation at our Institute, where therapy with anticholinergic drugs and botulinum toxin injections was introduced in the suspicion of dystonic tremor, with mild clinical benefit. At a clinical re-evaluation, brief and sudden jerks were observed in the right upper limb; at electromyographic recording of arms muscles, short jerks (duration ranging from 50 to 200 ms) occurring at rest and during posture with pseudo-rhythmic pattern were found in the distal right arm, with co-contraction or alternating contraction of antagonist muscles. Clinical and familiar history, along with findings from neurophysiological examination were suggestive for myoclonic dystonia, and a DYT11 gene mutation could be suspected. Genetic counseling and molecular analysis with NGS panel testing including genes associated with isolated/combined dystonia were performed.

*Conclusions:* Recurrent deletion c.907_909del (p.Glu303del) of the TOR1A gene was found. Thus, we concluded for an atypical presentation of DYT1 dystonia with segmental dystonia and myoclonus. Clonazepam was initiated with great clinical benefit.

**P99**

## A case of idiopathic lower limb dystonia treated with combined use of botulinum toxin type A and phenol nerve block

*Edoardo Bianchini*[1], A. Massimiani[1], J. Bemporad[2], M. Giovannelli[1]

[1] Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2] Department of Physical Medicine and Rehabilitation, San Giovanni Battista Hospital, ACISMOM, Rome, Italy

*Introduction:* Among focal dystonias, lower limb dystonia (LLD) is rather rare [1]. The most effective treatment is botulinum neurotoxin type A (BoNTA), but the evidence for LLD is less robust [2]. Nerve block (NB) is a chemodenervation technique used successfully in spasticity [3], but evidence for dystonia is very scarce [4].

*Objective:* Here we report a case of focal LLD successfully treated with BoNTA and NB combined.

*Methods:* A 50-year-old man, former long-distance runner, developed abnormal posture of the right foot and toe in 2014, which initially occurred only during running and was not elicited by other exercises, but over time also affected normal walking and persisted at rest. Physical examination showed inversion, plantarflexion, and internal rotation of the right foot and hyperextension of the toe at rest, with worsening during walking. No other neurological symptoms were found. Instrumental investigations were normal, and other causes of LLD were excluded. The patient underwent Abobotulinumtoxin-A therapy with initial improvement but progressively reduced response since 2018, despite dosage increase. The patient had also tried oral medications and physiotherapy without significant improvement. Ultrasonographic evaluation showed altered echogenic pattern of the right leg muscles.

*Results:* To test the hypothesis of a structural muscle alteration affecting the effectiveness of BoNTA [5], a diagnostic NB of the tibial nerve with 2.5% lidocaine injection was performed. After the procedure, foot internal rotation and plantarflexion improved and a therapeutic NB with 5% phenol was performed. Toe hyperextension was successfully treated with Abobotulinumtoxin-A. The combined treatment resulted in marked improvement with a lasting response that remained consistent with repeated treatment.

*Conclusions:* The case presented here suggests that NB might be a viable option, in patients with focal LLD refractory to BoNTA treatment, to assess residual response to chemodenervation and to help achieve effective symptoms control before considering more invasive strategies.

**References:**

[1] Jinnah HA, Berardelli A, Comella C, DeFazio G, DeLong MR, Factor S, et al. The focal dystonias: Current views and challenges for future research: Unanswered Questions in Focal Dystonias. Movement Disorders. 2013 Jun 15;28(7):926–43.
[2] Dressler D, Altavista MC, Altenmueller E, Bhidayasiri R, Bohlega S, Chana P, et al. Consensus guidelines for botulinum toxin therapy: general algorithms and dosing tables for dystonia and spasticity. J Neural Transm (Vienna). 2021 Mar;128(3):321–35.
[3] Kirazli Y, On AY, Kismali B, Aksit R. Comparison of phenol block and botulinus toxin type A in the treatment of spastic foot after stroke: a randomized, double-blind trial. Am J Phys Med Rehabil. 1998;77(6):510–5.
[4] Kim JS, Lee KS, Ko YJ, Ko SB, Chung SW. Idiopathic foot dystonia treated with intramuscular phenol injection. Parkinsonism Relat Disord. 2003 Aug;9(6):355–9.

[5] Picelli A, Bonetti P, Fontana C, Barausse M, Dambruoso F, Gajofatto F, et al. Is spastic muscle echo intensity related to the response to botulinum toxin type A in patients with stroke? A cohort study. Arch Phys Med Rehabil. 2012 Jul;93(7):1253–8.

**P100**

## Fatigue in Parkinson's disease: differences between caregiver's report and self-evaluation

*Valeria Sant'Elia*[1], M. Siciliano[1,2], R. De Micco[1], S. Aloisio[1], S. Aramini[1], E.N. Mosca[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

*Introduction:* Fatigue is one of the most prevalent and disabling non-motor symptoms in Parkinson's disease (PD), negatively impacting patients' quality of life and daily activities [1]. One of the core themes related to fatigue in PD is the desire for relatives and caregivers to understand the patients' fatigue experience [2]. However, no study has explored the differences between self-evaluation (SE) and caregiver reporting (CR) of fatigue in PD [3].

*Objectives:* 1) To investigate the differences in fatigue prevalence according to the point of view from which fatigue is reported (SE versus CR); 2) to identify the possible correlates between each of the two evaluations (SE and CR) and the main motor and non-motor symptoms.

*Methods:* Eighty-five patients with early PD (45.05% male; age 63.61±9.37 years; disease duration 3.43±2.28 years) were assessed using the Fatigue Severity Scale (FSS) in its SE version (FSS-SE). The CR version of FSS (FSS-CR) was made ad hoc to collect the point of view of the caregiver about the patients' fatigue experience. Correlations between fatigue experience and motor and non-motor burden were also assessed.

*Results:* No difference in fatigue prevalence was found between FSS-SE (30.6%) and FSS-CR (40%) (Chi-square= 1.648, p= 0.199). The multivariate linear regression analyses showed that FSS-SE was associated with Parkinson's Disease Sleep Scale (B=-0.21, p=0.039), while FSS-CR was related to Parkinson Anxiety Scale (B= 0.27, p= 0.042) and Apathy Evaluation Scale – caregiver (B= 0.26, p= 0.035).

*Conclusion:* Although no difference was found between self-evaluation and caregiver reporting of fatigue prevalence in PD, the caregivers understood the patients' fatigue experience in terms of anxious or apathetic symptoms. This evidence should encourage involving the caregivers in the assessment and treatment of fatigue to reduce the patients' frustration and distress induced by the lack of understanding of their own experience of fatigue.

**References:**

[1] B.M. Kluger, L.B. Krupp, R.M. Enoka, Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy, Neurology 80 (2013) 409-416. https://doi.org/10.1212/WNL.0b013e31827f07be.
[2] D.D. George, N.K. Baer, J.M. Berliner, J. Jones, B.M. Kluger, What Fatigue Means to Persons Living with Parkinson's Disease? A Qualitative Study, Mov Disord Clin Pract. 8 (2021) 919-924. doi: 10.1002/mdc3.13270.
[3] R. Radakovic, R. Davenport, J.M. Starr, S. Abrahams, Apathy dimensions in Parkinson's disease, Int J Geriatr Psychiatry. 33 (2018) 151-158. doi: 10.1002/gps.4697.

**P101**

## Mitochondrial respiration pattern of peripheral blood cells in patients with Parkinson's disease

*Davide Mascioli*[1], H. Zenuni[1], I. Salvatori[2,1] P. Grillo[1], C. Valle[2,3], N.B. Mercuri[1,2], A. Ferri[2,3], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, Tor Vergata University of Rome, Rome, Italy
[2]IRCCS Fondazione Santa Lucia, Rome, Italy
[3]National Research Council, Institute of Translational Pharmacology (IFT), Rome, Italy

*Introduction:* Mitochondrial dysfunction is a key element in Parkinson's disease (PD) pathogenesis. Accordingly, they emerge as novel potential therapeutic targets although further elucidations directly from patients are needed. Peripheral blood mononucleate cells (PBMCs) exhibit typical PD-neuropathology signatures and participate to the pathogenic cascade of the disease, representing an ideal tissue to analyze the molecular events underlying PD in vivo.

*Objective:* To evaluate the pattern of mitochondrial respiration in PBMCs of PD patients and the respective correlations with clinical features and levels of CSF neurodegeneration biomarkers.

*Methods:* Mitochondrial respirometry was conducted on PBMCs from 16 PD patients and 14 controls using Seahorse Bioscience technology. Bioenergetic parameters were correlated with clinical scores of main motor or non-motor scores and the CSF levels of α-synuclein, amyloid-β peptides, and tau proteins.

*Results:* PBMCs baseline oxygen consumption rate was similar between patients and controls (PD=22.4±10.6 OCR; controls=20.8±8.8). ATP-linked respiration was higher in PD (40.2±23.4) than controls (26.3±9.4), although not statistically significant. Both maximal respiration (PD=155.6±115.0; controls=79.3±29.9, p=0.038) and the spare respiratory capacity (PD=134.8±108.2; controls=58.5±28.04, p=0.02) were significantly higher in PD. The maximal respiration and the spare of respiratory capacity directly correlated with the disease duration, MDS-UPDRS part III and the Hoehn and Yahr scores; the spare respiratory capacity was directly associated with the CSF amyloid-β-42 and the amyloid-β-42/40 ratio (R=0.68, p=0.02 and R=0.66, p=0.04, respectively).

*Discussion:* PBMC mitochondria in PD patients had a peculiar pattern of respiration, with increased maximal and spare respiratory capacities, probably reflecting the increased energetic requirement due to the clinical–pathological progression of the disease or to compensatory adaptations.

**P102**

## Age effect on striatal dopamine transporter binding in *de novo* Parkinson's disease: exploring the different contribution of caudate denervation and age at onset on cognitive deficits

*Sara Giannoni*[1], G. Palermo[2], L. Tommasini[2], D. Frosini[2], T. Depalo[3], D. Volterrani[3], R. Morganti[4], L. Guidi[1], G. Siciliano[5], R. Ceravolo[2,5]

[1]Neurology Unit, Ospedale San Giuseppe, Empoli, Italy
[2]Center for Neurodegenerative Diseases – Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[3]Regional Center of Nuclear Medicine, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[4]Section of Statistics, University of Pisa, Pisa, Italy
[5]Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

*Introduction:* Older age at onset and baseline caudate dopaminergic denervation are either reported risk factors for cognitive impairment in Parkinson's disease (PD). Moreover, they are also strictly interlaced, making it challenging to identify their differential contribution to cognitive outcomes.

*Objective:* To assess whether early cognitive performances in PD could be linked to an age-related decline in caudate dopamine transporter (DAT) availability and to capture the relative contribution of age at onset and baseline caudate binding to the development of longitudinal cognitive deficits.

*Methods:* We investigated the relationship between baseline dopaminergic striatal dysfunction (measured by using [123I]-FP-CIT SPECT), age at disease onset and neuropsychological performance of 126 drug-naïve PD patients, using the putaminal and caudate binding values of 77 healthy controls (HC) for a comparative exploration of age-dependent loss of DAT availability in normal aging. In addition, we explored whether age at onset and DAT binding value of caudate could be independent predictors of cognitive changes during a median follow-up of 7 years.

*Results:* [123I]-FP-CIT-SPECT binding values had significant negative correlation with age in both PD and HC, but in PD aging was associated with a steeper slope for the caudate than putamen (-4.0% and -3.7% per decade in PD vs -3.3% and -4.9% in HC). Older age at onset and lower caudate uptake were associated with either worse global cognitive function and performance in specific neuropsychological tests at baseline and demonstrated to be significant independent predictors of both MCI and dementia at follow-up.

*Conclusions:* Our findings confirm a different age effect on [123I]-FP-CIT binding in the striatal subregions of *de novo* PD patients. Notably, we found a less age-related attrition of dopamine neurons in the putamen than in the caudate [1] reflecting likely the superimposition of compensatory mechanisms and the increased predisposition of old onset PD patients to develop cognitive disturbances [2-3].

**References:**

[1] Lee CS, Kim SJ, Oh SJ, Kim HO, Yun SC, Doudet D, Kim JS. Uneven age effects of [(18)F]FP-CIT binding in the striatum of Parkinson's disease. Ann Nucl Med. 2014 Nov;28(9):874-9. doi: 10.1007/s12149-014-0882-1. Epub 2014 Jul 10. PMID: 25008292.

[2] Li H, Hirano S, Furukawa S, Nakano Y, Kojima K, Ishikawa A, Tai H, Horikoshi T, Iimori T, Uno T, Matsuda H and Kuwabara S (2020) The Relationship Between the Striatal Dopaminergic Neuronal and Cognitive Function With Aging. Front. Aging Neurosci. 12:41. doi: 10.3389/fnagi.2020.00041.

[3] Yousaf T, Pagano G, Niccolini F, Politis M. Predicting cognitive decline with non-clinical markers in Parkinson's disease (PRECODE-2). J Neurol. 2019 May;266(5):1203-1210. doi: 10.1007/s00415-019- 09250-y. Epub 2019 Feb 28. PMID: 30820739; PMCID: PMC6469665.

**P103**

## An analysis of gender differences in the clinical profile of Parkinson's disease patients

*Maria Laura Nasi*[1], L. Weis[2], E. Fiorenzato[1,3], V. Cianci[2], F. Pistonesi[2], A. Antonini[2,3], R. Biundo[1,3,4]

[1]Department of General Psychology, University of Padova, Padova, Italy
[2]Parkinson's Disease and Movement Disorders Unit, Department of Neuroscience, Centre for Rare Neurological Diseases (ERN-RND), University of Padova, Padova, Italy
[3]Study Center for Neurodegeneration (CESNE), University of Padova, Padova, Italy
[4]IRCCS San Camillo Hospital, Venezia, Italy

*Introduction:* Parkinson Disease (PD) is the second most common neurodegenerative disease. Over the years several studies have reported gender differences in the clinical profile at onset, rate of progression of cognitive impairments, presence of specific motor symptoms, rate of quality of life, and treatment [1]. However, the mechanisms behind these differences, as well as their evolution over time are not entirely clear [1]. The importance of understanding and investigating these differences in depth is paramount to provide better care, to understand in depth how PD develops, and to provide a more personalised and effective care to all patients.

*Objective:* The present study aimed at characterising in depth the overall clinical profile of male and females PD patients.

*Methods:* Data from 731 PD patients was used in the current study. Clinical data from these patients was collected during routine clinical examinations carried out to assess the presence and progression of PD symptoms (both motor and non-motor).
A series of non-parametric Mann-Whitney test were conducted to assess the presence of gender differences in any of the global cognitive tests and assessment scales.

*Results:* Preliminary results showed statistically significant differences between males and females patients for scores in the ADL scale ($z(730)=-2.02$, $p<0.05$), in which males appeared to have higher scores than females, and in the PDQ8 scores ($z(730)=-3.49$, $p<0.001$), in which females appeared to have higher scores than males. A significant difference was also found for the type of treatment, the results showed that females were found to use apomorphine more often than males ($z(730)=-1.97$, $p<0.05$).

*Conclusions:* From these results it appears that females have a much more complex clinical presentation of the disease with worse baseline autonomy, worse overall quality of life, and need to utilise apomorphine pumps more often than males. Moreover, differences found in the scores of the ADL scale, without the presence of a significant difference in global cognitive scores or in rate of dementia between the two groups, might reflect a motor bias influencing the scoring of this scale.

**References:**
[1] Russillo et al., 2022. Brain Sci., 12, 917.

**P104**

## The role of impulse control disorders in predicting dimensions of cardiac interoception in Parkinson's disease

*Chiara Baiano*[1], F. Morgante[2], D. Goeta[2], M. Amboni[3,4], C. Vitale[3,5], E. Makovac[6], G. Santangelo[7*], L. Ricciardi[2*]

[1]IRCCS San Camillo Hospital, Venice, Italy
[2]Neurosciences Research Centre, St George's University of London, London, UK
[3]Institute of Diagnosis and Care (IDC), Hermitage-Capodimonte, Naples, Italy
[4]Department of Medicine, Surgery and Dentistry, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Salerno, Italy
[5]Department of Motor Sciences and Wellness, University "Parthenope", Naples, Italy
[6]Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, Kings College London, UK
[7]Department of Psychology, University of Campania Luigi Vanvitelli, Caserta, Italy

[*]Shared senior authorship

*Introduction:* So far, research underlined alterations of insular related networks, and of internal signals perception (i.e. interoception) in Parkinson's disease (PD). However, how emotional, and behavioral symptoms, as compulsive conducts, are related to multidimensional levels of interoceptive processing is still opaque.

*Objective:* The present study aimed at exploring the possible role of impulse control behaviours, anxiety, depression and demographic and clinical aspects (i.e. age, gender, disease duration, Levodopa Equivalent Daily Dose, (LEDD), severity of motor symptoms) on multiple dimensions of interoception in PD.

*Methods:* Fifty non-demented PD patients completed tasks assessing multiple dimensions of cardiac interoception (i.e. cardiac interoceptive accuracy, subjective sensibility, and metacognitive awareness). The Montreal Cognitive Assessment assessing global functioning and questionnaires assessing impulse control disorders (ICDs, by the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease- Rating Scales, QUIP-RS), anxiety (by the Hamilton Anxiety Rating Scale, HAM-A), and depression (by the Hamilton Depression Rating Scale, HDRS) were administered.

*Results:* Results of the multiple linear regressions showed that ICD severity positively predicted both cardiac interoceptive accuracy ($\beta = .43$; $t = 2.77$; $p = .009$), and sensibility ($\beta = .521$; $t = 3.05$; $p = .005$). However, interoceptive awareness was negatively predicted by LEDD ($\beta = -.498$; $t = -2.87$; $p = .008$). Moreover, anxiety symptoms significantly correlated with severity of ICD ($r = .331$; $p = .023$).

*Conclusions:* In the present study subjective and objective, but not metacognitive dimensions of interoception were predicted by ICD levels. These results are in line with neurocognitive models of addictive impulsive behaviours, explaining compulsive disorders as the result of a dysfunctional activity of interoceptive system. Moreover, further investigation on the possible role of anxiety levels on the link between ICD and interoceptive abilities is required.

**P105**

## Sway analysis in patients affected by Parkinson disease with and without self-reported neuropsychiatric symptoms

*Antonio Volzone*[1], C. Ricciardi[2,3], D. Calderone[2], M. Cesarelli[3,4], M.C. Calabrese[1], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Department of Electrical Engineering and Information Technology, University of Naples "Federico II", Naples, Italy
[3]Bioengineering Unit, Institute of Care and Scientific Research Maugeri, Pavia, Italy
[4]Optolectronics Group, Department of Engineering, University of Sannio, Benevento, Italy

*Introduction:* Neuropsychiatric symptoms (NPS) are the most common non motor features in Parkinson disease (PD) [1]. Previous studies suggested that PD patients have abnormal postural sway, incresing with disease progression [2] and correlated with dysfunctional cognition [3].

*Objectives:* To assess balance in PD patients with and without self-reported NPS in comparison with de novo PD patients by means a short sway test.

*Methods:* Patients were assessed with MDS-UPDRS and classified as having (NPS+) or not (NPS-) NPS based on the clinical opinion and according to an arbitrary cut-off, namely the sum of the first six elements of MDS-UPDRS part IA $\geq 3$. To extract the sway features, a standing phase of five seconds with BTS Gait Lab system was performed. Clinical and demographical data were analysed. The One-way ANOVA Test with post-hoc Bonferroni correction was chosen to perform the statistical analysis trough the software SPSS.

*Results:* Twenty-five patients were classified as PD NPS+, whereas 25 patients as PD NPS-. In addition, 25 de novo PD patients were chosen to be a control group. As expected, regarding clinical and demographical data, ANOVA test with post hoc analysis showed differences in disease duration, Hoehn and Yahr scale, daily LEDD dose, part 3 and 4 of MDS-UPDRS in de novo PD patients as compared with both NPS+ and NPS-, whereas NPS+ and NPS- were comparable, except for total and part 1 and 2 of MDS-UPDRS. Sway parameters, namely longitudinal oscillation range, mean radius, equivalent radius, path lenght and mean velocity, resulted significantly different in NPS+ vs de novo PD patients.

*Conclusions:* A short sway test proves that PD NPS+ patients display higher postural instability parameters with consequent increased risk of falling. Screening for NPS may aid to identify a PD subpopulation at increased risk of instability and therefore suitable for an early rehabilitation process.

**References:**

[1] Weintraub D et al., 2022. Lancet Neurol; 21(1):89-102.
[2] Frenklach A et al., 2009. Mov Disord; 15;24(3):377-85.
[3] Apthorp D et al., 2020. BMJ Neurol Open; 5;2(2):e000086.

## P106

### Gait pattern in single and in dual-task in patients affected by Parkinson disease with and without camptocormia

*Antonio Volzone*[1], C. Ricciardi[2,3], S. Adamo[2], A. Iavarone[4], C. Vitale[5], F. Amato[2], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Department of Electrical Engineering and Information Technology, University of Naples "Federico II", Naples, Italy
[3]Bioengineering Unit, Institute of Care and Scientific Research Maugeri, Pavia, Italy
[4]Neurological Unit, CTO Hospital, AORN "Ospedali dei Colli", Naples, Italy
[5]Institute of Diagnosis and Health, IDC-Hermitage Capodimonte, Naples, Italy; Department of Motor Sciences and Wellness, University "Parthenope", Naples, Italy

*Introduction:* Camptocormia (CC) is a postural deformity in Parkinson disease (PD), defined as "involuntary, non-fixed, pathological forward flexion of the trunk in standing position and walking, reversible when the patient is lying" [1]. Upper CC refers to the angulation of the different vertebrae along the spine, whereas Lower CC relates to the hip-angle [2]. Previous studies on small samples suggested that gait in PD patients with CC is characterized by reduced step and stride lenght [3].

*Objectives:* To asses gait pattern in single and in dual-task in PD patients with and without CC.

*Methods:* Patients were classified as Camptocormic (CC+) or not (CC-) based on the angle of Upper CC measured with "CamptoApp" [2] in according to a cut off of 40°. Clinical and demographical parameters were analyzed. All subjects performed gait analysis through an optoelectronic system of BTS by using Davis Protocol in single-task (GAIT) and in motor and cognitive dual-task (MOT, COG). Finally, a t-test for independent samples was performed through SPSS statistics in order to compare demographic, clinical and gait spatiotemporal parameters between CC+ and CC-.

*Results:* Forty PD patients were classified as CC+, whereas 40 as CC-. CC+ had a mean age of 64.8 ± 9.1 years, while CC- had a mean age of 64.0 ± 1.0 years. Among clinical parameters, MDS-UPDRS total score was higher, as a trend, in patients CC+ vs CC-. Regarding gait parameters, the mean lenght cycle resulted statistically significant higher in CC+ as compared to CC- both in MOT and COG tasks.

*Conclusions:* CC in PD is associated with increased gait instability, especially in dual-task condition, with consequent risk of falling. Early identification of CC should lead to employ integrated rehabilitation strategy aimed at improving dynamic balance especially in dual-task condition, thus reducing the risk of falling.

**References:**

[1] Doherty KM et al., 2011. Lancet Neurol; 10(6):538-49.
[2] Margraf NG et al., 2018. Parkinsonism Relat Disord; 52:1-5.
[3] Tramonti C et al., 2017. Gait Posture; 57:130-135.

**P107**

## Systematic review of the assessment tools for quality of life in patients with Parkinson's disease

*Ilaria Ruotolo*[1,3], G. Sellitto[1,3], A. Berardi[2], E. Amadio[1], F. Panuccio[1], M. Tofani[2], G. Galeoto[2]

[1]Sapienza University of Rome, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]MS Center, S. Andrea Hospital, Sapienza University, Rome, Italy

*Introduction:* Disability in people with Parkinson's disease (PD) leads to a low quality of life (QoL), that includes clinical, social and economic implications; these aspects have a significant impact for individuals with PD. Information regarding QoL of patients with PD and studies about the relationship between QoL and motor and cognitive function are necessary for both research and clinical use to make informed decisions in healthcare and rehabilitation. In 2021 a systematic review was performed about tools to assess QoL in patients with PD, but in the recent years a considerable number of studies was published about this topic.

*Objective:* The aim of this study was to update this systematic review exploring the most used outcome measures to assess QoL in patients with PD.

*Methods:* A literature search was conducted on MEDLINE, Scopus, CINAHL, PsycINFO, and Web of Science. PRISMA checklist guidelines were used. Three authors independently identified eligible studies based on predefined inclusion criteria: quantitative studies that evaluate the psychometric properties of the outcome measures, validations and cross-cultural adaptations of outcome measures that assess quality of life inherent to PD; studies on tests, questionnaires and self-reported and performance-based outcome measures; moreover, articles published from January 2020 to January 2023 were considered. Methodological quality of the studies and the risk of bias were assessed using the COSMIN checklist.

*Results:* 167 studies were included, and 87 different instruments were identified. The most frequently used scales were the 39-items and 8-items Parkinson's Disease Questionnaire (PDQ-39) (PDQ-8).

*Conclusions:* These results suggest further investigation of existing QoL in PD outcome measures would be useful for patients, researchers, and clinicians. Validated and universal outcome measures are necessary to allow comparisons across practice; therefore, it is recommended for future researchers use a common set of outcome assessments based on results of this review.

**P108**

## Camera - and viewpoint-agnostic evaluation of axial postural abnormalities in people with Parkinson's disease through augmented human pose estimation

*Stefano Aldegheri*[1], C.A. Artusi[2,3], S. Camozzi[4], R. Di Marco[1], C. Geroin[4], G. Imbalzano[2,3], L. Lopiano[2,3], M. Tinazzi[4], N. Bombieri[1]

[1]Department of Computer Science, University of Verona, Strada le Grazie 15, 37134, Verona, Italy
[2]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[3]Neurology 2 Unit, A.O.U, Città della Salute e della Scienza di Torino, Turin, Italy
[4]Neurology Unit, Movement Disorders Division, Department of Neurosciences Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Axial postural abnormalities (APA) are common features of Parkinson's disease (PD) and manifest in over 20% of patients during the course of the disease. APA form a spectrum of functional trunk misalignment, ranging from a typical parkinsonian stooped posture to progressively greater degrees of spine deviation [1-2].

*Objective:* There is a lack of agreement on validated, user-friendly, automatic tools for measuring and analyzing the differences in the degree of PA in different moments of the day, according to patients' therapeutic conditions and tasks. In this context, human pose estimation (HPE) software based on deep learning could be a valid support as it automatically extrapolates spatial coordinates of the human skeleton keypoints from images or videos.

*Methods:* AutoPosturePD is a software that augments the human skeleton extrapolated by HPE software at the state of the art from RGB pictures with exact bone points for posture evaluation trough computer vision post-processing primitives. It doesn't require any calibration and can be coupled with images taken using commercially available sensors, like the one found in smartphones.

*Results:* The software is tested for robustness and accuracy on the processing of 76 RGB images with different resolutions and sensor-subject distances from 55 PD patients with different degrees of anterior and lateral trunk flexion, showing accordance within a tolerance of 5 degrees with respect of virtual palpation.

*Conclusions:* AutoPosturePD is a novel low-cost software-based automatic and portable tool for the evaluation of axial postural abnormalities in people with Parkinson's Disease, which only relies on the use of off-the-shelf RGB cameras.

**References:**

[1] Tinazzi, M.; Geroin, C.; Bhidayasiri, R.; Bloem, B.R.; Capato, T.; Djaldetti, R.; Doherty, K.; Fasano, A.; Tibar, H.; Lopiano, L.; et al. 364 Task Force Consensus on Nosology and Cut-Off Values for Axial Postural Abnormalities in Parkinsonism. Movement Disorders 365 Clinical Practice 2022.
[2] Artusi, C.A.; Geroin, C.; Tinazzi, M.; Imabalzano, G.; Camozzi, S.; Aldegheri, S.; Bombieri, N. Assessment of Axial Postural 402 Abnormalities in Parkinsonism: Software for An Automatic Picture Analysis. Movement Disorders Clinical Practice 2023, in press.

**P109**

## Assessment tools for freezing of gait in patients with Parkinson's disease: a systematic review

*Giovanni Sellitto*[1,3], I. Ruotolo[1,3], A. Berardi[2], E. Amadio[1], M. Tofani[2], G. Galeoto[2]

[1]Sapienza University of Rome, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]MS Center, S. Andrea Hospital, Sapienza University, Rome, Italy

*Introduction:* Freezing of gait (FOG) is defined as brief and temporary absence or marked reduction of forward progression of the feet despite the intention to walk. FOG increases fall risk in patients with Parkinson's disease (PD), reducing their independence and significantly impairing their quality of life (QoL). For this reason, it is recommended an accurate evaluation of FOG to process a suitable rehabilitation program for individuals with PD.

*Objective:* The aim of this systematic review is to identify the rehabilitation outcome measures used to assess FOG in PD patients and describe their methodological qualities and cultural adaptations.

*Methods:* Three independent reviewers consulted Scopus, MEDLINE, Web of Science and CINAHL for literature search and no restrictions were applied regarding year of publication, country and language. The authors followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) and the methodological quality of selected study was assessed using the COSMIN Checklist. The following inclusion criteria were used for the selection of studies: quantitative studies evaluating psychometric properties of outcome measures; validation studies and cultural adaptation conducted on individuals affected by PD; studies published in languages understandable to reviewers.

*Results:* The search identified 627 matches. The three independent reviewers, after reading titles and abstracts and eliminating duplicates 119 studies were included; a careful reading of the full text was performed and 41 articles were included. The most used tool seems to be the FOG-Q (validated in several languages), but innovative tools for evaluation of FOG have also been identified.

*Conclusions:* All the included tools have good reliability, but further validations are necessary with a greater number of patients and in other languages to reach gold standards. Since FoG is a highly disabling disorder for patients with DP and difficult to measure, the development of new assessment tools is recommended.

**P110**

## Video-based automatic analysis of axial postural abnormality in static and dynamic conditions

*Carlo Alberto Artusi*[1,2], C. Geroin[3], S. Aldegheri[4], R. Di Marco[4], G. Imbalzano[1,2], S. Camozzi[3], L. Lopiano[1,2], N. Bombieri[4], M. Tinazzi[3]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]Neurology 2 Unit, A.O.U, Città della Salute e della Scienza di Torino, Turin, Italy
[3]Neurology Unit, Movement Disorders Division, Department of Neurosciences Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[4]Department of Computer Science, University of Verona, Verona, Italy

*Introduction:* The current body of research has not yet led to a sufficient understanding of pathophysiology and management of axial postural abnormalities (PA) in Parkinson disease (PD) due to lack of agreement on validated, harmonized tools for measurements. Moreover, PA have been only measured in static conditions, but they may get worse in dynamic conditions, leading to different degrees of severity when compared with the static assessment.

*Objective:* To develop a software based on Deep Learning for marker-less and automatic video-analysis of axial PA in PD to systematically quantify changes of PA in both static and dynamic conditions of PD subjects.

*Methods:* A total of 168 minutes videos from 7 PD patients with different degrees of anterior and lateral trunk flexion were used for the development and pilot validation of a new software called AutoPosturePD++ (APP++); the patients were asked to complete different tasks: standing still, standing still while reading (dual task), walking straight back and forth for 2 minutes and walking straight back and forth for 2 minutes while reading (dual task). Postural abnormalities were measured in lateral and posterior view during the patients' activity.

*Results:* From the software accuracy point of view, we confirmed an excellent agreement between APP++ and the gold standard for static assessments (NeuroPostureApp®). For dynamic assessments, we quantified constraints for the video shooting (i.e., subject-camera distance and field of view for both lateral and posterior view) to preserve such accuracy. The preliminary results from included patients, while indicating the robustness of the software for dynamic posture analysis, suggest the presence of significant modifications of posture during dual task and while walking.

*Conclusions:* APP++ can be a valid tool for marker-less spine flexion measurement in PD, accurately supporting the measurement of posture during dynamic conditions and informing on the modifications of posture during different tasks.

## P111

**Daily multidisciplinary intensive outpatient rehabilitation program versus home-based self-treatment program in Parkinson's disease: short-term preliminary results are influenced by baseline levels of motor impairment**

*Francesca Lea Saibene*[1], F. Merlo[1], A. Salvatore[1], P. Arcuri[1], A. Castagna[1], E. Farina[1], M. Alberoni[1], E. Calabrese[1], T. Bowman[1], D. Anastasi[1], D. Cattaneo[1,2], J.S. Navarro[1], C. Arienti[1], M. Meloni[1,3]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]University of Milan, Milan, Italy
[3]UOC Neurologia; Azienda Ospedaliero-Universitaria, Cagliari, Italy

*Introduction:* Although there are several studies about improvement after intensive and multidisciplinary treatments in People with Parkinson's Disease (PwPD) on different domains and abilities [1, 2], there is no comprehensive information on the factors that may have the greatest impact on the response to rehabilitative treatment.

*Objective:* The main aim of the present study was to evaluate whether PwPD allocated to the multidisciplinary intensive outpatient rehabilitation treatment (Experimental Group=EXP) show different short-term effects on motor and/or cognitive domains than PwPD allocated to the home-based self-managed stretching treatment (Control Group=CTRL). In addition, our work aimed at exploring which baseline factors may have influenced the effects of either treatments.

*Methods:* 43 PwPD [19CTRL/24EXP; 23F/20M; Age(years): 69.6±6.5; mH&Y: 1.5-3; Disease Duration(years): 8.87±6.3] were enrolled. All subjects underwent a neurological and neuropsychological assessment at baseline (T0) and after 6 weeks of treatment (T1). Motor and overall cognitive functioning were assessed respectively by the MDS-UPDRS-Part III [3] and the Montreal Cognitive Assessment (MoCA Test) [4].

*Results:* EXP-PwPD had a reduction of 5.75 points compared to the CTRL-PwPD on MDS-UPDRS-Part III. This difference is more meaningful in those who were more compromised at T0 MDS-UPDRS-Part III scores. In fact, in the group with higher T0 motor score (MDS-UPDRS-Part III >40 -median score-), EXP-PwPD showed a significant improvement on motor symptoms at MDS-UPDRS-Part III (-10.12; p=0.014) with respect to CTRL-PwPD. The same difference is not significant (-3.29; p=0.15) in the group with T0 motor score lower than 40 points. No statistically significant effect has been found on MoCA score in the EXP-PwPD compared to the CTRL-PwPD (-0.34; p=0.6).

*Conclusions:* Our findings suggest that a daily multidisciplinary intensive outpatient rehabilitation treatment instead of home-based rehabilitation treatment may induce relevant motor improvement in PwPD. Remarkably, we observed that this improvement was significant in PwPD with more compromised motor functions at baseline.

**References:**

[1] Meloni, M., Saibene, F. L., Di Tella, S., Di Cesare, M., Borgnis, F., Nemni, R., & Baglio, F. (2021). Functional and Cognitive Improvement After an Intensive Inpatient Multidisciplinary Rehabilitation Program in Mild to Severe Parkinson's Disease: A Retrospective and Observational Study. Frontiers in Neurology, 12, 626041.
[2] Ferrazzoli, D., Ortelli, P., Zivi, I., Cian, V., Urso, E., Ghilardi, M. F., ... & Frazzitta, G. (2018). Efficacy of intensive multidisciplinary rehabilitation in Parkinson's disease: a randomised controlled study. Journal of Neurology, Neurosurgery & Psychiatry, 89(8), 828-835.
[3] Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., ... & LaPelle, N. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale

presentation and clinimetric testing results. Movement disorders: official journal of the Movement Disorder Society, 23(15), 2129-2170.
[4] Santangelo, G., Siciliano, M., Pedone, R., Vitale, C., Falco, F., Bisogno, R., ... & Trojano, L. (2015). Normative data for the Montreal Cognitive Assessment in an Italian population sample. Neurological Sciences, 36, 585-591.
[5] Nucci, M., Mapelli, D., & Mondini, S. (2012). Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. Aging clinical and experimental research, 24, 218-226.

**P112**

## Assessment of axial postural abnormalities in parkinsonism: automatic picture analysis software

*Christian Geroin*[1], C.A. Artusi[2,3], G. Imbalzano[2,3], S. Camozzi[1], S. Aldegheri[4], L. Lopiano[2,3], M. Tinazzi[1], N. Bombieri[4]

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[3]Neurology 2 Unit, A.O.U, Città della Salute e della Scienza di Torino, Turin, Italy
[4]Department of Computer Science, University of Verona, Verona, Italy

*Background:* Software-based measurements of axial postural abnormalities in Parkinson's disease (PD) are the gold standard but may be time-consuming and not always feasible in clinical practice. An automatic and reliable software to accurately obtain real-time spine flexion angles according to the recently proposed consensus-based criteria would be a useful tool for both research and clinical practice.

*Objective:* We aimed to develop and validate a new software based on Deep Neural Networks to perform automatic measures of PD axial postural abnormalities.

*Methods:* A total of 76 pictures from 55 PD patients with different degrees of anterior and lateral trunk flexion were used for the development and pilot validation of a new software called AutoPosturePD (APP); postural abnormalities were measured in lateral and posterior view using the freeware NeuroPostureApp® (gold standard) and compared with the automatic measurement provided by the APP. Sensitivity and specificity for the diagnosis of camptocormia and Pisa syndrome were assessed.

*Results:* We found an excellent agreement between the new APP and the gold standard for lateral trunk flexion (ICC 0.960, IC95% 0.913-0.982, $p < 0.001$), anterior trunk flexion with thoracic fulcrum (ICC 0.929, IC95% 0.846-0.968, $p < 0.001$) and anterior trunk flexion with lumbar fulcrum (ICC 0.991, IC95% 0.962-0.997, $p < 0.001$). Sensitivity and specificity were 100% and 100% for detecting Pisa syndrome, 100% and 95.5% for camptocormia with thoracic fulcrum, 100% and 80.9% for camptocormia with lumbar fulcrum.

*Conclusions:* APP is a valid tool for spine flexion measurement in PD, accurately supporting the diagnosis of Pisa syndrome and camptocormia.

**References:**

[1] Tinazzi M, Gandolfi M, Ceravolo R, et al. Postural abnormalities in Parkinson's Disease: an epidemiological and clinical multicenter study. Mov Disord Clin Pract 2019; 6: 576-585.
[2] Tinazzi M, Geroin C, Bhidayasiri R, et al. Task force consensus on nosology and cut- off values for axial postural abnormalities in parkinsonism. Mov Disord Clin Pract 2022; 9:594-603.
[3] Margraf NG, Wolke R, Granert O, et al. Consensus for the measurement of the camptocormia angle in the standing patient. Parkinsonism Relat Disord 2018; 52: 1-5.
[4] Tinazzi M, Gandolfi M, Artusi CA, et al. Validity of the wall goniometer as a screening tool to detect postural abnormalities in Parkinson's disease. Parkinsonism Relat Disord 2019; 69: 159-165.

**P113**

## Rehabilitation treatment in painful shoulder in Parkinson's disease: outcome research

*Giovanni Galeoto*[2], E. Amadio[1], G. Sellitto[1,3], M. Tofani[2], I. Ruotolo[1,3], A. Berardi[2]

[1]Sapienza University of Rome, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]MS Center, S. Andrea Hospital, Sapienza University, Rome, Italy

*Introduction:* This study is focused on treating patients with Parkinson's desease and associated shoulder pain due to the high incidence of this problem, which causes elevated levels of disability of upper limbs.

*Objective:* The objective is to evaluate the efficacy of rehabilitation treatment aimed at treating painful shoulder in Parkinson's disease patients, monitoring improvements in shoulder conditions and how much shoulder disabilities influence daily activities, quality of life, mood-behaviourand balance in relation to gait and static.

*Methods:* Eight participants (five males and three females) with a mean age of 67,25±10,57, diagnosis of Parkinson's disease (PwPD) and an associated painful shoulder, H&Y =< 2, no other diseases, were enrolled at "Policlinico Umberto I" in Rome. The following outcome measures were used: Berg Balance Scale (BBG), Disability of the Arm, Shoulder, and Hand (DASH), Parkinson's Disease Questionnaire-39 (PDQ-39), Short From Health Survey-12 (SF-12) and Community Integration Questionnaire Revised (CIQ-R), Medical Research Council (MRC) and the shoulder range of motion (R.O.M.) was assessed. Physiotherapy programmes are based on 10 sessions with a biweekly frequency of 50-60 minutes for each patient.

*Results:* Data were statistically significant at the end of the treatment ($p < 0.05$) for results concerning active shoulder movements: flexion, abduction, external rotation on transverse plane, and external rotation on sagittal plane, internal rotation on sagittal plane. Statistically significant data in passive shoulder movements are external rotation on transverse plane, external rotation on sagittal plane and internal rotation on sagittal plane. Most improved muscles in terms of strength are: rotator cuff, serratus anterior and pectoralis major. As regards evaluation scales, BBS, DASH, PCS12, CIQ-R total scores are statistically significant.

*Conclusions:* Conclusions show effectiveness of this rehabilitative approach. This is determined by results obtained in mobility, strength and scales for assessment of balance, quality of life, mood-behaviour and activities of daily living.

**P114**

## Art therapy in patients with Parkinson's disease: a pilot study

*Rosina Paletta*, V. Raimondi, V. Visconti, N. Brezzolari, A. Zito, L. Caputi

UOC Neurologia, ASST Crema, Crema, Italy

*Introduction:* Several neuroimaging evidence provided functional and anatomical correlates of the efficacy of Art Therapy (AT) in patients with Parkinson's disease (PD) [1-2]. AT, may be considered as a novel rehabilitation strategy able to improve the cognitive and sensorimotor functions [3]. However, the AT-efficacy on impaired visual perception, a PD-common feature associated with negative motor outcomes, still remains unknown.

*Objective:* This pilot study aimed to evaluate the impact of AT on visual perception in PD patients, using a neuropsychologic approach.

*Methods:* Clinical and neuropsychological data were acquired from 12 participants (6 PD patients and 6 age-matched controls). To assess the cognitive performance in all participants, we used a complete neuropsychological battery including: MOCA, TMTA, TMTB, Rey-Osterrieth Complex Figure Test, Benton Visual test, FAB, phonemic fluency, and backward digit range; PHQ9, GAD7 and PDQ39 to assess quality of life and MFIS for fatigue. Patients were tested before and after AT (follow-up period). AT-intervention consisted of 13 sessions lasting approximately 90 minutes, once a week, with the exposure to visual art forms and techniques.

*Results:* A significant cognitive improvement in MOCA test (P=0,03), Rey-Osterrieth Complex Figure Test (p=0,05) and TMTB (p=0,05), was found in PD-treated with AT at follow-up evaluation as compared to baseline.

*Conclusions:* This study improves the knowledge on the efficacy of AT in PD. Our results encourage a new method of rehabilitation suggesting that AT leads to an improvement in visual spatial function that could also lead to motor improvement in Parkinson's disease.

**References:**

[1] Cucca A. et al. Complementary Therapies in Medicine 40 (2018) 70–76.
[2] Cucca A. et al. Parkinsonism and Related Disorders 84 (2021) 148–15.
[3] Hamedani A.G. et al. Mov. Disord. 35 (9) (2020) 1542–1549.

**P115**

## Efficacy of the combined treatment physiotherapy and dietary supplement based on whey protein with high biological value in people with Parkinson's disease: outcome research study

*Giovanni Sellitto*[1,3], A. Berardi[2], I. Ruotolo[1,3], M. Tofani[2], G. Galeoto[2]

[1]Sapienza University of Rome, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]MS Center, S. Andrea Hospital, Sapienza University, Rome, Italy

*Introduction:* Sarcopenia is one of the main problems in the most common neurological diseases; it leads to hypomobility and reduction of activities of daily life (ADL). This contributes to manifestation of fatigue, both physical and cognitive, in people with Parkinson's disease (PD). Physiotherapy has already manifested its positive correlation in the regression of sarcopenia; whey protein concentrate high in cysteine showed effectiveness on muscle tissue in people with severe chronic conditions.

*Objective:* The primary objective of our study is to combine the physiotherapy treatment to that of a new supplement on the market based on whey protein with high biological value, based on the concentration of the seriousness of late high in cysteine, in the reduction of fatigue in people with PD starting from the biological principle of sarcopenia reduction. The secondary objectives are to assess the impact of treatment also on Quality of Life (QoL) and walking.

*Methods:* People with PD diagnosed according to the Movement Disorder Society Clinical (MDSC) criteria were enrolled at Policlinico Umberto I in Rome from January to March 2023. Fatigue assessments were carried out before treatment (T0), after six weeks (T1) and twelve weeks (T2) using as outcome measures: Parkinson's Fatigue Scale (PFS-16), Fatigue Saverity Scale (FSS), Performance-Oriented Mobility Assessment (POMA) and Parkinson's Disease Questionnaire (PDQ-39). The combined treatment included two weekly physiotherapy sessions and the concomitant intake of two daily sachets of Fortiral® for the duration of the study.

*Results:* 15 people with PD average age 73±6 years were recruited (M:9; 60%). We found statistically significant results on fatigue and QoL.

*Conclusions:* The combined treatment of physiotherapy and dietary supplement intake based on protein concentrate and cysteine has already shown at six weeks a positive impact both on fatigue and QoL in people with PD. The 12-week figure was consolidated and reinforced by an improvement in walking and balance.

**P116**

## Multidisciplinary treatment for convergence insufficiency and movement disorders in Parkinson's disease: a pilot study

*Ilaria Ruotolo*[1,3], A. Marini Padovani[1], G. Sellitto[1,3], A. Berardi[2], M. Tofani[2], G. Galeoto[2]

[1]Sapienza University of Rome, Rome, Italy
[2] Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3] MS Center, S. Andrea Hospital, Sapienza University, Rome, Italy

*Introduction:* Parkinson's disease is characterized by movement disorders that affect Quality of Life (QoL); movement disorders can be due to visual symptoms that influence falls risk.
Asthenopia is the most common visual impairment in PD patients; eye strain while reading is accompanied by double vision. These disorders are often related to convergence insufficiency (CI). Patients with PD often have significant exodeviations especially at close range. Several studies have shown a reduced convergence amplitude in patients with PD.

*Objective:* The objective of this study is to evaluate the efficacy of a multidisciplinary intervention including orthoptic visual rehabilitation and physical therapy and its impact on QoL of patients with PD and falls risk.

*Methods:* Patients with PD diagnosed according to the Movement Disorder Society Clinical (MDSC) criteria, presenting IC and absence of concomitant ocular pathologies were recruited at Policlinico Umberto I (Rome) from December 2022 to April 2023.
The orthoptic rehabilitation training consisted in a weekly session lasting 45 minutes, over a period of 6 weeks, while physical therapy program consisted in 2 weekly sessions with the same duration.
The following outcome measures were used before (T0) and at the end of the treatment (T1): Convergence Insufficiency Symptoms Survey (CISS), Parkinson's Disease Questionnaire (PDQ-39), Parkinson's Disease Fatigue Scale (PFS-16), 12-item Berg Balance Scale and Performance-Oriented Mobility Assessment (POMA).

*Results:* 10 subjects were included. Average age was 69±6 (M:7; 70%). Statistically significant results were found as regards CISS, PDQ-39 and Berg Balance Scale.

*Conclusions:* The multidisciplinary rehabilitation program led to an improvement of QoL, CI and decreasing of falls risk after 6 weeks. These results show the effectiveness of orthoptic and physiotherapy treatments in patients affected by PD with CI. Further studies including a larger sample are necessary to demonstrate the efficacy of this intervention.

**P117**

## Physiotherapy as a non-pharmacological treatment for sleep disturbances in Parkinson's Disease

*Susanne Buechner*[1], A. Eisendle[1], C. Raccagni[1,2,3]

[1]Department of Neurology, Provincial Hospital of Bolzano (SABES-ASDAA), Bolzano-Bozen, Italy
[2]Lehrkrankenhaus der Paracelsus Medizinischen Privatuniversität, Salzburg, Austria
[3]Department of Neurology, Innsbruck Medical University, Innsbruck, Austria

*Introduction:* Sleep disturbances (SDs) are common in persons with Parkinson's Disease (PD)[1]. SDs can be very annoying and have a negative impact on life quality of patients and caregivers[2]. SDs include nocturnal and diurnal complaints such as insomnia, REM sleep behavior disorder, sleep fragmentation, and excessive daytime sleepniness[1-3]. The causes of SDs are manifold, and comorbidities such as obstructive sleep apnea syndrome and benign prostatic hypertrophy may further worsen the sleep quality. Treatment of SDs in PD is often unsatisfactory, and the intake of other medications complicates the pharmacologic strategy. The number of non-pharmacological treatments (NPT) that can improve sleep quality is growing fast, showing less adverse effects compared to medication[4]. Among NPT, physiotherapy has been described as a useful tool against SDs, which also improves motor performance and overall life quality of PD patients[5-6].

*Objective:* Our aim is to investigate whether intensive physiotherapy can subjectively improve SDs in PD patients.

*Methods:* To date, 8 PD patients (H&Y stage 1,5-2; age 46-73 years; 4 female, 4 males; without SDs medication) have been interviewed before and after 7 weeks of intensive physiotherapy using the Epworth Sleepiness Scale and the Parkinson Disease Sleep Scale-2[7-8].

*Results:* Our preliminary results have shown no statistically significant improvement in sleep problems from baseline to post-physiotherapeutic intervention, as measured by both validated questionnaires.

*Conclusions:* The interest in NPT for SDs in PD patients is increasing. In the study results available so far, no relevant improvement of SDs after physiotherapy could have been demonstrated. Certainly, studies with much larger patients' cohorts and subdivision into groups according to SDs severity are needed to determine the effect of physiotherapy on SDs in PD, as we can only speculate that NPT may be a useful tool for SDs in PD.

**References:**

[1] Suzuki K, Miyamoto M, Miyamoto T, Iwanami M, Hirata K. Sleep disturbances associated with Parkinson's disease. Parkinsons Dis. 2011;2011:219056. doi: 10.4061/2011/219056. Epub 2011 Aug 17. PMID: 21876839; PMCID: PMC3159123.

[2] Chahine LM, Amara AW, Videnovic A. A systematic review of the literature on disorders of sleep and wakefulness in Parkinson's disease from 2005 to 2015. Sleep Med Rev. 2017 Oct;35:33-50. doi: 10.1016/j.smrv.2016.08.001. Epub 2016 Aug 31. PMID: 27863901; PMCID: PMC5332351.

[3] Loddo G, Calandra-Buonaura G, Sambati L, Giannini G, Cecere A, Cortelli P, Provini F. The Treatment of Sleep Disorders in Parkinson's Disease: From Research to Clinical Practice. Front Neurol. 2017 Feb 16;8:42. doi: 10.3389/fneur.2017.00042. PMID: 28261151; PMCID: PMC5311042.

[4] Lee J, Kim Y, Kim YL. Non-pharmacological therapies for sleep disturbances in people with Parkinson's disease: A systematic review. J Adv Nurs. 2018 Apr 27. doi: 10.1111/jan.13694. Epub ahead of print. PMID: 29700848.

[5] Amara AW, Wood KH, Joop A, Memon RA, Pilkington J, Tuggle SC, Reams J, Barrett MJ, Edwards DA, Weltman AL, Hurt CP, Cutter G, Bamman MM. Randomized, Controlled Trial of Exercise on Objective and Subjective Sleep in Parkinson's Disease. Mov Disord. 2020 Jun;35(6):947-958. doi: 10.1002/mds.28009. Epub 2020 Feb 24. PMID: 32092190; PMCID: PMC8826749.

[6] Raccagni C, Goebel G, Gaßner H, Granata R, Ndayisaba JP, Seebacher B, Schoenherr G, Mitterhuber J, Hendriks P, Kaindlstorfer C, Eschlboeck S, Fanciulli A, Krismer F, Seppi K, Poewe W, Bloem BR, Klucken J, Wenning GK. Physiotherapy improves motor function in patients with the Parkinson variant of multiple system atrophy: A prospective trial. Parkinsonism Relat Disord. 2019 Oct;67:60-65. doi: 10.1016/j.parkreldis.2019.09.026. Epub 2019 Sep 24. PMID: 31621609.

[7] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991 Dec;14(6):540-5. doi: 10.1093/sleep/14.6.540. PMID: 1798888.

[8] Trenkwalder C, Kohnen R, Högl B, Metta V, Sixel-Döring F, Frauscher B, Hülsmann J, Martinez-Martin P, Chaudhuri KR. Parkinson's disease sleep scale--validation of the revised version PDSS-2. Mov Disord. 2011 Mar;26(4):644-52. doi: 10.1002/mds.23476. Epub 2011 Feb 10. PMID: 21312275.

## P118

# Alpha-synuclein RT-QuIC seeding activity in olfactory mucosa of GBA-associated Parkinson's disease

*Fabiana Colucci*[1], R. Cilia[1], C.M.G. De Luca[2], M. Fusar Poli[3], G. Devigili[1], A.E. Elia[1], N. Golfrè Andreasi[1], L.M. Romito[1], F. Cazzaniga[2], S. Prioni[3], P. Amami[3], S.H.M.J. Piacentini[3], F. Moda[2], R. Eleopra[1]

[1]Parkinson and Movement Disorders Unit, Department of Clinical Neurosciences, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Unit of Neurology 5 and Neuropathology, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[3]Clinical Neuropsychology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

*Introduction:* RT-QuIC assay may detect abnormal α-syn seeding activity in olfactory mucosa (OM) samples of patients with Parkinson's disease (PD) with approximately 60% sensitivity. [1-2] PD patients carrying heterozygous GBA mutations (GBA-PD) present more aggressive disease course3, which might be associated with a different pattern of α-syn seeding activity.

*Objective:* To investigate the pattern of α-syn seeding activity by RT-QuIC in OM of GBA-PD and PD-noncarriers.

*Methods:* Nasal brush was performed in 24PD-GBA carriers and 24 PD-noncarriers, matched by age and disease duration. Demographic, neurological, and neuropsychological data were collected. A sample was considered to induce α-syn seeding activity (positive) when at least two of four replicates exceeded the fluorescence threshold (30,000 AU before 20 hours), and lag time was calculated by averaging the time required to reach the fluorescence threshold.

*Results:* No differences were found in clinical features between two groups, excepted from higher prevalence of olfactory dysfunction was found in GBA-PDs than PD-noncarriers (p=0,004). We found trend towards lower positive α-syn seeding in OM of 25% GBA-PD vs. in 50% of PD-noncarriers (p=0.074). GBA-PD with positive seeding had lower MDS-UPDRS-III (p=0.044) than those without seeding. The mean RT-QuIC lag time was significantly longer in GBA-PD (p=0.039) and correlated to (a) MDS-UPDRS parts I (p=0.013) and II (p=0.012); (b) NMSS sleep/fatigue (p=0.005) and perceptual domain (p=0.031); (c) COMPASS-31 urinary domain(p=0.042).

*Conclusion:* We found lower α-syn seeding activity in GBA-PD than noncarriers. This might be explained by different α-syn conformation and binding to RT-QuIC primers. Alternatively, GBA-PD might exhibit increased OM neurons degeneration, resulting in suboptimal tissue samples. Analysis of α-syn strains in OM by electronic microscopy may clarify these results.

**References:**

[1] Shahmoradian, S. H., et al., (2019). Lewy pathology in Parkinson's disease consists of crowded organelles and lipid membranes. Nature Neuroscience, 22(7), 1099–1109.
[2] Chahine, L. M., (2020). In vivo distribution of α-synuclein in multiple tissues and biofluids in Parkinson disease. Neurology, 95(9), E1267–E1284.
[3] Brockmann, K., et al. (2015). GBA-associated Parkinson's disease: reduced survival and more rapid progression in a prospective longitudinal study. Movement Disorders: Official Journal of the Movement Disorder Society, 30(3), 407–411.

**P119**

## Dynamic and kinematic analysis of gait in Parkinson's disease: markers for diagnosis

*Pasquale Maria Pecoraro*[1,2], L. Raiano[3], M.L. Caminiti[1,2], V. Di Lazzaro[1,2], L. di Biase[1,2,4]

[1]Research Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine and Surgery, University Campus Bio-Medico of Rome, Rome, Italy
[2]Operative Research Unit of Neurology, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy
[3]NeXT: Neurophysiology and Neuroengineering of Human-Technology Interaction Research Unit, Campus Bio-Medico University, Rome, Italy
[4]Brain Innovations Lab, University Campus Bio-Medico of Rome, Rome, Italy

*Introduction:* Gait of Parkinson's disease (PD) patients differs from healthy subjects (HS) for both kinematic and dynamic features. However, which kind of analysis (dynamic or kinematic) is more informative to discriminate PD and HS gait features is a question still open.

*Objective:* The present study aims to evaluate the discrimination potential of dynamic and kinematic gait analysis between PD and HS.

*Methods:* In the present retrospective study, from two datasets were extracted gait dynamic and kinematic features of 108 PD patients and 88 HS. Gait data were collected through an instrumented force-sensitive insole placed in subjects' shoes.

*Results:* For all the dynamic central and dispersion indices, statistical analysis showed a non-significant difference between HS and PD. Conversely, kinematic features showed statistically significant differences between PD patients and HS for: gait speed, time-Up-and-Go test and for dispersion indices like standard deviation and interquartile range of stance, swing and double support time.

*Conclusions:* Despite a directly mathematical relationship between kinematics and dynamic features, the results of the present study highlighted the so-called force/rhythm dichotomy, due to the greater informativeness of kinematic features than dynamic ones in discriminating PD vs HS.

**P120**

## Correlation between voice intensity and swallowing function in subjects with Parkinson disease

*Baldanzi Cinzia*[1], V. Crispiatico[2], G. Fusari[1], F.L. Saibene[1], M. Meloni[1,3], D. Cattaneo[1,4], C. Vitali[1]

[1]IRCSS Fondazione Don Carlo Gnocchi, Milano, Italy
[2]UOC Neuorehabilitation, Ospedale G. Salvini, ASST-Rhodense, Garbagnate Milanese, Milano, Italy
[3]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy
[4]Department of Physiopathology and Transplants, University of Milano, Milano, Italy

*Introduction:* People with Parkinson's disease (PwPD) may experience a variety of motor and non-motor impairments, including decreased voice loudness and dysphagia [1]. Dysphagia involves oral, pharyngeal, or esophageal phases of swallowing [2], leading to malnutrition and dehydration, pneumonia, and even death [3]. Instrumented vocal parameters seem useful for identifying PwPD with dysphagia since recent evidence has shown organs related to swallowing and speech are structurally and neurologically intertwined [4-5-6].

*Objective:* The aim of this study was to investigate: the relationship between voice intensity and swallowing function and determine if disease severity could affect this correlation.

*Methods:* 30 PwPD according to the MDS Clinical Diagnostic Criteria were recruited at IRCCS Don Gnocchi Foundation (Milan, Italy). The MDS-UPDRS Part III [7] was used to evaluate motor disability; sustained /a/ intensity and the intensity of 1 minute of spontaneous speech were analyzed with PRAAT software. The Penetration Aspiration Scale [8], the Dysphagia Severity [9] and Videofluoroscopic Dysphagia Scales [10] were used for swallowing evaluation during videofluoroscopy. Spearman correlation coefficient and logistic and linear model were used to analyze data.

*Results:* Speech intensity correlated with swallowing impairment (between -.42 and -.72 across scales), even when controlling for UPDRS motor scores (mean score= 47.2±13.8). Swallowing impairment is 56 times more likely ($p<0.01$) when the speech intensity is below the normal voice intensity cut-off score (> 60 dB). Furthermore, the positive predictive value indicates that among those who have a negative voice test (<60 dB), the probability of swallowing disorders is 93%.

*Conclusions:* The results of the present study confirm the correlation between voice and swallowing. Voice recording is a non-invasive, low-cost, easy-to-use assessment, potentially useful for clinicians to identify PwPD who need an instrumental examination investigating dysphagia, allowing timely management and reduction of complications, and improving life's quality.

**References:**

[1] Potulska A, Friedman A, Królicki L, Spychala A. Swallowing disorders in Parkinson's disease. Parkinsonism Relat Disord. 2003 Aug;9(6):349-53.
[2] Kwon, Miseon, and Jae-Hong Lee. Oro-Pharyngeal Dysphagia in Parkinson's Disease and Related Movement Disorders." Journal of movement disorders vol. 12,3 (2019): 152-160.
[3] Cosentino, G., Avenali, M., Schindler, A. et al. A multinational consensus on dysphagia in Parkinson's disease: screening, diagnosis and prognostic value. J Neurol 269, 1335–1352 (2022).
[4] Park A, Jang SJ, Kim NE, et al. Swallowing Outcomes Following Voice Therapy in Multiple System Atrophy with Dysphagia: Comparison of Treatment Efficacy with Parkinson's Disease. Dysphagia. 2022 Feb;37(1):198-206.
[5] Sharkawi AE. Swallowing and voice effects of Lee Silverman Voice Treatment (LSVT(R)): a pilot study. J Neurol Neurosurg Psychiatry. 2002;72(1):31–6.

[6] Miles A, Jardine M, Johnston F, de Lisle M, Friary P, Allen J. Effect of Lee Silverman Voice Treatment (LSVT LOUD®) on swallowing and cough in Parkinson's disease: A pilot study. J Neurol Sci. 2017 Dec 15;383:180-187.
[7] Fahn S,Elton R, Members of the UPDRS development committee. The unified Parkison's disease rating scale. In: Fahn S,Marsden CD,Calne DB,Goldstein M, editors. Recent developments in Parkinson's disease, Vol. 2. Florham Park, NJ: Macmillan Health Care Information; 1987. p 153–163, 293–304.
[8] Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. Dysphagia. 1996;11(2):93–8.
[9] O'Neil KH, Purdy M, Falk J, Gallo L. The Dysphagia Outcome and Severity Scale. Dysphagia. 1999 Summer;14(3):139-45.
[10] Kim J, Oh BM, Kim JY, Lee GJ, Lee SA, Han TR. Validation of the videofluoroscopic dysphagia scale in various etiologies. Dysphagia. 2014 Aug;29(4):438-43.

**P121**

## Salivary extracellular vesicles as a potential biomarker of Parkinson's disease

*Maurizio Zibetti*[1,2], A. Gurgone[1], V. Cardinale[1], C. Ledda[1,2], G. Imbalzano[1,2], L. Lopiano[1,2], M. Giustetto[1]

[1]Rita Levi-Montalcini Department of Neuroscience, University of Turin, Turin, Italy
[2]Neurology 2 Unit Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino Turin, Italy

*Introduction:* Extracellular vesicles (EVs) are small vesicles released by many cells, including neurons and can be isolated from body fluids, like saliva [1]. α-Synuclein (α-syn) has recently been detected in EVs and may contribute to the spreading of disease pathology in α-synuclein-related neurodegeneration2. The detection of α-syn in salivary EVs may contribute to find potential biomarker for Parkinson disease (PD) onset and progression.

*Objective:* 1) To establish the methodology to isolate EVs from saliva; 2) To examine both oligomeric (α-synOlig) and total α-Syn (α-synTotal) contained in the EVs to validate their potential diagnostic and prognostic value for PD.

*Methods:* Saliva samples were obtained from 48 PD patients (PDs) and 31 healthy controls (HCs). The EVs were isolated by differential ultracentrifugation [3]; western blot (WB) and Nanosight (NTA) were used to validate the protocol and to analyze EVs size and concentration. The transmission electron microscopy (TEM) was used to assess EVs morphology [4]. The concentration of α-synTotal, α-synOlig was determine by ELISA technique [5]. Diagnostic value and clinical relevance of salivary EVs α-syn were assessed by Receiver Operator Characteristic (ROC) curve and Pearson correlation [6].

*Results:* We first characterized the EVs by WB and TEM, the NTA showed that the concentration of EVs is higher in HCs than PDs, while the dimensions do not change. The ELISA test revealed that the level of both α-synTotal and α-synOlig are higher in PDs compared to the HCs (α-synTotal: sensitivity = 66%, specificity = 76%; α-synOlig sensitivity = 83%, specificity = 60%). We found correlations of α-synOlig with the duration of the disease and the mini mental state examination (MMSE).

*Conclusions:* These findings support the role of salivary EVs cargoes as a promising biomarker for PD and purpose to further investigate the possible correlation of α-Syn with disease severity, which could reveal α-Syn as a predictor of PD progression.

**References:**

[1] Atik, A., Stewart, T. & Zhang, J. Alpha-Synuclein as a Biomarker for Parkinson's Disease. Brain Pathol. 26, 410–418 (2016).
[2] Cerri, S. et al. The exosomal/total α-synuclein ratio in plasma is associated with glucocerebrosidase activity and correlates with measures of disease severity in PD patients. Front. Cell. Neurosci. 12, 1–10 (2018).
[3] Franquesa, M. et al. Update on controls for isolation and quantification methodology of extracellular vesicles derived from adipose tissue mesenchymal stem cells. Front. Immunol. 5, (2014).
[4] Pomatto, M. et al. Differential therapeutic effect of extracellular vesicles derived by bone marrow and adipose mesenchymal stem cells on wound healing of diabetic ulcers and correlation to their cargoes. Int. J. Mol. Sci. 22, 1–26 (2021).
[5] Vivacqua, G. et al. Abnormal salivary total and oligomeric alpha-synuclein in Parkinson's disease. PLoS One 11, 1–12 (2016).
[6] Cao, Z. et al. α-Synuclein in salivary extracellular vesicles as a potential biomarker of Parkinson's disease. Neurosci. Lett. 696, 114–120 (2019).

**P122**

## Olfactory mucosa seeding assay in the diagnosis of Parkinson's disease and α-synucleinopathies

*Mauro Catalan*[1], M. Bongianni[2], V. Tommasini[1], D. Perra[2], P. Polverino[1], C. Bertolotti[1], R. Baruca[3], G. Bellavita[1], L. Antonutti[1], G. Zanusso[2], P. Manganotti[1]

[1]Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy
[2]Department of Neurosciences, Biomedicine, and Movement Sciences, Policlinico G.B. Rossi, University of Verona, Verona, Italy
[3]Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy

*Introduction:* Parkinson's disease (PD), dementia with Lewy bodies (DLB) and multiple system Atrophy (MSA) are characterized by misfolding and aggregation of pathological a-synuclein (a-syn). Real-time quaking-induced conversion (RT-QuIC) is able to detect misfolded α-syn in cerebrospinal fluid (CSF) and other peripheral tissues of patients with a-synucleinopathies. The aim of this study is to investigate the proficiency of RT-QuIC in detecting the presence of pathological a-syn on the olfactory mucosa (OM) and cerebrospinal fluid (CSF) of patients with a-synucleinopathies.

*Methods:* 53 patients with neurodegenerative diseases has been enrolled in the Neurological Clinic of Trieste University. 37 patients (SYN group) received a diagnosis of PD (29), DLB (4) and MSA (4) while 16 patients (6 Alzheimer's disease, 3 progressive supranuclear palsy, 3 fronto-temporal dementia and 4 with other diagnosis) were included in the NO SYN group. OM was obtained through nasal swab in 45 patients while CSF, through lumbar puncture, in 42; 34 patients performed both examinations. Presence of pathological a-synuclein seeding activity was assessed by means of RT-QuIC, in the Neuropathology laboratory at the University of Verona.

*Results:* RT-QuIC resulted positive in 25/33 OM samples (75.8%) of SYN group, in 22/27 of PD patients (81.5%) and in 1/12 (8.3%) of NO SYN group. 23/27 (85.2%) SYN, 19/20 (95.0%) PD and 3/15 (20.0%) NO SYN patients, had α-syn seeding activity in the CSF. Among the 34 patients who underwent both examinations, 21/23 (91.3%) SYN patients, 18/18 (100%) PD patients and 1/11 (9.1%) NO SYN patients, tested positive for either OM or CSF.

*Conclusions:* RT-QuIC assay performed in OM and CSF of patients with α-syn-related disorders shows a comparable diagnostic accuracy. The advantage of non-invasiveness, suggests that OM sampling might be used as a first screening tissue. The combination of the two samples analysis, may improve diagnostic accuracy especially in PD patients.

**P123**

## The impact of dopaminergic therapy on sleep quality of fluctuating Parkinson's disease patients

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

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy

*Introduction:* Parkinson's disease (PD) is characterized by several nonmotor symptoms [1]. Among these, sleep dysfunction is highly prevalent (60%-98% of patients) [2-3]. The influence of various antiparkinsonian drugs on sleep quality has been evaluated so far, with conflicting results.

*Objective:* To analyze the correlation between sleep dysfunction (i.e., reduced sleep quality and excessive daytime sleepiness [EDS]) and dopaminergic therapy in a large cohort of advanced PD patients.

*Methods:* Patients consecutively evaluated for device-aided therapies eligibility were enrolled. Sleep dysfunction was measured by means of the PD Sleep Scale-2 (PDSS-2; score ≥18 indicates poor sleep quality [4]), and the Epworth Sleepiness Scale (ESS; score ≥10 indicates EDS).
The association between dopaminergic therapy (i.e., dopamine agonists [DA], nocturnal extended-release levodopa, DA-LEDD, levodopa-LEDD, and total LEDD) and disturbed sleep or EDS was evaluated with binary logistic regression analysis, correcting for age, sex, disease duration, motor impairment (Off-state MDS-UPDRS-III), and sleep treatment. Analysis of covariance was used to evaluate differences in PDSS-2 (total and sub-domains scores) and ESS between patients with and without DA treatment, and between patients treated with low or high doses of DA (cut-off: DA-LEDD=180 mg), correcting for the same potential confounders.

*Results:* We enrolled 281 patients (males: 66.5%; age: 60.3±7.9 years; disease duration: 11.6±3.7 years). 66.2% of patients reported poor sleep quality; 34.5% reported EDS. DA treatment was independently associated with a 2-fold lower odds of reporting relevant sleep disturbances (OR: 0.498; p=0.035), while DA-LEDD, levodopa-LEDD, total LEDD, and extended-release levodopa were not associated with disturbed sleep. EDS was not influenced by dopaminergic therapy. Patients with DA intake reported significant lower PDSS-2 total score (p=0.027) and "motor symptoms at night" domain score (p=0.044). Patients with higher doses of DA showed lower PDSS-2 total score (p=0.043).

*Conclusion:* Our study highlights the positive influence of DA on sleep quality, especially for high doses of DA.

**References:**

[1] Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021;397(10291):2284-2303.
[2] Mirelman, Anat et al. "Tossing and Turning in Bed: Nocturnal Movements in Parkinson's Disease." Movement disorders : official journal of the Movement Disorder Society vol. 35,6 (2020): 959-968.
[3] Trenkwalder C, Kohnen R, Högl B, Metta V, Sixel-Döring F, Frauscher B, Hülsmann J, Martinez-Martin P, Chaudhuri KR. Parkinson's disease sleep scale--validation of the revised version PDSS-2. Mov Disord. 2011 Mar;26(4):644-52.
[4] Muntean ML, Benes H, Sixel-Döring F et al (2016) Clinically relevant cut-off values for the Parkinson's disease sleep scale-2 (PDSS-2): a validation study. Sleep Med 24:87–92.

**P124**

## Hearing impairment in Parkinson's disease: another non-motor symptom to consider?

*Elena Garasto*[1], M. Conti[1], A. Viziano[2], A. Stefani[1], M. Pierantozzi[1], N.B. Mercuri[1], A. Moleti[3], R. Sisto[4], R. Cerroni[1]

[1]Parkinson's Center, Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]Department of Clinical Sciences and Translational Medicine, University of Rome "Tor Vergata", Rome, Italy.
[3]Department of Physics and NAST Centre, University of Rome "Tor Vergata", Via della Ricerca Scientifica, Rome, Italy
[4]INAIL Research, Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Monteporzio Catone (Rome), Italy

*Introduction:* Sensorial non-motor symptoms (NMS) in Parkinson's disease (PD), which include pain, olfactory disturbance, visual and hearing impairment (HI), are often underestimated and untreated in clinical practice. In our previous study [1], one important result was PD patients having worse hearing function with respect to controls, in accordance with other works [2].

*Objective:* The aim of the study was to investigate the possible correlation between NMS burden and quality of life (QoL) with HI in a large cohort of PD patients, by means of pure tone audiometry (PTA) and distortion product otoacoustic emissions (DPOAEs).

*Methods:* We selected patients with idiopathic PD, without other concomitant neurological diseases, dementia or diagnosis of any audiological/vestibular disease. Demographic and clinical data were collected (UPDRS III, disease duration, H&Y). Then, patients underwent otoscopic examination, audiological testing (PTA and DPOAEs) and questionnaires with NMSS and PDQ39. ANCOVA and partial correlation analysis with Pearson coefficient have been used for statistical analysis (p value<0,05).

*Results:* We selected two cohort of patients, 59 who performed PTA (31 with hearing threshold >25dB and 28 lower than 25dB) and 64 with low signal-to noise ratio DPOAEs. Patients with HI had similar disease duration, UPDRS III and H&Y with respect to patients without HI, but were different for age and gender, being older and prevalently male. Concerning NMSS and PDQ39, they showed higher scores in every subdomain except for cardiovascular (CV) and sexual function (SF) of NMSS. DPOAE variables showed significant correlation with age and every subdomain of scales, except for NMS-CV, SF and urinary function (U).

*Conclusion:* This study demonstrated that PD patients with HI have greater burden of NMS and lower related QoL and functioning. We supported the idea of PD being a systemic disease with multidomain involvement [3] and stress the importance of hearing evaluation, even in asymptomatic patients.

**References:**

[1] Sisto R, Viziano A, Stefani A, Moleti A, Cerroni R, Liguori C, Garasto E, Pierantozzi M. Lateralization of cochlear dysfunction as a specific biomarker of Parkinson's disease. Brain Commun. 2020 Sep 18;2(2):fcaa144.
[2] Vitale C, Marcelli V, Allocca R, Santangelo G, Riccardi P, Erro R, et al. Hearing impairment in Parkinson's disease: Expanding the nonmotor phenotype. Mov Disord. 2012;27(12):1530–5.
[3] Titova N, Padmakumar C, Lewis SJG, Chaudhuri KR. Parkinson's: a syndrome rather than a disease? J Neural Transm. 2017;124(8):907–14.

**P125**

## Plasma GFAP and NfL levels in a group of Parkinson's disease patients. A study on clinical parameters and motion sensor tests

*Alessandro Lupini*[1], A. Pilotto[1], C. Zatti[1], A. Rizzardi[1], V. Quaresima[1], M. Parigi[2], S. Giliani[2], A. Padovani[1]

[1]Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Brescia, Italy
[2]Nocivelli Institute for Molecular Medicine Spedali Civili and Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

*Introduction:* Glial fibrillary acid protein (GFAP) has been recently studied as a biomarker for diagnostic and prognostic purposes of Alzheimer's disease and other neurodegenerative, neuroinflammatory or traumatic brain conditions. Plasma neurofilament light chain (NfL) has been identified as one of the most promising biomarkers for predicting disease burden and progression in several neurological conditions [MOU1] . Recent studies suggest that mobile health technologies could be more sensitive in detecting motor impairment in patients affected by Parkinson's Disease (PD).

*Objective:* To measure plasma levels of GFAP and NfL in blood samples from drug naïve PD patients, and to compare these biomarkers with clinical parameters and motion sensors tests.

*Methods:* We measured plasma GFAP and NfL using Single molecule array (Simoa) assays in consecutive drug naïve PD patients. All PD patients underwent an extensive motor and non-motor assessment. In a subgroup of patients, the motor assessment included a kinematics study with inertial motion sensors. The correlation between plasma biomarkers and motor scores at baseline and at follow-up were evaluated using linear and partial correlation analyses, corrected for age and gender.

*Results:* forty-two PD patients entered the study. GFAP and NfL did not show any correlation with clinical parameters. In PD patients, both GFAP and NfL correlated with several motion sensors recorded parameters: for GFAP, normal pace step length (R= -0,340 '=0.039) balance in semi-tandem position (R=0.322 p=0.040), gait and timed up and go angular velocity (R=-0.379 p=0.032); for NfL: straight walk normal pace step length asymmetry (R=-0.329 p=0.050), dual task straight walk times, balance jerks (R=0.433 p=0.004), timed up and go maximum speed (R=-0.344, p=0.04)

*Conclusions:* Our study shows that plasma GFAP and NfL correlate with subtle differences in motor performances in drug naïve PD patients, not identifiable by standard UPDRS-III assessment but measurable by mobile health technologies.

**P126**

## Neurodegeneration and inflammation in Parkinson's disease: an insight from blood biomarkers

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

[1]Neurology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]Department of Geriatrics, Neurosciences and Orthopedics, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[3]Neuroscience Department, Università Cattolica del Sacro Cuore, Rome, Italy

*Background and aim of the study:* Parkinson's disease (PD) is the second most frequent neurodegenerative disorder and is characterized by a great phenotypical heterogeneity. Alfa-synuclein deposition plays a crucial role in PD development but also other mechanisms, including inflammation, seem to underlie PD pathogenesis and progression [1]. Recently, great attention has been put on biomarkers which could follow disease initiation and progression to both monitor disease progression and understand underlying pathophysiological mechanisms [2-3].
Our aim was to measure blood levels of neurodegeneration and inflammation biomarkers and correlate them with clinical and demographic data.

*Materials and Methods:* We consecutively enrolled PD patients and evaluated them by means of validated clinical scales (UPDRS, Hoehn and Yahr staging, MMSE, NMSQ). Then, serum levels of selected biomarkers (Neurofilament light chain, BDNF, IL-1β, IL5, IL-6, IFN, TNF-a, IL4 and IL10) were essayed using commercially available kits on an ELLA™ automated immunoassay system (Bio-Techne, San Jose, CA, USA). Descriptive statistics, parametric and non-parametric tests were used when necessary. Spearman correlation test was used to correlate clinical-demographical data and biological measures.

*Results:* 104 patients were enrolled with a mean age of 66.55 years and disease duration ranging from 0 to 29 years, with a mean of 8 +/-5 years. NfL levels showed a positive correlation with disease duration and UPDRS III score (respectively rho 0,348, p=0.014 and rho 0,258 and p=0.047). A correlation analysis between inflammatory markers and disease duration showed a trend in increase of pro-inflammatory citokynes in the first years, with a tendency to peak at 5 years from diagnosis and then a decrease. patietns with short disease duration (< 5years) had significantly lower consentrations of IL5, IL10 and IL17.

*Discussion:* In this study we confirm the role of NfL as a marker of disease progression, confirming its reliability also if measured in the serum of PD patients. If combined with more specific markers, it could play a significant role in monitoring disease progression and also be predictive of conversion to a clinical manifest phase in prodromal patients. Moreover, we also found an interesting trend showing an increase of pro-inflammatory cytokines in the earliest phases of the disease, followed by a decrease in the following years.

*Conclusion:* This study shows the association between serum NfL and disease burden and the tendency to manifest a pro-inflammatory status in patients in the earliest phases of the disease.

**References:**

[1] Lindestam Arlehamn CS, Dhanwani R, Pham J, Kuan R, Frazier A, Rezende Dutra J, Phillips E, Mallal S, Roederer M, Marder KS, Amara AW, Standaert DG, Goldman JG, Litvan I, Peters B, Sulzer D, Sette A. α-Synuclein-specific T cell reactivity is associated with preclinical and early Parkinson's disease. Nat Commun. 2020 Apr 20;11(1):1875. doi: 10.1038/s41467-020-15626-w. PMID: 32313102; PMCID: PMC7171193.

[2] Halloway S, Desai P, Beck T, Aggarwal N, Agarwal P, Evans D, Rajan KB; and the Chicago Health and Aging Project. Association of Neurofilament Light With the Development and Severity of Parkinson Disease. Neurology. 2022 May 31;98(22):e2185-e2193. doi: 10.1212/WNL.0000000000200338. Epub 2022 Apr 13. PMID: 35418452; PMCID: PMC9162164.
[3] Parnetti L, Gaetani L, Eusebi P, Paciotti S, Hansson O, El-Agnaf O, Mollenhauer B, Blennow K, Calabresi P. CSF and blood biomarkers for Parkinson's disease. Lancet Neurol. 2019 Jun;18(6):573-586. doi: 10.1016/S1474-4422(19)30024-9. Epub 2019 Apr 10. PMID: 30981640.

**P127**

## Abnormal sensory attenuation as a potential biomarker of fatigue in Parkinson's disease: results from a preliminary study

*Emanuela Pizzolla*, M. Fiorio, M.E. Andani, I.A. Di Vico, M. Tinazzi, A. Marotta

Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

*Introduction:* Fatigue is a core non-motor symptom of Parkinson's disease (PD), interfering substantially with patients' quality of life [1]. Mechanisms underlying fatigue remain unclear, thus limiting the development of treatment strategies to tackle this highly disabling symptom. A recent model has conceptualized fatigue as a disorder of sensory attenuation (SA, i.e., a perceptual phenomenon by which self-generated stimuli are perceived as less salient than external ones) [1-2]. Yet, experimental evidence on this model is still lacking.

*Objective:* We aimed to investigate whether reduced SA was related to fatigue in PD patients with fatigue (PDFatigue) compared with patients without it (PDNo fatigue) and healthy controls (HC).

*Methods:* We enrolled 10 PDFatigue (mean age ± SD, 63.8 ± 9.9; 5M), 10 PDNo fatigue (mean age ± SD, 64.4 ± SD: 6.9; 9M), and 15 HC (mean age ± SD, 64.9 ± 6.4; 11M). Fatigue assessment was carried out through the Fatigue Severity Scale (cut off ≥4). To measure SA we used the force matching task (FMT) [3]. Participants were asked to match different target forces exerted on their left index finger, either by pressing directly on their finger (direct condition) or by operating an external device (indirect condition). Usually, participants overestimate the target force in the direct condition because of SA [4].

*Results:* We found no significant differences between the direct and indirect condition in the PDFatigue group, while a significant force overestimation in the direct condition compared to the indirect one was found in both the HC and in PDNo-Fatigue group with a tendency to significance. No significant differences between groups were found.

*Conclusions:* These preliminary data suggest a selective impairment of SA in PD patients with fatigue. The current study provides preliminary evidence on the role of SA in the pathophysiology of fatigue in PD.

**References:**

[1] Di Vico, I. A., Cirillo, G., Tessitore, A., Siciliano, M., Venturelli, M., Falup-Pecurariu, C., Tedeschi, G., Morgante, F., & Tinazzi, M. (2021). Fatigue in hypokinetic, hyperkinetic, and functional movement disorders. Parkinsonism & related disorders, 86, 114–123.

[2] Kuppuswamy A. The fatigue conundrum. Brain. 2017 Aug 1;140(8):2240-2245. doi: 10.1093/brain/awx153. PMID: 28899013; PMCID: PMC5806506.

[3] Pareés I, Brown H, Nuruki A, Adams RA, Davare M, Bhatia KP, Friston K, Edwards MJ. (2014). Loss of sensory attenuation in patients with functional (psychogenic) movement disorders. Brain, 137(Pt 11), 2916–2921.

[4] Shergill SS, Bays PM, Frith CD, Wolpert DM. (2003). Two eyes for an eye: the neuroscience of force escalation. Science, 301(5630), 187.

**P128**

## Kinematic gait patterns in patients affected by Parkinson disease with and without mild cognitive impairment

*Federico Di Filippo*[1], C. Ricciardi[2,3], M. Russo[2], A. Volzone[1], G. Ricciardelli[1], S. Cuoco[1], M. Romano[2], P. Barone[1], M. Amboni[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Department of Electrical Engineering and Information Technology, University of Naples "Federico II", Naples, Italy
[3]Bioengineering Unit, Institute of Care and Scientific Research Maugeri, Pavia, Italy

*Introduction:* Gait impairments and cognitive dysfunction are common in Parkinson's disease (PD) and both of them impact on physical and social health, since early stage. Previous studies suggested a close relationship between gait and cognition in PD [1].

*Objectives:* To assess biomechanical and kinematics changes in PD patients with (PD-MCI) and without mild cognitive impairment (PD-noMCI) in different gait settings, eventually phenotyping specific patterns.

*Methods:* Seventy-two PD patients (33 PD-MCI and 39 PD-noMCI) were evaluated with MDS-UPDRS, H&Y scale and gait analysis in three different conditions (normal gait, motor and cognitive dual-task). Kinematic variables were extracted. A univariate statistical analysis (t-Test for independent samples or Mann-Whitney U-test) was carried out to compare the two groups. Computation was supported by SPSS (v.27).

*Results:* PD-MCI, as compared with PD-noMCI patients, resulted older and affected by more disability and more severe motor symptoms, as indicated by higher H&Y scale and MDS-UPDRS part III. In the normal gait task, PD-MCI vs. PD-noMCI exhibited both increased plantarflexion and range of motion (ROM) in the ankle. In the motor dual-task, PD-MCI vs. PD-noMCI displayed significantly lower trunk maximum rotation, higher pelvic tilt and increased hip maximum flexion with consequent augmented ankle dorsiflexion [2]. In the cognitive dual-task, PD-MCI vs. PD-noMCI showed increased pelvic tilt and hip flexion with reduced ROM at both hip and knee and higher, likely compensatory, ankle plantarflexion [2].

Conclusions: PD-MCI vs.PD-noMCI patients display characteristic joints attitude with general lower limbs hyperflexion and reduction of ROM, especially in dual task conditions. Those kinematic changes could be propaedeutic for remodelling gait pattern and accounting for initial disability due to reduction of postural stability and strategical adaptability. On the one hand, these findings support the cognitive contribution to keep upright position during walking, on the other hand, they suggest early rehab intervention in PD patients with MCI.

**References:**

[1] Amboni M, Barone P, Hausdorff JM. Cognitive contributions to gait and falls: evidence and implications. Mov Disord. 2013 Sep 15;28(11):1520-33.
[2] Joseph B. Webster, Benjamin J. Darter Principles of Normal and Pathologic Gait, Chapter IV. 2019.

**P129**

## New insights on sensory-motor integration in Parkinson-related fatigue

*Angela Sandri*[1], I.A. Di Vico[1,2], M. Emadi Andani[1], G. Cirillo[3], S. Ottaviani[1], M. Venturelli[1], F. Morgante[4], M. Tinazzi[1]

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]The Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, NYU Langone Health, New York, USA
[3]Division of Human Anatomy - Laboratory of Morphology of Neuronal Network, Department of Mental, Physical Health and Preventive Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy
[4]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's, University of London, London, UK

*Background:* Fatigue is an extremely distressing symptom in Parkinson's disease (PD) that affects up to 50% of patients [1]. Imaging studies have linked fatigue to a disruption in connectivity of areas involved in motor preparation [2] and lack of pre-movement facilitation (PMF), [i.e. the increase of motor evoked potential (MEP) amplitude before movement onset] has been seen in fatigued patients with other neurological diseases [3].

*Aim:* We studied PMF in PD patients and tested the hypothesis that PD-related fatigue was related to reduced PMF.

*Methods:* We enrolled 15 patients with fatigue (PD-F), 16 patients without (PD-NF) and 16 Healthy controls (HC). Presence and severity of fatigue was measured with the Fatigue Severity Scale (FSS, cut-off≥4). We assessed PMF during a simple reaction time (RT) motor task using transcranial magnetic stimulation (TMS) and TMS was delivered within RT at 150, 100 and 50 ms before the estimated movement onset.

*Results:* The rate of increase in MEP amplitude at three different intervals during movement preparation compared to MEP at rest (MEPPMF/MEPREST) disclosed separate effects for 'and 'group' and post hoc analyses disclosed a statistically significant difference at 50 ms in all. HC group resulted statistically significant different from PD-F (p= 0.004**) and PD-NF (p = 0.014*), but PD-F and PD-NF did not differ from each other (p> 0.05).

*Conclusions:* These results provide preliminary evidence PMF is abnormally reduced in PD patients compared to HC, but independently from fatigue. Abnormally reduced pre-movement facilitation could represents a neurophysiological hallmark of PD patients but it is not a biomarker of fatigue in PD. Future studies are necessary to understand the mechanisms of fatigue and to verify the meaning of reduced PMF in PD patients, its meaning in clinical and research context.

**References:**

[1] Di Vico IA, Cirillo G, Tessitore A, Siciliano M, Venturelli M, Falup-Pecurariu C, Tedeschi G, Morgante F, Tinazzi M. Fatigue in hypokinetic, hyperkinetic, and functional movement disorders. Parkinsonism Relat Disord. 2021 May; 86:114-123. doi: 10.1016/j.parkreldis.2021.03.018. Epub 2021 Mar 29. PMID: 33839028.
[2] Siciliano M, De Micco R, Giordano A, Di Nardo F, Russo A, Caiazzo G, De Mase A, Cirillo M, Tedeschi G, Trojano L, Tessitore A. Supplementary motor area functional connectivity in "drug-naïve" Parkinson's disease patients with fatigue. J Neural Transm (Vienna). 2020 Aug;127(8):1133-1142. doi: 10.1007/s00702-020-02219-6. Epub 2020 Jun 27. PMID: 32594249.

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

**P130**

## Aberrant brain plasticity in patients with Parkinson's disease and levodopa-induced dyskinesias

*Pasquale Sanginario*[1], B. Angeloni[1], C. Piano[1,2], A.R. Bentivoglio[1,2], R. Di Iorio[2], F. Bove[2], P. Calabresi[1,2]

[1]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Neurology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

*Introduction:* Several alterations of physiological synaptic plasticity have been documented in patients with Parkinson's disease (PD) and Levodopa-Induced Diskinesias (LIDs). These alterations, in particular the failure of synaptic depotentiation, play a key role in the pathophysiology of LIDs.

*Objective:* We performed this monocentric cross-sectional study aimed to identify the alterations of cortical plasticity at primary motor cortex (M1) in PD patients with and without LIDs and to correlate the neurophysiological alterations with the severity of LIDs.

*Methods:* Each patient underwent a preliminary visit of enrolment and administration of clinical scales (MMSE, UPDRS and UDyRS). The patients underwent two sessions of theta-burst stimulation (TBS) in different days. In the first paradigm ("potentiation session"), a train of continuous TBS (cTBS) 300 stimuli was delivered over M1 followed by the 1-min voluntary contraction of the target muscle (cTBSc0). In the second paradigm ("depotentiation session"), the potentiation session (cTBSc0) was followed by the delivery of a train of cTBS 150 stimuli (cTBS150), which reversed the long-term potentiation-like plasticity previously induced.

*Results:* We recruited 24 PD patients, 13 without LIDs and 11 with LIDs. We found a significant depotentiation in the group of non-dyskinetic patients ($F = 4.55$, $p = 0.002$) and a not significant depotentiation in the group of dyskinetic patients ($F = 0.49$, $p = 0.7$). A negative correlation was found between depotentiation (measured by the % of MEP amplitude variation following cTBS150) and score of the UDyRS part III ($r=-0.7$, $p=0.005$).

*Conclusions:* Our results showed that PD patients with LIDs fail to respond normally to a depotentiation protocol and that impairment in depotentiation correlates with dyskinesias severity, so cTBS may represent a potential biomarker of LIDs in PD patients.

## P131

### Assessing the role of motor network excitability alterations in Parkinson's disease, a TMS-EEG study

*Mancuso Marco*[1], G. Leodori[1], M.I. De Bartolo[1], A. Fabbrini[1], L. Rocchi[2], D. Belvisi[1], A. Berardelli[1], A. Conte[1]

[1] Dipartiemnto di Neuroscienze Umane, La Sapienza Università di Roma, Rome, Italy
[2]Department of Medical Sciences and Public Health, Institute of Neurology, University of Cagliari, Cagliari, Italy

*Background:* Motor impairment in Parkinson's disease (PD) reflects changes in the basal ganglia-thalamocortical circuit converging on the primary motor cortex (M1) and supplementary motor area (SMA). In a previous study, using transcranial magnetic stimulation coupled with electroencephalography (TMS-EEG), we showed how moderate PD patients off medication had lower M1 and higher pre-SMA excitability, as reflected by alterations in early TMS-EEG responses [1]. These abnormalities were reverted by dopaminergic therapy. In this study, we aimed at understanding the pathophysiological and clinical meaning of these alterations by studying TMS-EEG responses in de novo (DNs) and early (EA) PD patients.

*Objectives:* To understand the role of pre-SMA and M1 excitability alterations in PD patients.

*Methods:* We compared TMS-evoked cortical potentials (TEPs) from M1 and pre-SMA contralateral to the most affected side between 15 de-novo (i.e. newly diagnosed, not taking dopaminergic medications) and 15 early (< 1 yr of history) PD patients tested off medications and 15 healthy controls (HCs). Also, a kinematic assessment of bradykinesia was performed on the most affected side and correlated to TEPs.

*Results:* When stimulating M1, DNs and EAs showed lower P30 than HCs, while DNs showed a less pronounced N45 than DNs. When stimulating pre-SMA, only EAs, but not DNs, showed a more negative N40 than HCs. No correlation was found between kinematic-based bradykinesia assessment and TEPs.

*Conclusions:* Here we confirmed a reduced M1 excitability from the early stages of PD patients that may offer a new disease biomarker. Also, we validated the finding of increased pre-SMA excitability in PD, which seems to parallel disease progression. Although dopaminergic medications reverted both abnormalities, these do not seem to be directly correlated with bradykinesia mechanisms.

**References:**

[1] Leodori G, De Bartolo MI, Guerra A, Fabbrini A, Rocchi L, Latorre A, Paparella G, Belvisi D, Conte A, Bhatia KP, Rothwell JC, Berardelli A. Motor Cortical Network Excitability in Parkinson's Disease. Mov Disord. 2022 Apr;37(4):734-744. doi: 10.1002/mds.28914. Epub 2022 Jan 9. PMID: 35001420.

**P132**

## Novel insights into the origin of subthalamic beta oscillations in Parkinson's disease

*Tommaso Bocci*[1,2], V. Levi[3], T. Albizzati[1], S. Rinaldo[3], R. Eleopra[3], M. Prenassi[4], S. Marceglia[4], A. Priori[1,2]

[1]Department of Health Sciences, University of Milan, Milan, Italy
[2]III Neurology Clinic, ASST-Santi Paolo e Carlo University Hospital, Milan, Italy
[3]Neurosurgery Department, Functional Neurosurgery Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[4]Department of Engineering and Architecture, University of Trieste, Trieste, Italy

*Introduction:* Neuronal subthalamic (STN) activity in Parkinson's disease (PD) is thought to be characterized by an excessive rhythm in beta-band frequency range (12-35 Hz), which is normalized by levodopa [1-2]. The aim of our study was to explore the origin of beta oscillations, by assessing possible changes of subthalamic LFPs in different moments during Deep Brain Stimulation (DBS) surgery [2]. That is of key importance because the beta rhythm is now considered the most reliable electrophysiological marker for guiding novel adaptive DBS approaches.

*Objective:* We started from two alternative hypotheses, that the LFPs of the STN play a central role in the "feed-forward" organization of movements or that β-band oscillations represent a mere epiphenomenon due to gamma-motoneuronal over-activity reflecting the patient's status.

*Methods:* STN signals were recorded in four patients (2 men, 2 women) in three different moments during DBS implantation: before sedation (T0), under the effect of both Propofol (2-3 microg/ml) and rocuronium (30 mg) (T1) and during Propofol alone (2-3 microg/ml) (T2). LFPs were analyzed in terms of both linear and non-linear analyses: power spectral density, sample entropy and multiscale entropy, as well as burst analysis.

*Results:* High values of Sample entropy have been observed at the level of the left posterior region in T2 (0.7045) compared to T1 (0.6375); even more effective was the burst analysis which shows significant increase in terms of mean amplitude ($p = 0.017$) on the same.

*Conclusions:* Whether there is an involvement of the peripheral system, or gamma-motoneurons, in the modulation of the hyper-synchronized β power is still a matter of debate, our work could highlight novel insights into the origin of the beta rhythm, possibly suggesting that these oscillations arise away from the basal ganglia network.

**References:**

[1] Bocci T, Prenassi M, Arlotti M, Cogiamanian FM, Borellini L, Moro E, Lozano AM, Volkmann J, Barbieri S, Priori A, Marceglia S (2021). Eight-hours conventional versus adaptive deep brain stimulation of the subthalamic nucleus in Parkinson's disease. NPJ Parkinsons Dis. 7(1):88.
[2] Averna A, Marceglia S, Arlotti M, Locatelli M, Rampini P, Priori A, Bocci T (2022). Influence of inter-electrode distance on subthalamic nucleus local field potential recordings in Parkinson's disease. Clin Neurophysiol. 133:29-38.

**P133**

## Data-driven clustering of neurodegenerative diseases based on EEG spectrum power-law decay: the DaCNES Study

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

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

*Background:* Neurodegenerative diseases are common causes of impaired mobility and cognition in the elderly. Among them, tauopathies (including Alzheimer's Disease, Progressive Supranuclear Palsy and Corticobasal Degeneration) and α-synucleinopathies (including Parkinson's Disease and Multiple System Atrophy) were considered. The neurodegenerative processes and relative differential diagnosis were addressed through a qEEG non-linear analytic method.

*Objectives:* To test accuracy of the power law exponent β applied to EEG in differentiating neurodegenerative diseases and to explore differences in neuronal connectivity among different neurodegenerative processes based on β.

*Methods:* N = 230 patients with a diagnosis of tauopathy or α-synucleinopathy and at least one artifact-free EEG recording were selected. Welch's periodogram was applied to signal epochs randomly chosen from continuous EEG recordings. Power law exponent β was computed as minus the slope of the power spectrum versus frequency in a Log-Log scale. A data-driven clustering based on β values was performed to identify independent subgroups.

*Results:* In bilateral frontal-temporal regions, β index values were significantly higher for Parkinson's Disease with respect to the atypical parkinsonisms; in parietal areas, differences remained significant only for Progressive Supranuclear Palsy and Corticobasal Degeneration. Data-driven clustering based on β differentiated tauopathies (overall lower β values) from α-synucleinopathies (higher β values) with high sensitivity and specificity. Tauopathies also presented lower values in the correlation coefficients matrix among frontal sites of recording.

*Conclusions:* Statistically significant differences in β index values were found between tauopathies and α-synucleinopathies. Hence, β index is proposed as a possible biomarker of differential diagnosis and neuronal connectivity.

**P134**

## Inhibitory cortical control in healthy subjects: modulation of beta and gamma oscillations in frontal cortical areas

*Marco Falletti*[1], I.B. Marc[2,3], V. D'Onofrio[4], F. Asci[1], S. Ferraina[2], A. Suppa[1,5]

[1]Department of Human Neurosciences, Sapienza University, Rome, Italy
[2]Department of Physiology and Pharmacology, Sapienza University, Rome, Italy
[3]Behavioral Neuroscience PhD Program, Sapienza University, Rome, Italy
[4]Padova Neuroscience Center, University of Padua, Padua, Italy
[5]IRCCS Neuromed Institute, Pozzilli (IS), Italy

*Introduction:* The inhibition of an ongoing response is a key component of executive control implying the voluntary suppression of inappropriate behaviours [1]. Physiological mechanisms underlying this response are based on an integrated cortical network, including the inferior frontal gyrus (IFG) and the dorsal premotor cortex (PMd) [2]. Inhibition of unwilling actions can be experimentally probed through a standardised paradigm, the Stop Signal Task (SST) [3-4], that requires subjects to start a movement as quickly as possible when a Go Signal is presented and to refrain from it if suddenly a Stop Signal appears during the reaction time (RT). This protocol allows for the assessment of the inhibitory ongoing response, reflected by the Stop Signal Reaction Times (SSRT). Recently, it has been demonstrated in healthy subjects (HS) that the activation of these cortical areas during specific behaviours is reflected by modulations of beta-/gamma- oscillations [5]. These oscillations can be experimentally and noninvasively modulated by transcranial alternating current stimulation (tACS) protocols.

*Objective:* The aim of this study is to explore the role of cortical beta-/gamma- oscillations in the physiology of inhibitory human behaviours through SST protocol performed during specific tACS paradigms, in HS.

*Methods:* Six HS performed the SST during three different tACS protocols (β-, γ- and sham-tACS) randomly delivered over the IFG and PMd, bilaterally, over two different days. The coordinates of right and left IFG and PMd were first assessed through neuronavigation. During the SST paradigm we quantified RT and SSRT.

*Results:* Preliminary results suggest that beta- and gamma- tACS differently modulate action inhibition in HS. A two-way repeated measures Anova revealed a significant interaction among the factors Area (IFG; PMd) and tACS(β; γ). Post-hoc comparisons pointed out a significant difference in γ-tACS modulation among the two areas ($p=.03$); gamma-tACS applied over the IFG decreased RTs, while the stimulation of the PMd increased RTs. Furthermore, gamma-tACS increased SSRTs when applied over both IFG and PMd.

*Conclusion:* We demonstrated that beta- and gamma- tACS can modulate cortical oscillations underlying physiological mechanisms of inhibitory control behaviours, in frontal cortical areas, in HS. These preliminary results provide the background for future applications in neurological disorders characterised by deficit of inhibitory control, such as Parkinson's Disease.

**References:**

[1] Jahanshahi et al., 2015a.Mov Disord;30:128–40.
[2] Pani P, et al., 2021.Cortex. 2022 Jul; 152:160-163.
[3] Vince M.A.,1948. Br J Psychol;38,149-157.
[4] Logan & Cowan,1984. Psychol Rev;295-327.
[5] Jahanshasahi et al., 2015b.Nat Rev Neurosci; 16:719–32.

**P135**

## Side-dependent subthalamic local field potential (LFPs) dynamics in Parkinson's disease

*Tommaso Bocci*[1,2], T. Albizzati[1], R. Ferrara[1], M. Prenassi[3], S. Marceglia[3], A. Priori[1,2]

[1]Department of Health Sciences, University of Milan, Milan, Italy
[2]III Neurology Clinic, ASST-Santi Paolo e Carlo University Hospital, Milan, Italy
[3]Department of Engineering and Architecture, University of Trieste, Trieste, Italy

*Introduction:* The role of dopaminergic neurons' brain asymmetries in Parkinson's disease (PD) motor symptoms is still undefined. LFP recordings from the subthalamic nucleus (STN) revealed some neurophysiological biomarkers of the disease: increased beta activity, increased low frequency activity, high frequency oscillations. Few data about STN-LFP asymmetry are available. Phase-amplitude coupling (PAC) coordinates the timing of neuronal activity and allows to determine the mechanism for communication within distinct regions of the brain.

*Methods:* We report the use of PAC to assess the differences between the two in 21 patients with PD before and after L-DOPA administration.

*Results:* We found a significant beta PAC disparity between the left and right hemisphere; whereas the left STN shows a higher phase-amplitude coupling within low-beta range in OFF condition as compared to the opposite side (Kruskal-Wallis test: $p < 0.001$), the right STN shows a significant coupling between high-frequencies (260-360 Hz) and low-beta in OFF condition as compared to the left one (Kruskal-Wallis test: $p = 0.006$). Interestingly, these findings are independent both from disease phenotype and side onset.

*Discussion:* These findings have important implications for the origin of neural signals and may provide an exhaustive insight into STN dynamics, possibly suggesting the use of novel adaptive DBS approaches (e.g. aDBS) to only one STN.

## P136

### Neurophysiological markers of motor reserve in Parkinson's disease

*Massimiliano Passaretti*[1], S. Rinaldo[2], E. Orunesu[3], D. Rossi Sebastiano[4], G. Devigili[2], G. Barbiera[2], A. Braccia[2], G. Paparella[1], M. De Riggi[1], P. Lanteri[4], A. Berardelli[1], S. Antonio[5], M. Bologna[1], R. Eleopra[2], R. Cilia[2]

[1]Sapienza University of Rome, Department of Human Neuroscience, Rome, Italy
[2]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy
[3]Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Nuclear Medicine Unit, Milan, Italy
[4]Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Neurophysiology, Milan, Italy
[5]University of Toronto, Krembil Brain Institute, UHN & Brain Health Imaging Centre, Campbell Family Mental Health Research,Institute, CAMH, Toronto, Canada

*Introduction:* Motor reserve (MR) is defined as the resilience mechanisms of the brain coping with neurodegeneration in idiopathic Parkinson's disease (PD) [1]. No investigation of MR focused on lateralized PD with bilateral binding reduction at dopamine transporter (DAT) imaging.

*Methods:* In this cross-sectional case-control study, we included 16 PD patients and 28 healthy control. Patients were included if their motor signs were unilateral (Hoehn and Yahr stage =1/5, two independent raters) but DAT density ([123I]-Ioflupane-SPECT, DATQUANTTM) was significantly reduced in bilateral putamina (Putamen z-score>0.5). Subjects were extensively investigated using the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS; part-III was videorecorded), Hoehn & Yahr (H&Y) stage.Transcranial magnetic stimulation (TMS) was performed on primary motor cortices (M1) in presymptomatic (PH) and symptomatic hemispheres (SH) for patients and on dominant hemisphere for HC. TMS measured cortical excitability, plasticity and interhemispheric-inhibition (IHI).

*Results:* TMS testing revealed asymmetries in corticospinal excitability with higher values in the PH. SH demonstrated lower M1-plasticity (compared to the asymptomatic hemisphere). Finally, we found reduced IHI from PH to SH. Interestingly, reduced putamen binding was predicted by reduced ICF in SH and by higher plasticity and reduced IHI in PH. Reduced putamen binding was predicted by enhanced plasticity and reduced IHI in PH, and by reduced ICF in SH. Putamen/caudate ratio was directly associated with corticospinal excitability in PH and inversely associated with cortical plasticity in symptomatic hemisphere. MRC distinguished PH from SH (AUC 0.9844). It was associated in SH with PAS increment, IHI and corticospinal excitability reduction.

*Conclusions:* Response to PD neurodegeneration involves a M1-putamen network, and cortico-M1 connections, responsible for excitability and plasticity changes, depending on caudate activity and becoming more effective with binding reduction in putamen. Further insight on PD MR networks is relevant for novel neuromodulation approaches, aimed at reducing motor burden in daily life.

**References:**

[1] Hoenig, M.C., Dzialas, V., Drzezga, A., van Eimeren, T., 2022. The Concept of Motor Reserve in Parkinson's Disease: New Wine in Old Bottles? Mov. Disord. Off. J. Mov. Disord. Soc. https://doi.org/10.1002/mds.29266.

**P137**

## GABAergic and glutamatergic alterations in prodromal and early Parkinson's disease

*Andrea Rizzardi*[1], A. Benussi[1], A. Pilotto[1], C. Tirloni[1], V. Cantoni[2], C. Zatti[1], B. Borroni[1], A. Padovani[1]

[1] Department of Clinical and Experimental Sciences, Neurology Unit, University of Brescia, Brescia, Italy
[2] Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

*Introduction:* Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique able to detect the impairment of specific neurotransmitter circuits in vivo. The aim of this study was to detect alterations within GABAergic and glutamatergic circuitries in Parkinson's disease (PD) patients, including *de novo* PD (naïve), and prodromal Parkinson's disease, namely rapid eye movement (REM) sleep behaviour disorder (RBD) patients.

*Methods:* The study enrolled consecutive patients with PD, polysomnography-confirmed RBD and age-matched healthy controls. Each subject underwent an extensive motor and cognitive assessment and a TMS paired-pulse protocol evaluating GABA A ergic circuits (short interval intracortical inhibition, SICI), and glutamatergic circuits (intracortical facilitation, ICF).

*Results:* Seventy-seven subjects entered the study, namely 46 PD patients (including 24 drug-naïve and 22 under dopaminergic treatment), 13 RBD and 18 age-matched healthy controls (HC). Compared to HC, SICI and ICF resulted significantly impaired in PD (both drug-naïve and under dopaminergic treatment). All RBD subjects exhibited impaired SICI, whereas ICF was reduced in 6 and increased in 7 subjects.

*Conclusions:* GABAergic and glutamatergic alterations are a prominent feature of PD from prodromal stages. The differences observed in ICF patterns in subset of RBD might indicate divergent risk of conversion to PD or dementia with Lewy bodies (DLB). Further longitudinal studies are thus warranted to extend these findings.

**P138**

## Clinical effects of sensorimotor anodal transcranial direct current stimulation in patients with early-onset Parkinson's disease: a pilot study

*Clara Simonetta*[1], J. Bissacco[1], M. Conti[1], C. Salimei[2], V. Ferrari[1], M. Pierantozzi[1], A. Stefani[1], N.B. Mercuri[1], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]Department of Clinical Sciences and Translational Medicine, University of Rome Tor Vergata, Rome, Italy

*Introduction:* Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation increasingly used for therapeutic modulation of central nervous system excitability in various neurological diseases [1], including Parkinson's disease (PD) [2]. Early-onset PD (EOPD) is a PD subtype with severe impact on patients' quality of life. tDCS has never been specifically applied to EOPD patients, although it could represent a valid integrative therapeutic option.

*Objective:* To evaluate the clinical effects of an anodal tDCS treatment in a group of EOPD patients.

*Methods:* We recruited 12 idiopathic EOPD patients. tDCS was administered with the anode placed over the left sensorimotor area and the cathode over the contralateral supraorbital ridge. The protocol included 10 sessions of stimulation (2mA intensity) of 20 minutes each, over two weeks. Participants were assessed at baseline and at the end of the protocol with MDS-UPDRS part III, Non-motor symptoms scale (NMSS), PD-cognitive rating scale (PD-CRS), and PD Quality of Life Questionnaire-39 (PDQ-39). Paired T-test was used to compare changes in clinical scores.

*Results:* Significant changes occurred in NMSS score (M 32,36±29,07 vs 17,45±20,92, p=0.001) and PD-CRS (M 100,82±13,95 vs 106,55±13,97, p=0. 040). Total MDS-UPDRSIII score did not change; conversely the rigidity items score significantly reduced (M 0,67±0,78 vs 0,42±0,70, p=0.05). PDQ-39 score was unmodified. No relevant side effects were recorded. The treatment was well tolerated by all participants.

*Conclusions:* This pilot study showed that a 10 session-long protocol of anodal sensorimotor tDCS might exert beneficial clinical effects in EOPD patients. Most relevant improvements occurred in non-motor symptoms and cognitive performances, consistently with a direct effect of the stimulation on cortical cognitive network. Motor disturbances did not significantly change, albeit some amelioration was notice for rigidity. Further confirmation in larger samples, with sham-controlled subjects, is now needed. However, tDCS emerges as a safe, well-tolerated, promising therapeutic option for EOPD.

**References:**

[1] Woods AJ, Antal A, Bikson M, et al. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clin Neurophysiol. 2016;127(2):1031-1048. doi:10.1016/j.clinph.2015.11.012.
[2] Brak IV, Filimonova E, Zakhariya O, Khasanov R, Stepanyan I. Transcranial Current Stimulation as a Tool of Neuromodulation of Cognitive Functions in Parkinson's Disease. Front Neurosci. 2022;16:781488. Published 2022 Jul 12. doi:10.3389/fnins.2022.781488.

**P139**

## Phase Locking Value as a tool to evaluate brain connectivity in Parkinson's disease

*Pasquale Maria Pecoraro*[1,2], L. Ricci[1,2], M. L. Caminiti[1,2], S. P. Carbone[1,2], V. Di Lazzaro[1,2], L. di Biase[1,2,3]

[1]Research Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine and Surgery, University Campus Bio-Medico of Rome, Rome, Italy
[2]Operative Research Unit of Neurology, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy
[3]Brain Innovations Lab, University Campus Bio-Medico of Rome, Rome, Italy

*Introduction:* Among neurophysiological techniques electroencephalogram (EEG) is one of the most versatile and wide available technique, these features combined with its good balance between temporal and spatial resolution, lead this technology to be explored in several studies for PD biomarkers research. Phase Locking Value (PLV) is a non-linear measure of pairwise functional connectivity used to quantify the phase coupling between two EEG signals.

*Objective:* The present study explores the discrimination ability of PLV, in differentiating Parkins's disease (PD) patients from Healthy Controls (HC), during rest and a motor task of lower limbs.

*Methods:* High-density EEG data from 26 PD patients and 13 HC were analyzed. EEG signals were recorded both during a motor task of lower limbs and at rest. PLV was calculated for each group during the two conditions for the following frequency bands: 2-4 Hz (delta); 5-7 Hz (theta); 8-12 Hz (alpha); 13-29 Hz (beta); 30-60 Hz (gamma). The diagnostic performance of PLV for the binomial discrimination of PD vs HC discrimination was evaluated for both conditions.

*Results:* During the resting state no significant differences in PLV connectivity between the two groups was showed. Conversely, during the motor task in HC compared to PD patients results showed a higher PLV connectivity in delta band. Furthermore, diagnostic performance analysis, showed a sensitivity of 100%, a negative predictive value (NPV) of 100% and an area under the ROC (AUC) of 0.75.

*Conclusions:* HC demonstrated higher ability in modulating neuronal synchronization in delta band during motor tasks respect to PD patients, highlighting the influence of movement on connectivity. This neurophysiology analysis could be explored as a potential screening biomarker for PD patients in future studies.

**P140**

## The role of the descending 'diffuse noxious inhibitory control' (DNIC) in patients with Restless Legs Syndrome: a study with laser evoked potentials (LEPs)

*Angela Sandri*[1], E. Antelmi[1], G.M. Squintani[2], M. Lippolis[2], S.M. Cartella[1], M. Tinazzi[1]

[1]Neurology Unit, Parkinson Disease and Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]UOC Neurologia A, Department of Neurosciences, AOUI, Verona, Italy

*Introduction:* Restless legs syndrome (RLS) is a complex sensorimotor disorder occurring with a typical circadian fashion [1]. Symptoms worsen towards evening and at rest, and they are temporarily relieved by movement [2]. Symptoms are perceived as painful in up to 45% of cases [3], and nociception seems involved also given the opioids' efficacy and the physiologic dopamine-pain control link [4].

*Objective:* To assess the descending diffuse noxious inhibitory control (DNIC) in RLS patients.

*Methods:* 22 RLS patients (mean age: 58±16 years; 11 females) and 20 matched controls (mean age: 55±11 years; 12 females) underwent a conditioned pain modulation protocol. Cutaneous heat stimuli were delivered via Laser evoked potentials (LEPs) on the dorsum of the right hand (UL) and foot (LL). N2/P2 amplitude and pain ratings (NRS) were recorded before (baseline), during (DNIC), and after (post) the application of a heterotopic noxious conditioning stimulation, where subjects submerged their left foot into an ice water bath (0°C).

*Results:* Non-parametric analyses in both RLS patients and controls show a physiological (N2/P2 amplitude) and subjective (NRS) reduction during the DNIC condition in both UL and LL in comparison to baseline and post conditions (all, $p<0.002$). For the N2/P2 amplitude, the post conditions were significantly lower in both groups with respect to the baselines (all, $p <0.002$), but not for NRS ratings. Between groups comparisons revealed a significant difference at the N2/P2 amplitude during the DNIC condition only for the LL ($p=0.011$), with RLS patients having a lower amplitude reduction than controls.

*Conclusions:* The lower physiological reduction during the DNIC condition at LL in RLS patients suggest a defect in the endogenous inhibitory pain system. Further studies should clarify the causal link with these findings also investigating the circadian modulation of this paradigm.

**References:**

[1] Manconi et al., 2021. Nat Rev Dis Primers; 7:80.
[2] Allen et al., 2014. Sleep Med; 15:860-873.
[3] Bassetti et al., 2001. Eur Neurology; 45:67–74.
[4] Millan, 2002. Progress Neurobio; 66:355–474.

**P141**

## A tremor in the family

*Tommaso Carrer*, G. Bonato, M. Carecchio

Parkinson and Movement Disorders Unit, Department of Neuroscience, University of Padua, Padua Italy

*Introduction:* We describe the case of a 66 year-old woman with onset at age 54 of head and upper limb tremor, worsened by stressful events, not invalidating but slightly progressive over time. Through the years she also developed a subjective sensation of dizziness and disequilibrium. The neurological examination showed a normal based gait with reduced arm swing and some difficulties in tandem gait; positive pull test and Romberg test with marked retropulsion; head tremor with cervical dystonia and mild vocal tremor; at the upper limbs mild rest and postural tremor, worsened by specific positions, not responsive to propranolole and levodopa. DAT-SPECT demonstrated no significant uptake reduction of the radiotracer, whereas a brain MRI showed a mild cerebellar atrophy. The patient has two children affected by X-fragile syndrome and she reported to have a sibling and an aunt with tremor and extrapyramidal symptoms. She is carrier of a premutation of the gene FMR1 (104 CGG repeats) with unbalanced inactivation and functional exclusion by methylation of the normal FMR1 allele. She was diagnosed with FXTAS (Fragile X–Associated Tremor/Ataxia Syndrome). Her medical history was relevant for depression and premature ovarian insufficiency, both linked to FMR1 premutation.

**P142**

## Not every tremor is essential: a challenging case of young-onset tremor

*Alessandro Magliozzi*[1,3], A. De Luca[2], V. Di Lazzaro[1,3], M. Marano[1,3]

[1]Department of Neurology, Università Campus Bio-Medico di Roma, Roma, Italy
[2]Medical Genetics Division, IRCCS Fondazione Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy
[3]Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy

*Case description:* A 29-year-old girl presented to our clinic with a long-standing diagnosis of essential tremor. However, her history was a 6-year progressive ataxia, appendicular tremor, and neck stiffness. No other relevant history was reported, and no family history of neurological disorders was described by the proband parents. At the neurological examination she was able to walk unaided, at the tandem walk test, despite the presence of a slight unsteadiness. A mild to moderate postural and kinetic dystonic tremor hampered most of the clinical tests, interrupted by frequent myoclonic jerks. Despite she complained of anterior neck stiffness, no clear dystonic features were detected. Her brain magnetic resonance showed only a mild atrophy of the right hippocampus and an enlarged metabolic screening for tremor syndromes (blood cell count with red cell smear analysis, electrolytes, liver and renal function markers, ammonia, thyroid hormones) was unremarkable. In the clinical suspicion of myoclonus-dystonia, an extensive panel of genes for dystonia was performed. Next generation sequencing analysis of a panel of genes test revealed a heterozygous c.592G>A missense variant [p. (Glu198)Lys] of the TUBB4A gene of the proband and of her 64 years old healthy mother and 20 years old sister. Levodopa, benzodiazepines, anticholinergic medications were administered without seeing any major clinical benefit. Low dose clonazepam showed a mild response. The patient was evaluated on regular basis for a two-year period and no substantial changes in clinical picture were observed.

*Discussion:* TUBB4A mutations can be causative of a variety of neurological disorders, embracing a wide scale of clinical phenotypes such as the hypomyelinating leukodystrophy with basal ganglia and cerebellum atrophy or disabling dystonia syndromes. Missense mutation or deletion of TUBB4A gene segregates mainly with a full autosomal dominant pattern, even if reduced penetrance is described. [1-2] Our case suggests that TUBB4A mutations can express with reduced penetrance and manifest with milder phenotype.

**References:**

[1] Erro, R., Hersheson, J., Ganos, C., Mencacci, N. E., Stamelou, M., Batla, A., Thust, S. C., Bras, J. M., Guerreiro, R. J., Hardy, J., Quinn, N. P., Houlden, H., & Bhatia, K. P. (2015). H-ABC syndrome and DYT4: Variable expressivity or pleiotropy of TUBB4 mutations? Movement disorders: official journal of the Movement Disorder Society, 30(6), 828–833. https://doi.org/10.1002/mds.26129.

[2] Ferreira, C., Poretti, A., Cohen, J., Hamosh, A., & Naidu, S. (2014). Novel TUBB4A mutations and expansion of the neuroimaging phenotype of hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC). American journal of medical genetics. Part A, 164A (7), 1802–1807. https://doi.org/10.1002/ajmg.a.36526.

**P143**

## Distal upper limb tremor during walking in Parkinson's disease

*Carolina Cutrona*[1], M. Costanzo[1], G. Leodori[1,2], M.I. De Bartolo[1], A. Fabbrini[2], G. Vivacqua[3,4], A. Conte[1,2], G. Fabbrini[1,2], A. Berardelli[1,2], D. Belvisi[1,2]

[1]IRCCS Neuromed, Pozzilli, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]Department of Experimental Morphology and Microscopy - Integrated Research Center (PRAAB) - Campus Biomedico University of Rome, Rome, Italy
[4]Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Sapienza University of Rome, Rome, Italy

*Introduction:* Distal upper limb tremor during walking (TW) is frequently observed in Parkinson's disease (PD). To date, it is unknown whether TW reflects rest tremor facilitated by walking or is a different form of tremor [1-2].

*Objective:* To characterize the occurrence and the clinical features of TW compared to other PD tremors (i.e., rest, re-emergent, and postural tremor).

*Methods:* Fifty-one PD patients with rest tremor were evaluated off- and on-treatment. Patients underwent a clinical examination and were videorecorded for tremor assessment during rest, posture holding, and walking. Tremor occurrence, body distribution, severity and latency of tremor onset were assessed with and without dopaminergic treatment.

*Results:* In PD patients with rest tremor, we observed that TW was present in 79% of cases. TW body distribution and severity were similar to those of rest and re-emergent tremor, but different from postural tremor. TW was present on the most bradykinetic and rigid side. TW latency, observed in 85% of patients, was on average 5.8 sec. Dopaminergic treatment induced a significant improvement of TW, rest and re-emergent tremor severity, but left TW latency unaffected.

*Conclusions:* TW is a clinical variant of rest tremor occurring during automatic movements. The association with bradykinesia and rigidity distribution suggests that TW may be due to abnormal "stability" resulting from a reduced symmetry in arm swing amplitude [3-4].

**References:**

[1] Rajput, A. H., Rozdilsky, B. & Ang, L. Occurrence of resting tremor in Parkinson's disease. Neurology 41, 1298–1298 (1991).
[2] Uchida, K. et al. Tremor is attenuated during walking in essential tremor with resting tremor but not parkinsonian tremor. Journal of Clinical Neuroscience 18, 1224–1228 (2011).
[3] Belvisi, D. et al. Re-emergent tremor in Parkinson's disease: the effect of dopaminergic treatment. Eur J Neurol 25, 799–804 (2018).
[4] Dirkx, M. F., Zach, H., Bloem, B. R., Hallett, M. & Helmich, R. C. The nature of postural tremor in Parkinson disease. Neurology 90, e1095–e1103 (2018).

**P144**

## Retinal structural and vascular changes as biomarker in Parkinson's disease

*Sandra Perillo*[1], L.G. Di Maio[1], G. Cennamo[1,2], D. Montorio[1], G. De Michele[1], N. Cuomo[1], C. V. Russo[1], L. Baratto[1], A. Giglio[1], A. Filla[1], V. Bresciamorra[1], G. De Michele[1], C. Costagliola[1], A. De Rosa[1]

[1]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2]Public Health Department, University of Naples Federico II, Naples, Italy

*Introduction:* Parkinson's disease (PD) is a common neurodegenerative disorder characterized by bradykinesia, resting tremor, and muscle rigidity. Visual disturbances have been described among non-motor features.

*Objective:* We aimed to investigate the structural and vascular changes in retinal and choroidal vascular networks, and to evaluate any relationship with motor and non-motor symptoms (NMS) in patients affected with PD.

*Methods:* A total of 48 eyes from 24 PD patients and 50 eyes from 25 controls (Ctrl) were assessed. Ganglion cell complex (GCC), retinal nerve fiber layer (RNFL) and subfoveal choroidal thickness (SFCT) were examined using Spectral Domain-Optical Coherence Tomography (SD-OCT). The vessel density (VD) of retinal and choriocapillary (CC) vascular networks in macular area and the foveal avascular zone (FAZ) area were evaluated by OCT Angiography (OCTA). All patients underwent clinical evaluation using motor section of Unified PD Rating Scale (UPDRS-III) and Hoehn and Yahr (HY) scale.

*Results:* At SD-OCT, GCC and RNFL were significantly thinner in patients compared to Ctrl. At OCTA exam, PD subjects showed lower values in VD of superficial capillary plexus (SCP) and radial peripapillary capillary plexus in comparison to Ctrl, whereas FAZ area resulted significantly increased in patients. We found a negative correlation between the age at onset and VD of SCP, and between HY score and RNLF thickness and FAZ area. UPDRS-III score was negatively correlated with VD of deep capillary plexus (DCP). Interestingly, we observed a negative relationship between SCOPA-AUT questionnaire score and VD of DCP, between Hamilton-Anxiety score and RNFL thickness, and between Epworth Sleepiness Scale score and FAZ area. Parkinson Fatigue Scale-16 score was negatively related to VD of SCP and DCP, and RNFL thickness.

*Conclusions:* The impairment of retinal structure and microvascularization suggests the role of the SD-OCT and OCTA measurements as potential valid biomarkers for disease severity and progression in PD.

**P145**

## Dystonia in untreated Early Onset Parkinson's disease

*Roberta Bovenzi*[1], M. Conti[1], C. Simonetta[1], P. Grillo[1], R. Cerroni[1], M. Pierantozzi[1], A. Stefani[1,3], N.B. Mercuri[1,2], T. Schirinzi[1]

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

*Introduction:* Dystonia may represent the initial sign in Parkinson's disease (PD), especially in patients with age at onset (AAO) lower than 50 years (early-onset PD, EOPD) [1,2]. Pathophysiological mechanisms underlying such peculiar PD presentation are still unknown; likewise, it is unclear if dystonia at onset might identify a distinct clinical PD subtype.

*Objective:* To outline main clinical and genetic features of *de novo* EOPD patients presenting with dystonia by a single-center retrospective longitudinal cohort study.

*Methods:* Clinical charts of 170 *de novo* (newly diagnosed and untreated) EOPD patients prospectively followed-up were screened, selecting patients presenting with dystonia (EOPDdyst). Demographics, genetics, motor and non-motor features, therapies, complications, rate of change in Hoehn and Yahr score and levodopa equivalent daily dose (LEDD) were analysed in EOPDdyst cohort in comparison to EOPD *de novo* patients without dystonia.

*Results:* Dystonia had a prevalence of 14.1%. EOPDdyst patients had lower AAO than the non-dystonic (41.5 ± 6.1 vs 44.2 ± 5.2, p=0.03). Pathogenic genetic variants were more frequent in EOPDdyst (29.2% vs 9.6%, p=0.001), mostly in autosomal recessive genes (57.1%). PRKN variants were the most common in the EOPDdyst group (42.9%), GBAvariants in the non-dystonic group (50%). EOPDdyst patients had symmetrical motor presentation (16.7% vs 2.7%, p=0.004) and suffered with earlier levodopa induced dyskinesias (LIDs) (1.00 ± 0.91 years vs 2.79 ± 2.55 years, p=0.049). Adjusting the analysis for the genetic origin, the two groups did not show significant differences in any item.

*Conclusions:* Main clinical milestones seem to not differ in EOPDdyst patients. However, dystonia in EOPD mostly imply a genetic origin, especially of recessive forms, which accounts for earlier onset and probably a wider motor network impairment.

**References:**

[1] A.S. Shetty, K.P. Bhatia, A.E. Lang, Dystonia and Parkinson's disease: What is therelationship?, Neurobiol Dis. (2019). https://doi.org/10.1016/j.nbd.2019.05.001.
[2] R. Mehanna, Age Cutoff for Early-Onset Parkinson's Disease: Recommendations from the International Parkinson and Movement Disorder Society Task Force on Early Onset Parkinson's Disease, Movement Disorders Clinical Practice. (2022). https://doi.org/10.1002/mdc3.13523.

## P146

### Impact of fatigue on the caregiver's burden in Parkinson's disease

*Gabriele Di Francesco*[1,2], C. Defilippi[1], L.M. Broscautanu[1], C. Ledda[1,2], M. Tangari[1,2], A. Covolo[1,2], C.A. Artusi[1,2], E. Montanaro[1,2], M. Zibetti[1,2], M.G. Rizzone[1,2], M. Bozzali[1,2,3], L. Lopiano[1,2], A. Romagnolo[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy
[3]Department of Neuroscience, Brighton & Sussex Medical School, University of Sussex, Brighton, UK

*Introduction:* Fatigue, defined as a decreased level of energy and/or an exaggerated perception of effort during specific activities, is a frequent non-motor symptom of Parkinson's disease (PD) [1]. It is a key determinant of patient's disability, with detrimental effect on quality of life [2]. However, the impact of fatigue on caregiver's burden has not been evaluated so far.

*Objective:* To assess the impact of fatigue on caregiver's burden on a cohort of PD patients

*Methods:* We evaluated consecutive PD patients and their primary informal caregivers. Patients' fatigue was evaluated with validated scales for PD [3-4], with consistent cut-offs for defining the presence of significant fatigue, the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (mFIS). The Zarit Burden Interview (ZBI) [5] was used to define the caregiver's burden. Analysis of covariance was used to evaluate differences in the ZBI score between caregivers of patients with and without fatigue, correcting for potential confounders: patients' and caregivers' age, disease duration, motor disability (MDS-UPDRS-III score). Correlations between ZBI, FSS, and mFIS scores were calculated by means of linear regression analysis, corrected for the same confounders.

*Results:* We enrolled 53 patients (males: 66.0%; age: 70.53±8.36 years; disease duration: 11.11±7.44 years) and their caregivers. More than 70% of patients reported significant fatigue. After correcting for potential confounders, caregivers of patients with fatigue reported 2-fold higher ZBI scores, both using FSS ($p=0.013$) and mFIS ($p=0.002$) to define significant fatigue. ZBI showed significant correlation with fatigue, in particular with total mFIS (Beta=0.712; $p<0.001$) and mFIS subdomains (Physical: Beta=0.568, Cognitive: Beta=0.645, Psychosocial: Beta=0.408; $p<0.001$).

*Conclusion:* Fatigue is a frequent yet overlooked symptom of PD. Our study demonstrated that fatigue, along with its detrimental effect on patient's quality of life, is an independent determinant of caregiver's distress. Exhaustive diagnostic and therapeutic approaches are needed to ameliorate both patients' and caregivers' well-being.

**References:**

[1] Siciliano M, Trojano L, Santangelo G, De Micco R, Tedeschi G, Tessitore A. Fatigue in Parkinson's disease: A systematic review and meta-analysis. Mov Disord. 2018 Nov;33(11):1712-1723.
[2] Havlikova E, Rosenberger J, Nagyova I, Middel B, Dubayova T, Gdovinova Z, van Dijk JP, Groothoff JW. Impact of fatigue on quality of life in patients with Parkinson's disease. Eur J Neurol. 2008 May;15(5):475-80.
[3] Friedman JH, Alves G, Hagell P, Marinus J, Marsh L, Martinez-Martin P, Goetz CG, Poewe W, Rascol O, Sampaio C, Stebbins G, Schrag A. Fatigue rating scales critique and recommendations by the Movement Disorders Society task force on rating scales for Parkinson's disease. Mov Disord. 2010 May 15;25(7):805-22.
[4] Schiehser DM, Ayers CR, Liu L, Lessig S, Song DS, Filoteo JV. Validation of the Modified Fatigue Impact Scale in Parkinson's disease. Parkinsonism Relat Disord. 2013 Mar;19(3):335-8.
[5] Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist. 1980 Dec;20(6):649-55.

**P147**

## Writing tremor in Parkinson's disease: frequency and associated clinical features

*Marcello Mario Mascia*[1], *G. Orofino*[1], *P. Cimino*[1], *G. Cadeddu*[1], *T. Ercoli*[1], *G. Defazio*[2]

[1]University Hospital of Cagliari, Cagliari, Italy
[2]Department of Transation Biomedicine and Neuroscience (DiBraiN), University of Bari "Aldo Moro", Bari, Italy

*Introduction and objectives:* Action tremor in Parkinson's disease may present in up to 46% of patients, either as postural or kinetic tremor. How action tremor may affect handwriting has been the object of some investigations; however clinical features of writing tremor in Parkinson's disease are still not well characterised.

*Methods:* One hundred consecutive patients with idiopathic Parkinson's disease were included in the study. Demographic and clinical data were collected through a standardized questionnaire. Patients were assessed for the presence of rest, action and writing tremor in on condition. The effect of a standardised sensory trick was also investigated in all patients with action tremor.

*Results:* Writing tremor was found in 10% of patients (26% of patients with postural/kinetic tremor, either alone or in combination with rest tremor). Severity of writing tremor did not correlated to that of the other tremor variants and to the other clinical variables. Writing tremor was task-specific in 4/10 patients, no task-specific in 6/10. Sensory trick was effective on writing tremor in two patients but did not improve action tremor in any of the study patients.

*Conclusions:* Results showed that writing tremor in Parkinson's disease is less common than other tremor variants, may be associated with other forms of action tremor, and may sometimes have dystonic features, including task-specificity and sensitivity to sensory trick.

**P148**

## A treatable parkinsonism: lesson learned from a case of NMDARE autoimmune encephalitis

*Alfonso Giordano*, N. Setola, V. Campana, R. De Micco, M. Cirillo, A. Tessitore

Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy

A 25-years-old man without any previous relevant medical history referred to our outpatient clinic for a few days progressive onset of slowness of movements and muscle rigidity. Three months before he was admitted to a psychiatry service for visual hallucinations, episodes of nonsensical speech and acute paranoia with aggressiveness complicated by a tonic-clonic seizure during the hospital stay. He received a diagnosis of psychosis and was treated with haloperidol (6 mg/die) and benzodiazepines. At the admission, neurological examination showed catatonic abnormal postures, hypomimia, generalized bradykinesia of upper and lower limbs (left more than right) and postural tremor of the left hand (video 1). Brain MRI was normal while EEG showed periodic lateralized epileptiform discharges in the right temporal region. In the contest of a new onset of psychosis, seizure, rapidly progressive parkinsonism, with normal brain MRI and EEG abnormalities a diagnosis of possible autoimmune limbic encephalitis was considered. Cerebrospinal fluid analysis revealed slight increases of protein level and IgG index, a normal cell count and antibodies against NR1/NR2 heteromers of NMDA-receptor. No systemic tumour was identified by combined CT scan with 18F-fluorodeoxyglucose PET. He was started on intravenous IgG and methylprednisolone that resulted in a complete and rapid improvement within four days of both parkinsonism and psychiatric symptoms (video 2). Early recognition of a rapidly immune-mediated parkinsonism caused, in our case, by either autoimmunity against the basal ganglia and intolerance to neuroleptics is crucial because of the potential for recovery of signs and symptoms after first line immunotherapy [1].

**References:**

[1] Balu R, McCracken L, Lancaster E, Graus F, Dalmau J, Titulaer MJ. A score that predicts 1-year functional status in patients with anti NMDA receptor encephalitis. Neurology. 2019.

**P149**

## Effects of dopaminergic medication on reactive and proactive inhibitory control

*Giovanni Mirabella*[1,2], E. Olivola[2], A. Rizzardi[1], V. Di Caprio[2], E. Ferrari[1], N. Modugno[2], A. Pilotto[1], A. Padovani[1]

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

*Objective:* In this study, we addressed the effects of dopaminergic treatment (DT) on the two domains of motor inhibition, i.e., reactive (the ability to react to a stop signal) and proactive inhibition (the ability to adapt the motor strategies according to the current context flexibly) according to the stage of Parkinson's disease (PD).

*Methods:* We recruited cognitively unimpaired PD patients under DT in the early (H&Y 1/1.5, n=20), intermediate (H&Y 2, n=20), and moderate/advanced (H&Y 2.5/3, n=20) stages and 30 age-matched healthy controls. Each participant underwent a standardized motor and cognitive assessment and stop-signal task (SST). Covariance analyses adjusted for the effect of age, sex, and UPDRS3 evaluated the differences between the performance in the SST (in terms of reactive and proactive inhibition) in DT ON and OFF and each stage of the disease as well as in comparison with controls.

*Results:* We found that reactive and proactive inhibition are progressively impaired along the disease. However, DT negatively affects reactive inhibition in the early and proactive inhibition in the intermediate PD stage. By contrast, DT does not impact motor inhibition in H&Y 2.5/3 patients. Relevantly, these effects are not only generated by the administration of dopamine agonists but also by L-Dopa.

*Conclusions:* In PD's early and intermediate stages, the DT negatively impacts reactive and proactive inhibition, respectively, despite improving motor symptoms. Such evidence supports the dopamine overdose hypothesis [1], which suggests that the administration of DT in the first stages of PD benefits dopamine-depleted dorsal striatal circuitries improving motor symptoms but overdose the more intact dopamine-dependent circuitries of the ventral striatum, impairing executive functions relying on it. Such findings suggest that the DT has to be titrated carefully to maximize patients' quality of life in the first stages of PD.

**References:**

[1] Vaillancourt et al (2013) Mov Disord. 28:1920-9.

**P150**

## Arm swing reduction in Parkinson disease: a study with a network of wearable sensors

*Martina Patera*[1], L. Pietrosanti[2], A. Zampogna[1], A. Calado[2], A. Pisani[3,4], F. Fattapposta[1], C.M. Verrelli[2], V. Rosati[5], F. Giannini[2], G. Saggio[2], A. Suppa[1-6]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy
[3]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[4]IRCCS Mondino Foundation, Pavia, Italy
[5]A.O.U. Policlinico Umberto I, Rome, Italy
[6]IRCCS Neuromed, Pozzilli, Italy

*Introduction:* Parkinson's disease (PD) commonly manifests with arm swing reduction during gait [1]. Previous kinematic studies using traditional gait analysis have shown decreased arm swing range, amplitude, and velocity in PD compared with controls. The pathophysiology of arm swing abnormalities in PD is still under debate since it would reflect bradykinesia or articular limitation due to rigidity [2-3]. We have recently reported more advanced measurements of reduced arm swing in PD, by using a wearable sensors network in an ecological experimental setting.

*Objective:* The first aim is to describe new objective arm-swing features extracted by a frequency-based analysis in patients performing the timed-up and go (TUG) test. A second aim is to correlate the extracted instrumental measures with specific UPDRS subitems for bradykinesia, rigidity, and tremor.

*Methods:* We recruited 44 PD patients in the early stage of the disease (H&Y<2) and never exposed to L-Dopa (drug-naïve) and 31 age-matched healthy controls. We performed a sensor-based analysis of arm swing during gait. The collected data were FFT transformed, and the frequency content was further analysed. The Spearman's test was used to correlate specific harmonic features with upper limb clinical scores.

*Results:* The kinematic analysis demonstrated that arm-swing reduction in PD can be objectively described in terms of decreased amplitude of all harmonics extracted from kinematic analysis of upper limb movements. Specific kinematic features highly correlated with rigidity and, in a lesser extent, with bradykinesia; there was no significant correlation with upper limb tremor.

*Conclusions:* The kinematic analysis based on our wearable sensors network demonstrated arm-swing reduction objectively during gait in PD patients performing a TUG test in an ecological setting. Our findings also suggest that reduced arm swing in PD would more likely reflect the severity of rigidity rather than bradykinesia.

**References:**

[1] V. Navarro-López et al., "Arm-swing kinematics in Parkinson's disease: A systematic review and meta-analysis," Gait Posture, vol. 98, pp. 85–95, Oct. 2022, doi: 10.1016/j.gaitpost.2022.08.017.
[2] K.-Y. Kwon, M. Kim, S.-M. Lee, S. H. Kang, H. M. Lee, and S.-B. Koh, "Is reduced arm and leg swing in Parkinson's disease associated with rigidity or bradykinesia?," J. Neurol. Sci., vol. 341, no. 1–2, pp. 32–35, Jun. 2014, doi: 10.1016/j.jns.2014.03.041.
[3] A. Winogrodzka, R. C. Wagenaar, J. Booij, and E. C. Wolters, "Rigidity and bradykinesia reduce interlimb coordination in Parkinsonian gait," Arch. Phys. Med. Rehabil., vol. 86, no. 2, pp. 183–189, Feb. 2005, doi: 10.1016/j.apmr.2004.09.010.

**P151**

## Safinamide effect on bladder function in PD Patients

*Livia Brusa*[1], E. Casula[2], A. Stefani[3], G. Koch[4], C. Iani[1]

[1]UOC Neurologia Ospedale S.Eugenio, Roma, Italia
[2]Dipartimento Medicina dei Sistemi Università Tor Vergata, Roma, Italia
[3] Clinica Neurologica Università di Tor Vergata, Rome, Italia
[4]Dipartim Neuroscienze e Riabilitazione Universita' di Ferrara, Ferrara, Italia

Among autonomic disorders, bladder dysfunction is one of the most disabling complain in patients with Parkinson's disease (PD).
Dopamine seems to play a key role in central bladder control, either in normal animals, or PD animal models or in patients affected by the disease.
Safinamide is a reversible, selective, monoamine oxidase b inhibitor (MAO-B-i) and glutamate modulator with therapeutic indication as an add-on to levodopa in fluctuating PD patients.
On these bases, this study tested safinamide effect on Lower Urinary Tract behavior in a group of moderate motor fluctuating PD patients complaining of bladder dysfunction.
Twenty-nine moderate motor fluctuating PD patients with Hoehn and Yahr score < 2.5 were included in the study.
All patients were evaluated first at baseline with IPSS questionnaire (International Prostate Symptoms Score questionnaire) and SCOPA OUT Questionnaire.
Following the first evaluating section, subjects added on their usual dopaminergic therapy a morning dose of Safinamide 50 mg for the sequent two months and at the end of this period all were re-evaluated in a second visit. A third section of evaluation with the same characteristics was administered following other two months of treatment with the same dopaminergic medication plus safinamide titrated to 100 mg per day.
Post-hoc analysis showed a significantly lower IPSS score after safinamide 50 mg ($p<0.001$) and 100 mg ($p<0.001$) compared to baseline evaluation; IPSS score was significantly lower also after Safinamide 100 mg compared to 50 mg ($p=0.004$). The evaluation of IPSS revealed a significant effect of Safinamide on the following items: urgency [EPC1] [$\chi2 = 39.169$; $p<0.001$], nicturia [EPC2] [EPC3] [$\chi2 = 31.871$; $p<0.001$] and frequency [EPC4] [$\chi2 = 49.854$; $p<0.001$][EPC5].
Analysis of total SCOPA OUT score revealed a significant effect of safinamide [$\chi2 = 48.713$; $p<0.001$]. Post-hoc analysis revealed a significantly lower SCOPA OUT score after safinamide 50 mg ($p<0.001$) and 100 mg ($p<0.001$) compared to baseline evaluation.
We performed a prospective open-label study to assess the effect of safinamide treatment on bladder function in patients with Parkinson's disease who have urinary symptoms. Our analysis showed a generalized improvement of total IPSS and SCOPA OUT score. We observed a relevant effect of safinamide on nicturia and frequency with an improvement also in motor functions.
Efficacy on nicturia is higher with safinamide 100 mg. A non dopaminergic effect of safinamide on different NMS (attention, mood, anxiety, sleep, cognitive functions and pain) suggested by different studies, could be relevant also for urinary symptoms.
In PD patients, the daily dose of 50 mg is required for reversible full inhibition of MAOB activity. The daily dose of 100 mg also inhibits glutamate release, an effect that may contribute to further efficacy on motor and NMS in fluctuating PD patients.

**P152**

## Retinal microvascular and choroidal structural changes in patients with Parkinson's disease and vascular parkinsonism: a pilot study

*Lanfranco De Carolis*[1], M. Di Pippo[2], M. Lodesani[2], S. Galli[1], D. Rinaldi[1], E. Bianchini[1], M. Alborghetti[1], S. Abdolrahimzadeh[2], F.E. Pontieri[1]

[1]Neurology Unit, Department of Neurosciences, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy
[2]Ophtalmology Unit, Department of Neurosciences, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy

*Introduction:* Diagnostic differentiation between patients with Parkinson's disease (PD) and vascular parkinsonism (VP) relies mainly on clinical and neuroimaging features. Nevertheless, noninvasive retinal imaging using Spectral-Domain (SD-OCT) and Optical Coherence Tomography Angiography (OCT-A) are increasingly recognized methods that may help to detect changes in neurodegenerative diseases.

*Objective:* To compare SD-OCT and OCT-A features between patients with PD, VP and healthy controls.

*Methods:* We collected clinical and OCT data on 14 PD patients, 7 VP patients and 17 healthy controls. Patients with diabetes mellitus, glaucoma, cataract, other retina and/or macular diseases, uncontrolled arterial hypertension were excluded. SD-OCT and OCT-A were used to assess: retinal nerve fiber layer (RNFL) average thickness, macular ganglion cell complex (GCC) thickness, central macular thickness (CMT), radial peripapillary plexus, choroidal thickness, vessel density of the superficial and deep capillary plexus, foveal avascular zone (FAZ) and choriocapillaris flow area. Total and luminal choroidal area and choroidal vascularity index (CVI) were also calculated using Image J software.

*Results:* Compared to healthy controls, PD and VP patients showed higher values of deep capillary plexus vessel density ($p=0.002$ and $p=0.049$ respectively), CVI ($p<0.001$ and $p=0.002$ respectively), total ($p<0.001$ and $p=0.046$ respectively) and luminal ($p<0.001$ and $p=0.011$ respectively) choroidal area. Furthermore, PD patients displayed higher CMT values ($p=0.036$). A tendency towards significance was found in choroidal thickness values difference between PD and VP patients ($p=0.08$).

*Conclusion:* These preliminary findings suggest that VP and PD patients differ in terms of SD-OCT and OCT-A findings from healthy controls. Albeit non-significant, VP and PD patients showed different values of choroidal thickness. Given these observations, microvascular and structural retinal and choroidal changes could constitute potential biomarkers that might enhance clinical individuation of PD and VP patients.

**P153**

## Gender differences in non-motor fluctuations in Parkinson's disease

*Giulia Donzuso*, C.E. Cicero, E. Vinciguerra, R. Sergi, A. Luca, G. Mostile, C. Terravecchia, M. Zappia, Alessandra Nicoletti

Department of Medical, Surgical Sciences and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy

*Background:* Non-motor symptoms (NMS) and Non-motor fluctuations (NMF) in Parkinson's disease (PD) are common, involving several domains and affecting quality of life [1].

*Objectives:* To estimate the burden of NMF in PD patients and to evaluate the possible gender effect.

*Methods:* PD patients fulfilling the MDS-PD diagnostic criteria attending the "Parkinson's Disease and Movement Disorders Centre" of the University of Catania were evaluated using the Non-Motor Fluctuations Assessment (NoMoFA) Questionnaire [2]. NoMoFA items were also grouped into the following domains: cognitive, mood, sleep/fatigue, dysautonomia, hallucination/perception and miscellaneous domains were identified.

*Results:* One-hundred and twenty-one patients with PD (67 men, 55.4%; mean age 70.2 ± 8.9 years, disease duration 8.3 ± 4.6 years) were evaluated. All PD patients reported at least one NMS, whereas 87 (71.9%) also reported NMF. "Feel sluggish or had low energy levels" (47.2%) along with "Feel excessively sleepy during the day" (40.0%) were the most common NMF reported in the whole sample. The majority of PD patients reported presence NMF during the OFF state (79, 65.3%). At multivariate analysis, NMF were positively associated with the female gender (adjusted OR 3.13; 95%CI 1.21-8.11 p-value 0.01). Women with PD had higher NMF scores especially in depression/anxiety, sleep/fatigue and dysautonomia domains.

*Conclusions:* Our study reported the presence of a gender-related pattern in the frequency of NMS and NMF in PD patients, with female gender associated with a higher risk of developing NMF, highlighting the need for personalized treatment strategies when addressing NMF.

**References:**

[1] Kim HS, Cheon SM, Seo JW, Ryu HJ, Park KW, Kim JW. Nonmotor symptoms more closely related to Parkinson's disease: Comparison with normal elderly. J Neurol Sci 2013; 324: 70–73.

[2] Kleiner G, Fernandez HH, Chou KL, et al; PSG NoMoFA Study Group. Non-Motor Fluctuations in Parkinson's Disease: Validation of the Non-Motor Fluctuation Assessment Questionnaire. Mov Disord 2021; 36: 1392-1400.

**P154**

## Phenotypical and molecular characterisation of a cohort of patients with GBA-related Parkinson's disease: focus on dysautonomic symptoms

*Eleonora Bertoncello*[1,2], G. Bonato[1], P. Cimino[1], L. Salviati[1], R. Biundo[1], A. Antonini[1], M. Carecchio[1]

[1]University of Padua, Department of Neuroscience, Padua, Italy
[2]University of Verona, Department of Neuroscience, Verona, Italy

*Introduction:* GBA is presently considered the most important genetic risk factor for Parkinson's disease (PD). A previous multicentric study (2020) revealed a significant prevalence of monoallelic variants of GBA (14,3%) in Italian PD patients, but centers from North-East of Italy were not included.

*Objective:* To assess clinical and genetic features of a cohort of patients with GBA-related-PD followed at Padova University and to compare them with results from previous studies. To assess potential differences in the clinical phenotype of GBA-related PD vs idiopathic-PD.

*Methods:* 20 patients with GBA-related-PD were included. Mutations were classified according to pathogenicity (ACMG guidelines) and clinical phenotyping was performed with motor and non-motor assessment scales, including COMPASS-31 for dysautonomia. The results were compared with a cohort of early-onset genetically-negative PD patients, matched for age, sex and disease duration. Lastly, results were compared with another group of late-onset idiopathic-PD patients with longer disease duration, not genetically tested.

*Results:* Mutational frequency of GBA was 11,76% (20/170). Patients with GBA-related-PD showed an earlier onset (mean 45.2 years), positive family history in 35% of cases and bradykinetic-rigid presentation in 65% of cases, with motor and non-motor complications over disease course, such as cognitive decline (75%), psychiatric disturbances (80%) and dysautonomia. The comparison with the two control groups demonstrated a higher severity of GBA-related-PD in terms of cognitive symptoms (p1=0,0003, p2=0,0002), disease progression (H&Y: 2,54, p1=0,00988, p2=0,02852) and dysautonomia, as confirmed by the higher average scores of COMPASS-31 (34,12400723, p=0,03662).
The most common mutations were N370S (9 patients) and D409H (4 patients), classified as mild and severe, respectively, according to residual GBA enzymatic activity. Other previously reported mutations were L444P and IVS2+1, both severe.

*Conclusions:* Our results are in line with previous research and demonstrate that GBA-related-PD has peculiar features compared to idiopathic, genetically-undetermined forms, particularly regarding cognitive and dysautonomic symptoms.

**P155**

## A juvenile case of Parkinson's disease associated with MAPT mutation

*Davide Greco*[1,2], S. Mombelli[1,2], S. Valente[1,2], F. Piattellini[1,2], G. Grigioni[2], L. Caremani[2], A. Govoni[2], B. Nacmias[1,2], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Department of Neuro-Muscular-Skeletal and Sensorials Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

*Introduction:* Parkinson's disease (PD) is defined primarily as a movement disorder, in addition to the defining dopaminerelated motor symptoms, however, PD is increasingly recognized as a heterogeneous multisystem disorder. Autosomal dominant mutations in the microtubule-associated protein tau (MAPT) gene were found to cause forms of parkinsonism and frontotemporal dementia.

*Objective:* We describe heterogeneous clinical manifestations in a 51 years old man with PD and carrying a mutation in MAPT gene.

*Methods:* Subject underwent serial neurological visits, Genetic Analysis, brain magnetic resonance imaging (MRI), brain 123I-FP-CIT SPECT, brain PET-FDG and neuropsychological assessments.

*Results:* We present the case of a man who was diagnosed with PD at the age of 47 years, beginning with right upper limb bradykinesia. The brain 123I-FP-CIT SPECT confirmed low uptake in the left caudate and putamen while the Brain MRI showed mild ventricular dilation. Therapy with dopamine-agonist, rasagiline and levodopa was started. Interestingly the gene analysis identified a pathogenic variant in exon 10 of MAPT gene (c. 1853C>T; p.Pro618Leu). Further diagnostic investigations highlighted left insular and temporo-parietal hypometabolism through Brain PET-FDG and deficit of attentive, executive e visuospatial skills. In the following years motor symptoms worsened, impulse control disorder occurred (with hyperphagia, hypersexuality, gambling and drug abuse) and the patient presented traits of aggression, requiring psychiatric intervention.

*Conclusions:* Tauopathies refer to a wide range of phenotypically diverse diseases characterised by the aberrant aggregation of tau in neurons and/or glia, tau dysfunction is sufficient for widespread central nervous system neurodegeneration. In this case we increase the knowledge about the possible role of tau dysfunction in non-motor clinical manifestation of Parkinson disease.

**P156**

## Genetics isn't enough: clinical and biochemical profile of GBA and non-GBA related Parkinson's disease in twins and non-twins brother

*Pierfrancesco Mitrotti*[1], G. Ongari[2], G. Cuconato[3], I. Palmieri[2], R. Zangaglia[2], S. Cerri[2], R. Calabrese[2], C. Tassorelli[1,2], C. Pacchetti[2], E.M. Valente[2,3], M. Avenali[1,2]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Molecular Medicine, University of Pavia, Pavia, Italy

*Introduction:* GBA mutations lead to impaired lysosomal-mediated autophagy leading to a-synuclein accumulation and synucleopathies development. However, not every individual carrying a variant in GBA gene develop Parkinson Disease (PD) due to incomplete penetrance of these variants. Investigate lysosomal dysfunction in GBA carriers compared to non-mutated PD individuals will help to identify risk factors that could contribute to disease development.

*Objective:* To characterize genetic, clinical, biochemical profile of GBA monozygotic sisters clinically discordant for PD and two non-twins PD brothers discordant for GBA mutations.

*Methods:* Genetic and clinical characterization were performed and lysosomal alterations (GCase, LAMP1, LIMP2, Saposin C) and alpha-synuclein levels were analyzed in peripheral blood lymphocytes.

*Results:* Two 66 years old monozygotic sisters had a heterozygous GBA N370S mutation (mild variant); one of them with an history of depression and anxiety developed at age of 56 bradykinesia and rigidity on the right upper limb with an initial good response to levodopa. After 6 years she developed motor fluctuations, cognitive decline and moderate psychotic symptoms requiring advance therapy intervention (duodopa infusion gel). Her sister had a normal neurological exam without parkinsonian symptoms.
The non-twins brothers both developed PD at age of 40 and 54 years and genetic analysis revealed a heterozygous GBA L444P mutation only in the latest. The GBA-PD carrier although developed PD later than the non-mutated brother had a more rapid and severe motor progression requiring STN-DBS implant after 6 years from onset. On the contrary, the non-mutated brother showed a milder non-motor and cognitive phenotype than GBA-PD brother, although the longer disease duration.

*Conclusions:* To the best of our knowledge no environmental factors or other genetic mutations were found in these subjects that could explain the different phenotypes. Biochemical investigation is currently ongoing to deeper explore the role of lysosomal dysfunction on clinical heterogeneity.

**P157**

## A case of ataxia and optic atrophy caused by NDUFA1 mutation

*Antonio Funcis*[1], S. Rossi[1], R. Carrozzo[3], A. Torraco[3], E.S. Bertini[3], G. Silvestri[1,2]

[1]Institute of Neurology, Catholic University of the Sacred Heart, Rome, Italy
[2]Institute of Neurology, Fondazione Policlinico A. Gemelli, Rome, Italy
[3]Neuromuscular and Neurodegenerative Disorders, Bambino Gesù Children's Hospital, IRCSS, Rome, Italy

*Objective:* To describe a novel association of a previously reported NDUFA1 mutation with slowly progressive sensory ataxia and optic atrophy.

*Case description:* A male born full-term from unrelated parents, had motor and speech developmental delayed acquisition and an IQ of 79. At the age of 5 he showed visual impairment, the fundus study showed an optic sub-atrophy. Brain MRI and MEP, both of which were unremarkable. At the age of 25 he was evaluated by a neurologist due to progressive gait instability. Neurological examination showed ataxic gait, positive Romberg sign, severely reduced visual acuity and pes cavus. Electroneurography documented sensory axonal polyneuropathy. Visual evoked potentials showed bilateral absence of P100. Lactate exercise test was positive, muscle biopsy was normal. Genetic tests for SCA 1,2,3,6,7 and FXN were negative. At 43 years old, he showed a worsening of balance. Second MRI, showed thinning of the optic nerves and slight vermian atrophy. The patient and his parents performed genetic testing through the Next Generation Sequencing Panel (Illumina), filtering results for genes associated to mitochondrial diseases.

*Results:* Genetic testing showed the hemizygous missense mutation c.55C>T; p.(Pro19Ser) on NADH-Ubiquinone Oxidoreductase Subunit A1 (NDUFA1) gene, which was inherited from his mother. To confirm pathogenicity, previous muscle biopsy testing by native blue gel electrophoresis showed a decrease in the enzyme activity of mitochondrial complex I. Gel electrophoresis showed a reduction in complex I subunits, especially NDUFA.

*Conclusion:* NDUFA1 codes for a subunit of CI and is fundamental for CI assembly and functioning [1]. The same mutation was previously described with young-onset Leigh syndrome [2]. Our case expands the phenotypic spectrum of NDUFA1 mutations, therefore should be considered among the causes of sensory ataxia with optic atrophy and further confirm the relevance of complex I for optic nerve integrity.

**References:**

[1] Janssen, R. J. R. J., Nijtmans, L. G., van den Heuvel, L. P. & Smeitink, J. A. M. Mitochondrial complex I: structure, function and pathology. J. Inherit. Metab. Dis. 29, 499–515 (2006).
[2] Fernandez-Moreira, D. et al. X-linked NDUFA1 gene mutations associated with mitochondrial encephalomyopathy. Ann. Neurol. 61, 73–83 (2007).

**P158**

## CSF biomarkers profile of patients with Parkinson's disease treated with different MAO-B inhibitors in add-on

*Henri Zenuni*[1], A. Ferri[2,3], C. Valle[2,3], S. Scaricamazza[2,3], V. Nesci[2,3], J. Bissacco[1], C. Simonetta[1], A. Stefani[1], N.B. Mercuri[1,2], T. Schirinzi[1]

[1]Unit of Neurology, Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]IRCCS Fondazione Santa Lucia, Rome, Italy
[3]Institute of Translational Pharmacology (IFT), Consiglio Nazionale delle Ricerche (CNR), Rome, Italy

*Introduction:* APO-ε genotype serves as a genetic risk factor for Alzheimer's disease (AD) and affects the progression rate of the disease. Recent findings also showed a role of APO-ε genotype as a determinant of motor and cognitive trajectories in Parkinson's disease (PD) [1-2]. However, the clinical and neurochemical correlates of the APO-ε genotype have not clearly established yet in PD patients.

*Objective:* To assess the association between different APO-ε genotypes and CSF neurodegeration-related biomarkers or main clinical features in PD patients.

*Methods:* The study involved 183 PD patients and 85 controls genotyped for APO-ε and grouped in APO-ε4 and non-APO-ε4 carriers(PD: APO-ε4 83.6%, non-APO-ε4 16.4%; controls: APO-ε4 85.7%, non-APO-ε4 14.3%). All participants underwent the measuremet of amyloid-β42 (Aβ42), amyloid-β40 (Aβ40), t-tau, p-tau and lactate CSF levels. Beta ratio (Aβ42/Aβ40) was also calculated. PD patients were evaluated through the MDS-UPDRS part III, MoCA, non motor symptoms scale (NMSS) and LEDD calculation. Clinical and neurochemical parameters were compared between the groups and correlated each other.

*Results:* APO-ε4 PD carrier group compared to the non APO-ε4 group presented with higher NMSS total score (50.7±7.1 and 40.8±3.0 respectively, p=0.037), lower Aβ-42 (779.1±54.2pmol/ml and 966.1±30.6pmol/ml respectively, p=0,018) and higher lactate (1.57±0.06mmol/ml and 1.46±0.03mmol/ml respectively, p=0.032) CSF level. CSF biomarkers did not differ in APO-ε control groups.

**References:**

[1] Pu JL, Jin CY, Wang ZX, et al. Apolipoprotein E Genotype Contributes to Motor Progression in Parkinson's Disease. Mov Disord. 2022;37(1):196-200. doi:10.1002/MDS.28805.
[2] Jo S, Kim SO, Park KW, Lee SH, Hwang YS, Chung SJ. The role of APOE in cognitive trajectories and motor decline in Parkinson's disease. Sci Reports 2021 111. 2021;11(1):1-10. doi:10.1038/s41598-021-86483-w.

**P159**

## A novel Beta synuclein mutation associated with neurodegeneration and beta-amyloid deposition causing dementia

*Elisabetta Gasparoli*[1], A. Codemo[1], A. Pontarin[6], L. Salviati[2], P. Cassina[2], D. Cecchin[3], C. Ruaro[4], M. Sandre[5], C. Gabelli[1]

[1]Centro Regionale per lo studio dell'Invecchiamento Cerebrale (CRIC), Dipartimento di Medicina (DIMED), Università di Padova, Padova, Italy
[2]Unità di Genetica Clinica, Dipartimento della salute della Donna e del Bambino, Università di Padova e Fondazione Istituto di Ricerca Pediatrica Città della Speranza, Padova, Italy
[3]Unità di Medicina Nucleare, Università di Padova, Padova, Italy
[4]Unità Ospedaliera di Psicologia, Aziena Ospedaliera Università di Padova, Padova, Italy
[5]Centro di Ricerca per le Malattie Neurodegenerative (CESNE), Università di Padova, Padova, Italy
[6]Unità di Geriatria, Ospedale di Dolo, Venezia, Italy

*Background:* Beta – synuclein (B-Syn) is a presynaptic protein encoded by the synuclein Beta locus (SNCB) on chromosome 13 and is predominantly expressed in the brain. B-Syn, together with alfa synuclein and gamma synuclein, forms a group of proteins dubbed "synucleins" [1]. Although the physiologic role of B-Syn has not been fully elucidated it has been shown to inhibit alpha synuclein aggregation while recent reports suggest that elevated B-Syn levels in cerobrospinal fluid is an early and specific diagnostic biomarker for Alzheimer's disease [7-12]. Mutations of SNCB previously described (P123H LB and V70M) were associated with clinical and neuropathological diagnosis of Lewy body dementia. [2-3-4-5-6]
We describe here two consanguineous female patients (cousins) carrying a heterozygous variant in the SNCB gene, NM_003085.5: c.382C>G p. (Gln128Glu), not reported in literature and rare in the general population (absent in the gnom AD database). The substitution alters a highly preserved amino acid residue. Both subjects had an early onset cognitive decline (pt 1=56 ys, pt 2=65 ys), in addition patient 1 has familial hypercholesterolemia, macular degeneration and amyloid angiopathy. Both of them show a similar onset of cognitive impairment with memory loss without motor signs. They have a comparable CSF profile typical of AD (A+T+N+) and both of them were positive at florbetaben PET brain scan and neurodegeneration at MR imaging indicative of Alzheimer's disease.

*Conclusions:* This is the first time for a SNCB mutation associated with diagnosis of Alzheimer Disease (A+T+N+). Although the specific mechanism remains undefined, previous studies and our findings suggest that alterations of beta-synuclein protein might play a role in the pathogenesis of AD clinical phenotypes and that alterations of B-Syn structure or function may play an amyloidogenic role.

**References:**

[1] Spillantini MG, Crowther RA, Jakes R, Hasegawa M, Goedert M. α-Synuclein in filamentous inclusions of Lewy bodies from Parkinson's disease and dementia with Lewy bodies. Proc Natl Acad Sci. maggio 1998;95(11):6469–73.
[2] Sharma K, Mehra S, Sawner AS, Markam PS, Panigrahi R, Navalkar A, et al. Effect of Disease-Associated P123H and V70M Mutations on β-Synuclein Fibrillation. ACS Chem Neurosci. Settembre 2020;11(18):2836–48.
[3] Ohtake H, Limprasert P, Fan Y, Onodera O, Kakita A, Takahashi H, et al. β-Synuclein gene alterations in dementia with Lewy bodies. Neurology. settembre 2004;63(5):805–11.
[4] Narhi L, Wood SJ, Steavenson S, Jiang Y, Wu GM, Anafi D, et al. Both Familial Parkinson's Disease Mutations Accelerate α-Synuclein Aggregation. J Biol Chem. aprile 1999;274(14):9843–6.
[5] Hashimoto M, Bar-on P, Ho G, Takenouchi T, Rockenstein E, Crews L, et al. β-Synuclein Regulates Akt Activity in Neuronal Cells. J Biol Chem. maggio 2004;279(22):23622–9.
[6] Sharma K, Mehra S, Sawner AS, Markam PS, Panigrahi R, Navalkar A, et al. Effect of Disease-Associated P123H and V70M Mutations on β-Synuclein Fibrillation. ACS Chem Neurosci. settembre 2020;11(18):2836–48.

[7] Tolö J, Taschenberger G, Leite K, Stahlberg MA, Spehlbrink G, Kues J, et al. Pathophysiological Consequences of Neuronal α-Synuclein Overexpression: Impacts on Ion Homeostasis, Stress Signaling, Mitochondrial Integrity, and Electrical Activity. Front Mol Neurosci. marzo 2018;11.
[8] Fujita M, Ho G, Takamatsu Y, Wada R, Ikeda K, Hashimoto M. Possible Role of Amyloidogenic Evolvability in Dementia with Lewy Bodies: Insights from Transgenic Mice Expressing P123H β-Synuclein. Int J Mol Sci. aprile 2020;21(8).
[9] Oeckl P, Metzger F, Nagl M, Arnim CAF von, Halbgebauer S, Steinacker P, et al. Alpha-, Beta-, and Gamma-synuclein Quantification in Cerebrospinal Fluid by Multiple Reaction Monitoring Reveals Increased Concentrations in Alzheimer′s and Creutzfeldt-Jakob Disease but No Alteration in Synucleinopathies. Mol Cell Proteomics. ottobre 2016;15(10):3126–38.
[10] Oeckl P, Halbgebauer S, Anderl-Straub S, Arnim CAF von, Diehl-Schmid J, Froelich L, et al. Targeted Mass Spectrometry Suggests Beta-Synuclein as Synaptic Blood Marker in Alzheimer's Disease. J Proteome Res. marzo 2020;19(3):1310–8.
[11] Halbgebauer S, Oeckl P, Steinacker P, Yilmazer-Hanke D, Anderl-Straub S, Arnim C von, et al. Beta-synuclein in cerebrospinal fluid as an early diagnostic marker of Alzheimer's disease. J Neurol Neurosurg Psychiatry. aprile 2021;92(4).
[12] J. Nilsson, J Constantinescu, B. Nellgard, P. Jakobsson, W.S. BRum, J. Gobom, L. Forsgren, K Dalla, R. Constantinescu, H.Zettenberg, O. Hansson, K. Blennow, D. Bacstrom, A. Brinkmalm. Cerebrospinal Fluid Biomarkers of Synaptic Dysfunction Are Altered in Parkinson's Disease and Related Disorders. Mov Disord .2022 Dec 12.

**P160**

## Sex differences in microRNA expression in levodopa-naïve PD patients

*Maria Claudia Russillo*[1], A. Vallelunga[2], T. Iannitti[3], G. Somma[1], M. Picillo[1], R. De Micco[4], L. Vacca[5], R. Cilia[6], E.C. Cicero[7], R. Zangaglia[8], G. Lazzeri[9], S. Galantucci[10], F.G. Radicati[5], A. De Rosa[11], M. Amboni[1], C.L. Scaglione[12], A. Tessitore[4], F. Stocchi[1,3,5], R. Eleopra[6], A. Nicoletti[7], C. Pacchetti[8], A.B. Di Fonzo[9], M.A. Volontè[10], P. Barone[1], M.T. Pellecchia[1]

[1] Department of Medicine Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Salerno, Italy
[2] Department of Life Sciences and Biotechnologies, University of Ferrara, Ferrara, Italy
[3] Department of Medical Sciences, Section of Experimental Medicine, University of Ferrara, Ferrara, Italy
[4] Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[5] IRCCS San Raffaele, Roma, Italy
[6] Fondazione IRCCS Istituto Neurologico Carlo Besta, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milano, Italy
[7] Neurologic Unit, AOU "Policlinico-San Marco", Department of Medical, Surgical Sciences and Advanced Technologies, G.F. Ingrassia, University of Catania, Catania, Italy
[8] Parkinson's Disease and Movement Disorders Unit, IRCCS Mondino Foundation, Pavia, Italy
[9] IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milano, Italy
[10] IRCCS San Raffaele Scientific Institute, Neurology Unit, Milano, Italy
[11] Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Napoli, Italy
[12] IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[13] University San Raffaele, Roma, Italy

*Introduction:* Parkinson's disease (PD) is the second most common neurodegenerative disorder that affects millions of individuals worldwide. Biological sex is an important factor influencing epidemiological and clinical features of the disease. MicroRNAs (miRNAs) are small non-coding RNAs which regulate gene expression at post-transcriptional level. Several studies have shown that specific panels of miRNAs are dysregulated in PD and other parkinsonian disorders [1,2].

*Objective:* Our goal was to evaluate gender differences in the expression of a panel of miRNAs (miR-34a-5p, miR-146a, miR-155, miR-29a, miR-106a) possibly involved in the pathophysiology or progression of disease.

*Methods:* Serum samples were obtained from 104 PD patients (58 men and 46 women) never treated with levodopa. All samples with severe hemolysis were excluded. We measured levels of miRNAs using quantitative PCR. Correlations between miRNA expression and clinical data were assessed using the Spearman's correlation test. We used STRING to evaluate co-expression relationship among target genes.

*Results:* MiR-34a-5p was significantly upregulated in PD male patients compared with PD female patients (fc: 1.62; $p < 0.0001$). No correlation was found with age, BMI, and disease severity, assessed by UPDRS III scale, in male and female patients. MiR-146a-5p was significantly upregulated in PD female compared with male patients (fc: 3,44; $p < 0.0001$) and a significant correlation was also observed between disease duration and mir-146a-5p. No differences were found in the expression of miR-29a, miR-106a-5p and miR-155 between genders. Predicted target genes for miR-34a-5p and miR-146-5p and protein interactions in biological processes were reported.

*Conclusions:* Our study supports the hypothesis that there are sex specific differences in serum miRNAs expression in PD patients, possibly affecting disease progression and response to treatment.

**References:**

[1] Zago E, Dal Molin A, Dimitri GM, Xumerle L, Pirazzini C, Bacalini MG, Maturo MG, Azevedo T, Spasov S, Gómez-Garre P, Periñán MT, Jesús S, Baldelli L, Sambati L, Calandra-Buonaura G, Garagnani P, Provini F, Cortelli P, Mir P, Trenkwalder C, Mollenhauer B, Franceschi C, Liò P, Nardini C; PROPAG-AGEING Consortium. Early downregulation of hsa-miR-144-3p in serum from drug-naïve Parkinson's disease patients. Sci Rep. 2022 Jan 25;12(1):1330. doi: 10.1038/s41598-022-05227-6. PMID: 35079043; PMCID: PMC8789812.

[2] Vallelunga A, Iannitti T, Capece S, Somma G, Russillo MC, Foubert-Samier A, Laurens B, Sibon I, Meissner WG, Barone P, Pellecchia MT. Serum miR-96-5P and miR-339-5P Are Potential Biomarkers for Multiple System Atrophy and Parkinson's Disease. Front Aging Neurosci. 2021 Jul 26;13:632891. doi: 10.3389/fnagi.2021.632891. PMID: 34381349; PMCID: PMC8350521.

**P161**

## Cerebellar ataxia associated with IRF2BPL pathogenic variant

*Antonella Muroni*[1], L. Polizzi[1], G. Defazio[1,2]

[1]Neurology Unit, Azienda Ospedaliero Universitaria di Cagliari, Cagliari, Italy
[2]Dipartimento di Biomedicina Traslazionale e Neuroscienze Università di Bari "A. Moro", Bari, Italy

*Introduction and objective:* Cerebellar ataxias represent a group of disorders with heterogeneous clinical presentation consisting in a pure cerebellar phenotype or various combinations with extracerebellar signs. We report a case of ataxia associated to IRF2BPL gene variant, an intronless gene mapped to 14q24.3 chromosome that codes for the interferon-regulatory-factor-2-binding-like-protein [1].

*Materials:* A 24-year-old woman came to clinical observation because of the appearance of myoclonic jerks and unsteady gait with frequent falls a few months before. Clinical examination showed multifocal myoclonic jerks, adult-onset intention tremor in the four limbs, and gait ataxia. The patient also reported a mild neuro-developmental disorder with regression and memory lapses starting when she was 7.

*Methods:* MRI brain-scan revealed six small T2/Flair-hyperintense supratentorial, bilateral gliotic lesions. Metabolic and genetic (SCA1, 2, 3, 6, 7, 17 and HTT genes) investigations resulted normal. Levetiracetam and Clonazepam consistently reduced the frequency of myoclonic jerks. Whole exome sequencing (WES) followed by Sanger sequencing revealed a de novo heterozygous pathogenetic variant (c.364C> T, p.Gln122Ter) in the IRF2BPL gene. WES performed in the parents of the patient didn't reveal any mutation. In addition to our case, a review of the literature identified 27 further patients carrying IRF2BPL variants was performed. Developmental delay and/or motor/speech regression of variable severity were present in all 28 patients, whereas ataxia was observed in 10.

*Conclusions:* The IRF2BPL mutation is to be added to the increasing number of genes implicated in cerebellar ataxias. The IRF2BPL variants should be considered in the diagnostic work up of patients with ataxia and extracerebellar signs, even though the condition is apparently sporadic. The absence of a family history should not preclude diagnosis because the great majority of previously reported probands had the disorder as the result of a de novo pathogenic variant.

**References:**

[1] Seizure 2022 Jul;99:12-15. doi: 10.1016/j.seizure.2022.04.010.

## P162

### Juvenile Parkinson disease and mutation in RFC1 replication factor

*Luca Caremani*[2], F. Piattellini[1,2], S. Valente[1,2], S. Mombelli[1,2], D. Greco[1,2], G. Grigioni[2], A. Govoni[2], S. Ramat[2]

[1]Neurologia1, Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Neurologia 1, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

*Introduction:* The biallelic repeat expansion (AAGGG)exp in the replication factor C subunit 1 gene (RFC1) is a frequent cause of cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) as well as late-onset ataxia [1]. The clinical spectrum from the outset has been shown to be diverse and non-classical phenotypes are often observed.

*Objective:* We present the case of a 61-year-old man with concomitant diagnosis of Parkinson Disease (PD) and CANVAS.

*Methods:* The patient underwent neurological examinations, radiological tests (brain MRI, Ioflupane-SPET), electrophysiological and genetic analysis (AAGGG intronic expansion of the RFC1 gene, on two alleles).

*Outcome:* The patient presented in 2020 with difficulty in fine movements of the left hand. But since 2013 he had decreased sensitivity/paresthesias in the lower limbs starting from the foot and then radiating to the knee, followed by slight paresthesias in the hands, greater on the left. EMG (2020): polyneuropathy, predominantly sensory and axonal type, motor almost exclusively at lower limbs, mixed and distal type. Brain MRI reperto incidentale of small aneurysmal formation partially thrombosed. Ioflupane-SPET (2021) showed reduction of DAT sites in the putamen, prevalent on the right. He had recurring cough and rhinorrhea. Not familiarity for PD, but family history of disability (2 maternal cousins wheelchair bound at age 6-7, unknown diagnosis).

*Conclusions:* Our results suggest that (AAGGG)exp in RFC1 is a rare cause of early-onset PD. The present case shows an association with PD, recently reported rare cases in the literature. Certainly, a greater number of cases of juvenile PD should be studied to find an effective correlation between the

**References:**

[1] Bhagwat NM, Joshi AS, Rao G, Varthakavi PK. Uncontrolled hyperglycaemia: a reversible cause of hemichorea-hemiballismus. BMJ Case Rep. 2013 Sep 6;2013:bcr2013010229. doi: 10.1136/bcr-2013-010229. PMID: 24014327; PMCID: PMC3794112.

**P163**

## A rapidly progressive PSP-FTD like phenotype in a carrier of the GBA L444P mutation

*Raffaella Di Giacopo*[1], F. Zappini[2], E. Monfrini[3], A.B. Di Fonzo[3]

[1]U.O Neurologia, Ospedale Santa Maria del Carmine di Rovereto, Trento, Italy
[2]Centro di Riabilitazione Neurocognitiva, Centro Interdipartimentale Mente Cervello, Università di Trento, Trento, Italy
[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

*Introduction:* Heterozygous GBA mutations increase the risk of PD, LBD and worsen the severity in other neurodegenerative disorder different from the alpha-synucleinopathies.Previous studies failed to report a significant association between tauopathies and GBA mutations [1].

*Objective:* To describe the phenotype of a patient with a FTD like-phenotype carrying a severe GBA pathogenic variant.

*Methods:* Phenotypic data were repeatedly collected along three years.

*Results:* A 58-year-old right-handed man came at our attention for a progressive language disorder. Family history was negative.The examination revealed photophobia,vertical and horizontal hypometric saccades with higher latency,mild dysphagia, and speach apraxia.Postural instability,parkinsonism,pyramidal and cerebellar signs were absent.The electromyography performed on the face and limbs was normal.The neuropsychological evaluation revealed a primary progressive aphasia associated to executive/attention difficulties. A PET-FGD scan showed a frontal widespread hypometabolism without cortical or midbrain atrophy.CSF biomarkers levels were normal.The course of the disease was remarkably aggressive.After 36 months the patient developed a frontal dementia,anartria, severe dysphagia without hypertonia or balance disturbances.Eight months later he developed diffuse myoclonus and died for pneumonia.Genetic analysis excluded C9ORF72 pathologic expansions.The Exome Sequencing failed to detect pathogenic variants in genes associated to fronto temporal dementia and revealed the L444P heterozygous mutation in the GBA gene.

*Conclusions:* We present a rapidly progressive PSP-FTD phenotype, mainly characterized by pseudobulbar involvement in a carrier of a severe GBA pathogenic variant. To the best of our knowledge,this mutation has been found only in one other case of PSP-like phenotype, mainly characterized by falls [2]. Recent evidence suggests that GBA mutations may influence the cognitive status of patients with ALS [3]. Several genes causing ALS and FTD, are related to lysosomal function and protein degradation.Moreover, mutations in genes that encode proteins important for endosome-lysosome function also occur in other age-dependent neurodegenerative diseases, including Alzheimer's and Parkinson's disease.A more understanding of the features of lysosome dysfunction in neurodegeneration will help guide the development of disease-modifiyng therapies.

**References:**

[1] Straniero et al., 2020. Neurolog Genet 6(6):e523.
[2] Picillo et al., 2016. Mov Disord Clin Pract. 4(3):444-446.
[3] Root et al., 2021. Neurobiol Dis. 154: 105360.

**P164**

## Mitochondrial disorders and Parkinson's disease: the clinical case of a patient with concomitant diagnosis of Parkinson disease and Leber's hereditary optic neuropathy

*Francesca Piattellini*[1,2], S. Valente[1,2], S. Mombelli[1,2], D. Greco[1,2], G. Grigioni[1,2], L. Caremani[2], A. Govoni[2], M.T.R. De Cristofaro[3], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2] Parkinson Unit, Department of NeuroMuscular-Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[3]Nuclear Medicine Unit, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy

*Introduction:* Mitochondrial diseases (MIDs) are a heterogeneous group of disorders caused by mitochondrial or nuclear DNA mutations, resulting in multiorgan disorders including the central and peripheral nervous system. Parkinsonism has been described in some cases of MIDs and some studies show a greater sensitivity of substantia nigra to mitochondrial dysfunction that represents a key event in the pathogenesis of Parkinson's disease (PD).

*Objective:* We present the case of a 70-year-old man with concomitant diagnosis of PD and Leber's hereditary optic neuropathy (LHON).

*Method:* The patient underwent neurological examinations, radiological tests (brain RMN, 123Ioflupane SPECT), electrophysiological and genetic analysis.

*Outcome:* Patient arrived at our attention at the age of 67 years, he suffered for PD diagnosed 7 years before and began with bilateral tremor in the upper limbs, greater on the left side. Brain NMR was normal and 123Ioflupane SPECT showed a severe reduction in the putamen uptake, more pronounced on the right side. Moreover, patient was diagnosed for LHON (mutation G11778A) and the same diagnosis was made for a brother and two maternal uncles. Family history was negative for PD, while the father suffered from Alzheimer's disease.

*Conclusions:* It is known that many genes involved in hereditary forms of PD encode for proteins with mitochondrial functions (Parkin, PINK1 and DJ1). Similarly extrapyramidal syndromes can occur in MIDs, in particular in patients carrying A8344G mutation or mutations in POLG1 and PEO1 genes. LHON is reported to be associated to some extrapyramidal symptoms, especially dystonia, chorea and tics. In this case we found an association of LHNO and PD, of which only very few cases have been reported, enriching the knowledge on the correlation between MIDs and movement disorders. Further studies are needed to understand the pathogenic role of mitochondrial dysfunction on PD.

**P165**

## A new pathogenic variant in GBA gene in a man with Parkinson's disease

*Alessandra Govoni*[1], G. Grigioni[1], L. Caremani[1], F. Piattellini[1,2], S. Valente[1,2], S. Mombelli[1,2], D. Greco[1,2], R. Tonin[3], M. Rinaldi[3], A. Morrone[3,4], S. Ramat[1]

[1]Parkinson Unit, Department of NeuroMuscular- Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[2]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[3]Laboratory of Molecular Biology of Neurometabolic Diseases, Neuroscience Department, Meyer Children's Hospital, IRCCS, Florence, Italy
[4]Department of NEUROFARBA, University of Florence, Florence, Italy

*Introduction:* GBA gene mutations are the most significant genetic risk factor for developing Parkinson's disease (PD) and a known cause of dementia with Lewy bodies (LBD). GBA-PD clinical features are earlier onset, more rapid progression and higher frequency and severity of non-motor symptoms.

*Objective:* We describe the clinical case of a 65-years-old PD patient heterozygous for two GBA mutations, enrolled in the MuTaParGa2018.0942 project.

*Methods:* The subject was selected from patients referred to the Parkinson Unit at AOU Careggi and screened for β-glucocerebrosidase (GBA) enzymatic activity on Dried Blood Spot using tandem mass spectrometry (LC-MS/MS). GBA gene analysis was performed using AmpliSeq for Illumina Custom DNA panel and identified variants were confirmed using Sanger sequencing.

*Results:* The disease was clinically diagnosed, supported by SPECT-Brain-DaTscan test, at the age of 60. Symptoms started 2 years earlier with bradykinesia and resting tremor (affecting the left side mostly) gait disturbance and postural instability. A prodromal phase with vivid dreams and sleeptalking was also reported. Levodopa and dopamine-agonist therapies improved the symptoms. The patient had a positive family history of PD (maternal uncle) and dementia (mother) and suffered from monoclonal gammopathy, maculopathy and allergic asthma. After 3 years the clinical course worsened both for motor and non-motor symptoms; particularly balance impairment increased. Brain FDG-PET tomography revealed a pattern compatible with LBD. Brain MRI highlighted calcium salts deposits in the basal nuclei. GBA enzymatic activity resulted reduced and compatible with carrier status. GBA gene analysis identified the presence of the common mutation c.1448T>C p.(Leu483Pro) and the new missense variant c.631G>A p.(Val211Ile). Unfortunately, CIS or TRANS allelic segregation analysis is not available.

*Conclusions:* The reported case confirms the known data relating to the clinical phenotype of patients with PD and GBA mutations and increases knowledge about the genotype of this category of patients.

**P166**

## A study on the correlations between acoustic speech variables and bradykinesia in advanced Parkinson's disease

*Francesco Cavallieri*[1], G. Di Rauso[2,3], A. Gessani[3], C. Budriesi[2,3], V. Fioravanti[1], S. Contardi[4], E. Menozzi[5], S. Pinto[6], E. Moro[7], F. Antonelli[3], F. Valzania[1]

[1] Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2] Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[3] Neurology, Neuroscience Head Neck Department, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy
[4] IRCCS Istituto delle Scienze Neurologiche di Bologna, Neurologia e Rete Stroke Metropolitana, Ospedale Maggiore, Bologna, Italy
[5] Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK
[6] Aix Marseille Univ, CNRS, LPL, Aix-en-Provence, France
[7] Grenoble Alpes University, Division of Neurology, Centre Hospitalier Universitaire de Grenoble, Grenoble Institute of Neuroscience, Grenoble, France

*Introduction:* Very few studies have assessed the presence of possible correlation between speech variables and limb bradykinesia in patients with Parkinson's disease (PD).

*Objective:* The objective of this study was to find the presence of correlation between different speech variables and upper extremity bradykinesia in different medication conditions in a cohort of advanced PD patients.

*Methods:* Retrospective data from advanced PD patients before and after an acute levodopa challenge were collected. Each patient was assessed through a perceptual-acoustic analysis of speech which included several quantitative parameters (i.e. maximum phonation time [MPT]; Shimmer Local dB); a neurological evaluation with the administration of the Unified Parkinson's Disease Rating Scale (UPDRS) (total scores, subscores and items) and a timed test (tapping test for 20 seconds) to quantify upper extremity bradykinesia. Pearson's correlation coefficient was applied to find correlation between the different speech variables and tapping rate.

*Results:* 53 PD patients (males: 34; disease duration: 10.66 [sd 4.37] years; age at PD onset: 49.81 years [sd 6.12]) were included. Levodopa intake significantly increased the MPT of sustained phonation ($p<0.01$) while significantly reduced speech rate ($p=0.05$). In the defined-OFF condition, MPT of sustained phonation correlated positively with both bilateral mean ($p= 0.044$, r-value: .299) and left ($p= 0.033$, r-value: .314) tapping.
In the defined-ON condition patients with a longer MPT performed well the tapping test with both arms.

*Conclusions:* This study confirms the presence of correlations between speech acoustic variables and upper extremity bradykinesia in a cohort of advanced PD patients. This may be due to common pathophysiological mechanisms.

**P167**

## Levodopa responsive asymmetric Parkinson's disease as clinical presentation of progranulin gene mutation: a case report

*Francesco Cavallieri*[1], G. Di Rauso[1,2], V. Fioravanti[1], E. Monfrini[3], A. Marti[1], F. Gasparini[1], D. Beltrami[1], S. Grisanti[4], J. Rossi[1,4], G. Toschi[1], A. Fraternali[6], A. Versari[6], M. Napoli[7], R. Pascarella[7], A.B Di Fonzo[3], F. Valzania[1]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Neurology Unit, Department of Biomedical, Metabolic and Neural Science, University of Modena and Reggio Emilia, Modena, Italy
[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy
[4]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena,Italy
[5]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[6]Nuclear Medicine Unit, Azienda Unità Sanitaria Locale-IRCCS of Reggio Emilia, Reggio Emilia, Italy
[7]Neuroradiology Unit, Radiology Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

*Introduction:* Mutations in the progranulin gene (GRN) are one of the major causes of autosomal dominant frontotemporal dementia (FTD). In this setting parkinsonism can develop over the course of FTD or may rarely be the presenting feature of the disease, mimicking idiopathic Parkinson's disease (PD) or atypical parkinsonism.

*Case presentation:* A 53 years-old man with a family history of PD (both parents and one paternal uncle) and dementia (one paternal uncle) came to our attention for rest tremor, bradykinesia, and rigidity in the right hand. Neurological examination confirmed the presence of a right-sided hemiparkinsonism. Brain-MRI was normal while DaTscan revealed bilateral reduction in presynaptic dopaminergic uptake. A diagnosis of PD was made and ropinirole was introduced with good motor response, followed two-year later by carbidopa/levodopa. Four years after diagnosis, the patient developed motor complication in the form of wearing-off episodes and peak-dose dyskinesia. In the following year cognitive decline appeared together with sleep disturbances, delusions, hallucinations and axial features. A new brain-MRI was repeated showing mild cortical diffuse atrophy, while cerebral 18F-FDG PET study showed bilateral hypometabolism involving frontal, parietal, and occipital cortices, precuneus, posterior cingulate cortex and basal ganglia. Neuropsychological assessment showed severe cognitive impairment involving mainly executive functions, attention, and visuospatial functions. A diagnosis of dementia associated with PD was made. Interestingly, a NGS screening of mutations in PD and dementia genes revealed a pathogenic monoallelic variant in the GRN gene p.R110X (class 1 ACMG).

*Conclusions:* This case underlying the phenotypic variability of GRN mutations that may rarely resemble an asymmetric levodopa-responsive idiopathic PD. Considering that clinical trials with recombinant monoclonal antibody against the GRN regulatory protein sortilin are ongoing, it appears extremely relevant to test for the presence of GRN mutations PD patients with early cognitive decline and a strong positive family history for PD or dementia.

**P168**

## Impulse control disorders in Parkinson's disease patients treated with dopamine agonists

*Stefano Mombelli*[1,2], F. Piattellini[1,2], S. Valente[1,2], D. Greco[1,2], G. Grigioni[2], L. Caremani[2], A. Govoni[2], S. Ramat[2]

[1]Department of Neurosciences, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
[2]Parkinson Unit, Department of NeuroMuscular-Skeletal and Sensorial Organs, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

*Introduction:* Impulse control disorders (ICDs) are a group of complex behavioral disturbances, characterized by the occurrence of repetitive and maladaptive behaviors that may be harmful to the individual or to others. ICDs such as pathological gambling (PG), hypersexuality (HS), compulsive eating and shopping (CE, CS) often occur as a non-motor complication of Parkinson's disease (PD) following, but not limited to, dopamine replacement therapy (DRT). Dopamine Agonists (DA) are the main risk factor but other factors include male sex, younger age or younger age at PD onset, a history of ICD symptoms, history of substance use or bipolar disorder.

*Objective:* We studied a cohort of patients with diagnosis of PD treated with DA, with former or current ICDs.

*Methods:* Subjects underwent neurological assessment at Parkinson Unit, Azienda Ospedaliero Universitaria Careggi, Florence in the period from January 2022 to January 2023.

*Results:* We describe 53 patients (32 Males, 21 Females) with former or current ICDs at the time of evaluation. Mean age at the time of the ICD onset was 66 (SD ± 8.78). The most frequent disorder was CE with 23 patients (43,4%). Thirteen patients (24,5%) developed CS, 12 (22,6%) with PG, 9 (16,9%) with HS, 4 (7,5%) with Hobbysm, 2 (3,7%) with Punding and in the end only one (1,8%) with Hoarning. Fourty-two patients developed only one ICD while 11 patients developed two ICDs. Twenty-six of these patients were treated with Pramipexole (mean 112.6 LEDD), 18 with Ropinirole (mean 187.1 LEDD), 6 with Rotigotine (mean 120 LEDD), 1 with Pramipexole and Rotigotine (mean 270 LEDD) and 1 with Pramipexole and Ropinirole (mean 185 LEDD). Mean time of ICD onset from the initiation of therapy with DA was 5.82 years (SD±4.12).

*Conclusions:* This study wants to describe the phenotypic spectrum of ICDs in PD patients.

**P169**

## Brain parenchyma sonography findings in patients affected by Parkinson's disease associated with GBA gene mutations

*Sabrine Othmani*[1], C. Frau[2], M.R. Murru[3], M.D. Azzena[4], C. Bagella[4], P. Solla[2], C.F. Bagella[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Unit of Neurology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
[3]Multiple Sclerosis Laboratory, Asl of Cagliari, Cagliari, Italy
[4]Unit of Nuclear Medicine, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

*Introduction:* Parkinson's disease associated with GBA mutations (PD-GBA) is a common cause of early onset PD, with a peculiar phenotype characterized by prominent non-motor features and even in the early stages of the disease. Single-photon emission computed tomography (SPECT) with DaT has high specificity and sensitivity, but in early stage of disease can be negative [1]. Brain Parenchyma Sonography (BPS) have been shown to be a useful tool in detecting early stage of PD and bilateral substantia nigra (SN) hyperechogenicity was detected in PD and already in the premotor stage [2]. Previous studies have found that BPS findings in PD-GBA is similar to those of patients with sporadic PD [3].

*Objective:* The aim of this study is to describe the BPS finding in a series of PD-GBA patients which could be consider as a biomarker both in early stages and in advanced PD-GBA.

*Methods:* Case series.

*Results:* Five patients affected by PD-GBA were investigated by BPS. Three patient carried the N370S mutation, one patient carried the E365K mutation and one patient was found to be carrier of a new mutation c.1312C>T. The age at onset was 48.5 ±9.9 years (range 40-59). The disease duration was 9.3 ±11.0 years (range 1-25). A DAT SPECT showed bilateral dopaminergic denervation in 4 patients and unilateral in one; a BPS revealed bilateral and symmetric hyperechogenicity of SN in 3 patients, asymmetrical hyperechogenicity, contralateral to the site of motor onset, in the others two.

*Conclusions:* GBA mutation carriers with PD have greater hyperechogenicity similar to sporadic PD. The mechanism underlying parkinsonism in these patients is still debated. The presence of this sonographic finding is consistent with iron deposition. Larger simple size is needed to explore possible differences in nigral echogenicity in PD patients with different genotipes.

**References:**

[1] De la Fuente-Fernandez R: Role of DaTSCAN and clinical diagnosis in Parkinson disease. Neurology 2012;78:696–701.
[2] Berg D, Seppi K, Behnke S, Liepelt I, Schweitzer K, Stockner H, Wollenweber F, Gaenslen A, Mahlknecht P, Spiegel J, Godau J, Huber H, Srulijes K, Kiechl S, Bentele M, Gasperi A, Schubert T, Hiry T, Probst M, Schneider V, Klenk J, Sawires M, Willeit J, Maetzler W, Fassbender K, Gasser T, Poewe W. Enlarged substantia nigra hyperechogenicity and risk for Parkinson disease: a 37-month Center study of 1847 older persons. Arch Neurol. 2011 Ju.
[3] Barrett MJ, Hagenah J, Dhawan V, Peng S, Stanley K, Raymond D, Deik A, Gross SJ, Schreiber-Agus N, Mirelman A, Marder K, Ozelius LJ, Eidelberg D, Bressman SB, Saunders-Pullman R; LRRK2 Ashkenazi Jewish Consortium. Transcranial sonography and functional imaging in glucocerebrosidase mutation Parkinson disease. Parkinsonism Relat Disord. 2013 Feb.

**P170**

## Parkinson disease and osteoporotic fractures: an observational retrospective study

*Albina Boreatti*, F. Nicolli, R. Ferrari, M.G. Caruso, A. Grecchi, R. Mattedi

Unità Operativa Medicina Fisica e Riabilitazione 1, Presidio Ospedaliero "Villa Igea", APSS Trento_ Trento, Italy

*Introduction:* In the guideline “Diagnosis, risk stratification and continuity of care”, the Italian National Institute of Health highlighted that Parkinson Disease (PD) patients are at high risk for osteoporotic fractures.

*Objective:* The aim of this observational retrospective study was to analyze osteoporotic fractures in PD patients underwent to physiatrist visit in “Villa Igea” Rehab Unit in Trento in 2022.

*Methods:* We included PD patients underwent to physiatrist visit in “Villa Igea” Rehab Unit in Trento in 2022. Datas collected were: sex, age, year of diagnosis, Hoehn e Yahr stage, levodopa treatment, history of falls, walking aid, history of osteoporotic fractures (year, number, site) and osteoporotic treatment.

*Results:* The patients included were 144: 74 females and 70 males; mean age 73 years. Median PD duration was 7 years, range few months -30 years. In 78% of the patients Hoehn-Yahr stage ranged from 2.5 and 4. Falls were reported in 49% of patients. Walking aid was used by 37% of patients. At least one osteoporotic fracture was occurred in 27 patients (19%), 22 women and 5 men. Femoral fracture was recorded in 11 patients: in 4 patients was occurred before 2020 (of whom 50% in osteoporotic treatment), in 7 patients after 2020 (of whom 28% in osteoporotic treatment). Vertebral fracture was recorded in 13 patients: in 5 patients was occurred before 2020 (of whom 80% in osteoporotic treatment), in 8 patients after 2020 (of whom 25% in osteoporotic treatment).
Wrist fracture was occurred in 6 patients, no one in osteoporotic treatment, regardless the date.

*Conclusions:* PD increases risk osteoporotic fracture and it doubles mortality fracture, but only few patients receive osteoporotic treatment. Maybe during Covid pandemic was harder undertake the right diagnostic-therapeutic process. After Covid pandemic Neurologists and Phisyatrists should ask PD patients about osteoporotic fracture and osteoporotic treatment.

**P171**

## The impact of increased perceived fatigue on postural control during a standing task in people with Parkinson's disease

*Thomas Bowman*[1], D. Anastasi[1], P. Arcuri[1], F. Baglio[1], R. Bertoni[1], A. Castagna[1], A. Crippa[1], M. Meloni[1,3], F.L. Saibene[1], M. Saresella[1], D. Cattaneo[1,2]

[1]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy
[2]Department of Physiopathology and Transplants, University of Milan, Milan, Italy
[3]UOC Neurologia; Azienda Ospedaliero-Universitaria, Cagliari, Italy

*Introduction:* Fatigue is a disabling symptom affecting from 30% to 70% of people with Parkinson's disease (PD). Even if several studies associate fatigue with the other non-motor symptoms, there is a lack of studies investigating the impact of increased perceived fatigue on postural control in people with PD.

*Objective:* To investigate the impact of increased perceived fatigue on the upright postural control during standing task in people with PD.

*Methods:* 14 people with PD (Age: 68,4±6,3 years, H&Y: 2-3, Male=7/Female=7) were recruited for this cross-sectional study. All participants wore optical markers (LAMB protocol) and performed a continuous overground walking task into a gait analysis laboratory equipped with a motion tracking system (SMART-TD and P6000, BTS S.p.A., Milan, Italy) until they reached perceived exertion of 17 (at lower limbs or breath) rated with the Borg scale [1]. Participants performed a standing task with eyes open (StandEO) and eyes closed (StandEC) on a force platform before (T0) and after (T1) the walking trial. Data were processed to extract range of motion of the trunk on the sagittal (TrunkSagROM) frontal (TrunkFrontROM) and horizontal (TrunkHorROM) plane, mean velocity (CoPVel) and ellipse area (CoPArea) of center of pressure. To verify the impact of perceived fatigue on postural variables, comparison of medians between T0 and T1 were analyzed using Wilcoxon sign rank test.

*Results:* Participants showed increase (T1-T0) in TrunkSagROM (1,1±3,3 deg), TrunkHorROM (1,4±3,3 deg) and in CoPArea (366,6±1037,7 mm2) during StandEO. Significant increases were detected in TrunkHorROM (2,2±3,2 deg; p=0,013) and CoPArea (382,2±468,9 mm2; p=0,028) during StandEC.

*Conclusions:* These preliminary findings suggest that increased perceived fatigue can somewhat affect the upright postural control in people with PD. Future studies should compare data of people with PD reporting increased perceived fatigue with individuals who do not report fatigue in the same task.

**References:**

[1] Penko AL, Barkley JE, Koop MM, Alberts JL. Borg scale is valid for ratings of perceived exertion for individuals with Parkinson's disease. Int J Exerc Sci. 2017 Jan 1;10(1):76-86.

**P172**

## Spectroscopic molecular characterization of saliva for the diagnosis and monitoring of Parkinson's disease

*Silvia Picciolini*[1], A. Gualerzi[1], M. Meloni[1,2], F.L. Saibene[1], D. Moscato[5], R. Conte[5], F. Rodà[1,3], V. Mangolini[1,4], A. Del Prete[1], L. Forleo[1], J.S. Navarro[1], M. Ceotto[5], M. Bedoni[1]

[1]IRCCS Fondazione Don Carlo Gnocchi Onlus, Milano, Italy
[2]UOC Neurologia, Azienda Ospedaliero-Universitaria, Cagliari, Italy
[3]Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, Brescia, Italy
[4]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[5] Università degli Studi di Milano, Milano, Italy

*Introduction:* Despite the plethora of proposed biomarkers for Parkinson's disease (PD), there are no specific molecules or signals able to early and uniquely identify the pathology onset, progression and stratification in easily accessible liquid biopsies. Saliva is a complex biofluid that contains multiple components shared with blood and cerebrospinal fluid, including PD related molecules. However, the limited analyte concentrations require high throughput and sensitive methods to use saliva in diagnostics. Raman spectroscopy (RS) is a label free vibrational technique able to detect the concomitant presence and concentration of different molecules, with demonstrated translatability to clinics [1].

*Objective:* The main aim of the present study was the identification of the molecular fingerprint of saliva of people with PD by RS, to be used as biomarker of disease onset and progression. Besides, our work was aimed at the identification of specific spectral assignment taking advantage of computational chemistry.

*Methods:* Saliva was collected from 25 people with PD and control subjects (33 healthy; 10 Alzheimer's patients). RS acquisition was performed on dry drops of saliva lied on aluminium slides. Multivariate statistical analysis was performed to compare data from the recruited subjects. Computational chemistry was used to investigate potential molecules involved in the observed PD associated spectral variations.

*Results:* The proposed procedure allows the collection of detailed and repeatable spectra using a fast protocol with minimal sample preparation. The selected groups of patients were discriminated with 89% accuracy and the salivary composition of PD samples was successfully correlated with levodopa equivalent daily doses, Hoehn&Yahr stages and UPDRS III [1]. Moreover, the preliminary computational chemistry results provide hints for the identification of the molecular contribution of alpha-synuclein to the salivary spectra.

*Conclusions:* The proposed pilot study paves the way to the use of the salivary Raman spectrum in order to assess PD onset and progression, having the potentiality to be transferred to clinics.

**References:**
[1] Carlomagno C et al., 2021. Front Neurosci; 15: 704963.

**P173**

## Home telemonitoring orthostatic hypotension in patients with Parkinson's disease: a new insight for a possibile telemedine service for degenerative diseases

*Marco Liccari*, M. Ajcevic, P. Polverino, M. Catalan, L. Antonutti, P. Manganotti

Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy

*Introduction:* In Parkinson's disease, orthostatic hypotension (OH) is a common but underappreciated symptom (PD). Information and communication technologies (ICT) have been essential in the management of chronic diseases like PD, especially during the COVID-19 epidemic, not only for assessing motor impairment but also for monitoring vital signs.

*Objective:* A real-life remote home monitoring system and procedure were to be proposed in this pilot project for PD patients with OH.

*Methods:* Vital metrics were collected by wireless devices and communicated to an ICT platform, which gave the healthcare provider data and smart notifications through an interactive web interface. Five-day monitoring was performed on eight patients with idiopathic PD and OH. Data were gathered and examined regarding OH episodes, therapeutic approaches, the effect on daily activities, and patient satisfaction.

*Results:* The suggested remedy made it possible to recognize episodes and then take appropriate medical action. 35 instances, mostly in the postprandial and afternoon records, were asymptomatic. Systolic and diastolic blood pressure were markedly lower during symptomatic episodes, while pressure declines were markedly greater when symptoms were present. High values for patient satisfaction and usefulness were seen.

*Conclusions:* The proposed home-monitoring system and methodology has shown to be effective in managing PD patients with OH during the COVID-19 pandemic by offering meaningful information and enabling quick responses.

**P174**

## Neurogenic orthostatic hypotension worsens gait performances in Parkinson's disease: an instrumental kinematic assessment

*Gabriele Imbalzano*[1,2], C. Ledda[1,2], M. Tangari[1,2], C.A. Artusi[1,2], E. Montanaro[2], M. Zibetti[1,2], M.G. Rizzone[1,2], M. Bozzali[1,2], L. Lopiano[1,2], A. Romagnolo[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy

*Introduction:* Recent studies based on clinical scales revealed that orthostatic hypotension (OH) could influence ambulatory capacity in patients with Parkinson's disease (PD). Preliminary use of kinematic assessment suggested their utility to predict risk of falls related to OH and found correlation between orthostatic arterial pressure and gait parameters like gait speed and stride length. However, the association between neurogenic OH (nOH) and gait parameters modification still needs further investigation.

*Objective:* To assess the influence of nOH on postural and gait parameters with APDM Mobility Lab™ motion sensors.

*Methods:* We evaluated consecutive advanced PD patients in their "best-on" state, with bedside assessment of nOH (using the DHR/DSBP ratio), and gait/balance parameters acquisition by means of wearable motion sensors (Sway test, 3-meters Timed-up and go test (TUG test), Two-minute walk test [2MWT]). We used analysis of covariance (adjusting for age, disease duration and Hoehn and Yahr stage [H&Y]) to evaluate differences in kinematic parameters between the two groups.

*Results:* We enrolled 91 patients, 18 with nOH (19.8%) and 63 without nOH (69.2%).The two groups showed similar age (62.3±7.3 vs. 60.3±8.3 years, p=0.094), levodopa equivalent daily dose and H&Y, while disease duration was longer in patients without nOH (12.8±5.4 vs. 10.2±2.3 years; p=0.03). After correcting for age, disease duration, and H&Y stage, patients with nOH showed lower stride length (p=0.011), lower gait speed (p=0.010), longer time of double support (p=0.042), and longer time of execution of TUG test (without reaching full statistical significance, p=0.062). Sway test presented no differences between groups.

*Conclusion:* nOH is independently associated with poorer objective gait performances in PD patients, probably due to a detrimental effect during prolonged walking. nOH assessment should be included in the evaluation of complicated gait issues, and its management could be of utmost importance in reducing falls, fractures, and other important PD complications.

**References:**

[1] Merola et al., 2016. Parkinsonism Relat Disord; 33: 65-71.
[2] Sturchio et al., 2021. J Neurol; 268(3): 1006-1015.
[3] Raccagni et al., 2020. Parkinsonism Relat Disord; 77:107-109.
[4] Norcliffe-Kaufmann et al., 2018. Ann Neurol; 83: 522-531.

**P175**

## Tele-assistance and role of the Case Manager: ensuring the care of patients with movement disorders

*Catia Leuzzi*[1], M. Gammone[1], M. Catotti[1], G.C. Moreschi[1], R. Cilia[2], R. Eleopra[3]

[1]Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[2]Clinical Neurology Unit, ASST Santi Paolo & Carlo and Department of Health Sciences, University of Milan, Milan, Italy
[3]Aldo Ravelli Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy

*Introduction:* The Covid-19 pandemic has highlighted some critical issues regarding the care and management of patients with neurological diseases, especially in patients with movement disorders such as Parkinson's Disease [1]. New strategies for the care and treatment of patients, such as telemedicine, have become necessary due to the difficulty of accessing hospitals [2]. For this reason, Fondazione IRCCS Istituto Neurologico Carlo Besta in Milan introduced the figure of the Case Manager (CM) who, through tele-assistance, responds to the clinical care problems of patients, and supports the figure of the caregiver.

*Objective:* To describe the role of the CM in responding to the compromised needs of the patient through tele-assistance, to provide personalized assessment and nursing care, contextualized to the care setting.

*Methods:* A descriptive analysis of the CM's work was conducted: the CM assists patients remotely and, through a semi-structured interview, following a specific flow-chart [3], identifies and manages the compromised need, administers validated measurement scales and guides the patient towards a resolution of the problem by activating, if necessary, other professional figures.

*Results:* From November 2020 to January 2023, 652 patients were taken under the care. There were 1855 'on demand' or 'proactive' events, 52% of which were managed independently by the CM. 19% were resolved by the CM after briefing with the neurologist and only 11.5% required direct action by the physician. The remaining 17.4% were managed by the multidisciplinary team at the hospital and territorial level, through collaboration with Rehabilitation Clinics or other specialists.

*Conclusions:* CM pays special attention to the caregivers' burden and ensures that the patient's compromised needs are taken under the care and monitored. This figure can contribute to the reduction of healthcare costs through the elimination of unnecessary services.

**References:**

[1] Cartella SM, Terranova C, Rizzo V, Quartarone A, Girlanda P. Covid-19 and Parkinson's disease: an overview. J Neurol. 2021 Dec;268(12):4415-4421. doi: 10.1007/s00415-021-10721-4. Epub 2021 Jul 27. PMID: 34313818; PMCID: PMC8313415.

[2] Hassan A, Mari Z, Gatto EM, Cardozo A, Youn J, Okubadejo N, Bajwa JA, Shalash A, Fujioka S, Aldaajani Z, Cubo E; International Telemedicine Study Group. Global Survey on Telemedicine Utilization for Movement Disorders During the COVID-19 Pandemic. Mov Disord. 2020 Oct;35(10):1701-1711. doi: 10.1002/mds.28284. PMID: 32833273; PMCID: PMC7461376.

[3] Cilia R, Mancini F, Bloem BR, Eleopra R. Telemedicine for parkinsonism: A two-step model based on the COVID-19 experience in Milan, Italy. Parkinsonism Relat Disord. 2020 Jun;75:130-132. doi: 10.1016/j.parkreldis.2020.05.038. Epub 2020 Jun 10. PMID: 32723588; PMCID: PMC7286232.

**P176**

## Prevalence of headache in a cohort of patients with Parkinson's disease

*Augusta Giglio*, C.V. Russo, L. Baratto, S. Perillo, N. Cuomo, G. De Michele, A. De Rosa

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

*Introduction:* Although Parkinson's disease (PD) is preeminently considered a movement disorder, most patients also present non-motor features, including autonomic and gastrointestinal dysfunction, cognitive impairment, psychiatric and sleep disturbances, and sensory symptoms. Until now, data about the prevalence of headache and migraine in PD are variable, the studies conducted so far are extremely heterogeneous and the results controversial.

*Objective:* Our aim was to assess the lifetime and last year prevalence and the phenomenology of the headache in a cohort of PD patients in comparison with control subjects (Ctrl).

*Methods:* We recruited 80 patients (36 F; 44 M) and 76 Ctrl (37 F; 39 M) selected among spouses and not consanguineous caregivers, comparable for age, sex and education. All participants underwent Beck Depression Inventory scale and a questionnaire assessing the presence of a history of headache and days with headache during the last year, describing characteristics of pain as well. Only patients were clinically evaluated by the motor section of Unified PD Rating Scale (UPDRS-III) and Hoehn and Yahr(HY) scale.

*Results:* Forty-seven patients (57%; 24 M/23 F) and 46 Ctrl (60%; 24 M/22 F; p=0.871) presented headache during the whole lifetime, whereas 28 patients (35%; 12 M/16 F) and 34 Ctrl (45%; 18 M/16 F; p=0.514) had suffered in the last year. No significant difference was observed in the overall prevalence of lifetime migraine among PD patients (30%; 5 M/9 F; p=0.387) compared to Ctrl (39%; 6 M/12 F; p=0.178), as well as the prevalence of tension-type headache (TTH) was comparable between the two groups (70% vs 61%; p=0.619). Migraine prevalence was significantly higher among women in both groups (11% M vs 25% F; p=0.067; 15% M vs 32% F; Ctrl: p=0.016). We found higher occurrence of headache family history (40% vs 13%; p=0.004), more common headache remission with age (p<0.001), particularly after the onset of motor symptoms (23%; p=0.037),among PD subjects rather than Ctrl. Furthermore, patients reported more common gradual onset of the pain (6% vs 16% p=0.068), less frequent visual aura (46% vs 64% p<0.001), and shorter attack duration than Ctrl (2% vs 13%; p=0.058).

*Conclusions:* The prevalence of migraine and TTH did not differ between PD subjects and controls. PD does not seem to act as a risk factor in the development of headache, but the dopaminergic pathway degeneration and progressive loss of DA activation on the trigeminal-vascular system might affect the severity and duration of the attacks and favor the improvement and remission of the headache in these patients.

**P177**

## Dopamine striatal availability in brain and body first Parkinson's disease patients

*Gabriele Bellini*[1], G. Palermo[1], E. Benevento[1], E. Belli[1], D. Frosini[2], E. Unti[2], E. Del Prete[2], R. Ceravolo[1,2,3]

[1]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Department of Medical Specialties, Neurology Unit, AOUP, Pisa, Italy
[3]Center for Neurodegenerative Diseases, Unit of Neurology, Parkinson's Disease and Movement Disorders, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

*Introduction:* Recently it has been suggested that there are two distinct subtypes of Parkinson's disease, brain-first (BR) and body-first (BO). In BR, the accumulation of a-synuclein (a-syn) starts in the brain and spreads to the enteric nervous system (ENS). In contrast, BO shows early autonomic dysfunction and RBD, and α-syn accumulation originates in the ENS, with more symmetrical nigrostriatal degeneration [1]. The purpose of this study is to evaluate possible differences in the 123I-FP-CIT SPECT ratios in patients with and without dysautonomia and RBD at diagnosis.

*Aim:* The purpose of this study is to evaluate possible differences in the 123I-FP-CIT SPECT ratios in patients with and without dysautonomia and RBD at diagnosis.

*Methods:* We retrospectively analyzed 56 PD patients undergoing 123I-FP-CIT SPECT at the time of diagnosis. We divided the patients into two groups: BO, those who already had RBD, constipation or orthostatic hypotension at the time of diagnosis, and BR. We evaluated striatal asymmetry index (SAI), 123I-FP-CIT SPECT specific binding ratio (SBR) and any differences between the two groups by t-test or Chi-square.

*Results:* The two groups were homogeneous in terms of age at the time of 123I-FP-CIT SPECT (62 ± 10.68 vs 66.38±10.15), levodopa equivalent dose (107.23 ± 161.17 vs 91.67 ± 109.11), lateralization and severity of motor symptoms (MDS-UPDRS III 18.51 ± 8.09 vs 15.73 ± 8.25). SAI revealed no significant differences in the two groups, while SBR at the left putamen (1.25 ± 0.37 vs 1.59 ± 0.38 p=0.003) and left striatum level (1.88 ± 0.46 vs 2.16 ± 0.38 p=0.036) were significantly reduced in BR patients compared to BO patients.

*Conclusions:* BR patients show a significant reduction at the level of the left striatum, particularly the putamen, compared to the BO group at the onset of the disease. However, there are no differences in SAI.

**References:**

[1] Horsager J, Andersen KB, Knudsen K, Skjærbæk C, Fedorova TD, Okkels N, Schaeffer E, Bonkat SK, Geday J, Otto M, Sommerauer M, Danielsen EH, Bech E, Kraft J, Munk OL, Hansen SD, Pavese N, Göder R, Brooks DJ, Berg D, Borghammer P. Brain-first versus body-first Parkinson's disease: a multimodal imaging case-control study. Brain. 2020 Oct 1;143(10):3077-3088. doi: 10.1093/brain/awaa238. PMID: 32830221.

**P178**

## Off-label 123I-FP-CIT SPECT use: a single-center, real-world study

*Roberto Avena*, M. Picillo, M.T. Pellecchia, P. Barone, R. Erro

Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Salerno, Italy

*Introduction:* Parkinsonian syndromes (PSs) are a group of disorders due to either neurodegenerative or non-neurodegenerative causes. Diagnosis is clinical, but 123I-FP-CIT SPECT, the only approved technique to assess the functional integrity of presynaptic nigrostriatal terminals, can assist in detecting neurodegenerative PSs [1]. Current formal indications include: I) differentiation between essential tremor (ET) and Parkinson's Disease (PD); II) differentiation between Dementia with Lewy Bodies and Alzheimer's disease.

*Objective:* To explore how often 123I-FP-CIT SPECT is prescribed off-label in clinical practice.

*Methods:* We collected the reason of requesting a 123I-FP-CIT SPECT, as formally indicated in the proforma request form to our Nuclear Medicine Department, during a 2-year period.

*Results:* Out of 70 scans, 37 (52.9%) were "on-label", differential diagnosis with tremor syndromes being the most common. Thirty-three scans (47.10%) were "off-label". About one-third of these were requested to differentiate degenerative from secondary parkinsonisms, especially drug-induced parkinsonism (DIP) (table 1), whereas 14.3% of the scans were solicited to detect presynaptic dopaminergic denervation in prodromal PD. The remaining were asked to confirm a clinical diagnosis of PD. Significant differences were noted when comparing requests from experts and non-experts in movement disorders.

*Conclusions:* We have here shown that the reasons for requesting a 123I-FP-CIT SPECT go far beyond the approved indications. We are aware our figures cannot be deemed representative of the overall use of 123I-FP-CIT SPECT in clinical practice because of potential biases due to the focus on movement disorders in our center, which might explain some "off-label" indications (i.e., differentiation between degenerative and secondary PSs and detection of prodromal PD) as suggested by the European Association of Nuclear Medicine [2]. Nevertheless, our results also show that there is the risk of inappropriateness in using this imaging technique (i.e., confirmation of PD), which calls for educative programs targeting general neurologists.

**References:**

[1] Balestrino R, Barone P, Filippi M, Erro R Unexpected (123I)FP-CIT SPECT findings: SWIDD, SWEDD and all DAT. J Neurol. 2022 Feb;269(2):758-770. doi: 10.1007/s00415-021-10809-x. Epub 2021 Sep 18. Erratum in: J Neurol. 2021 Dec 9;: PMID: 34537866.

[2] Morbelli S, Esposito G, Arbizu J et al (2020) EANM practice guideline/SNMMI procedure standard for dopaminergic imaging in Parkinsonian syndromes 1.0. Eur J Nucl Med Mol Imaging 47:1885–1912. https://doi.org/10.1007/s00259-020-04817-8.

**P179**

## Characterization of hemodynamic activity in resting-state networks associated with dementia in Parkinson's disease by fractal analysis

*Eleonora Fiorenzato*[1], A. Antonini[1], L. Weis[1], R. Biundo[2,3], V. D'Onofrio[4], F. Ferreri[1], S. Moaveninejad[1], C. Porcaro[1,5,6]

[1]Department of Neurosciences, University of Padua, Padua, Italy
[2]Department of General Psychology, University of Padua, Padua, Italy
[3]IRCCS San Camillo Hospital, Lido-Venice, Italy
[4]Unit of Neurology, Unit of Clinical Neurophysiology and Study Center for Neurodegeneration (CESNE), Department of Neuroscience, University of Padua, Padua, Italy
[5]Institute of Cognitive Sciences and Technologies (ISTC) - National Research Council (CNR), Rome, Italy
[6]Centre for Human Brain Health and School of Psychology, University of Birmingham, Birmingham, UK

*Introduction:* Changes in spontaneous neural activity have been reported in Parkinson's disease (PD) patients with cognitive deficits [1]. However, the frequency dependence of neuronal interaction activities, especially as measured by the fractional amplitude of low-frequency fluctuation (fALFF) and the degree of complexity of these interactions, remains still underinvestigated in PD with cognitive deficits.
Among complexity measures, the Higuchi's fractal dimension (FD) is emerging as being sensitive to capture the complexity of functional connectivity in neurological disorders [2, 3].

*Objective:* In the present study, we aimed to characterize the frequency dependence and the complexity changes of functional connectivity associated with PD cognitive decline.

*Methods:* As described in our previous work [4], 118 PD patients were matched for age, sex and education with 35 healthy controls (HC), and classified as 52 PD with normal cognition (PD-NC), 46 with mild cognitive impairment (PD-MCI), and 20 with dementia (PDD) based on an extensive cognitive evaluation. Rs-fMRI data was acquired on 1.5T scanner. Through spatial group ICA, 35 ICs were identified and sorted into 7 functional networks: basal ganglia, auditory (AN), visual, cerebellar, sensorimotor (SMN), cognitive executive (CEN), and default mode network (DMN). Further, a machine learning approach was used to test the best model based on distances between all FDs vs. fALFFs.

*Results:* The fALFF values in the DMN and CEN were decreased in PD, but increased in the AN, as compared to the HCs. PD-subgroups analyses highlighted that PDD had lower fALFF values than PD-NC/MCI in fronto-parietal internodes located within the CEN.

By contrast, PD patients showed increased complexity than HCs in the SMN, CEN and DMN. Namely, subgroups analyses showed that PDD had increased complexity compared to PD-NC/MCI, in fronto-parieto-occipital internodes located within the CEN and DMN.

Of note, the best model based on distances between all FDs reached the 78% accuracy in differentiating PD-cognitive states as opposed to the 62% accuracy between all fALFFs.

*Conclusions:* Our study indicates cognitive decline in PD is characterized by an altered spontaneous neuronal activity and an increased temporal complexity, involving namely the CEN and DMN and

reflecting an increased segregation of these networks. Hence, we proposed that FD may serve as a prognostic biomarker of PD-cognitive decline.

**References:**

[1] Rong S, Zhang P, He C, Li Y, Li X, Li R, et al. Abnormal Neural Activity in Different Frequency Bands in Parkinson's Disease With Mild Cognitive Impairment. Frontiers in Aging Neuroscience. 2021;13.
[2] Ziukelis ET, Mak E, Dounavi M-E, Su L, T O'Brien J. Fractal dimension of the brain in neurodegenerative disease and dementia: A systematic review. Ageing Research Reviews. 2022;79:101651.
[3] Smits FM, Porcaro C, Cottone C, Cancelli A, Rossini PM, Tecchio F. Electroencephalographic Fractal Dimension in Healthy Ageing and Alzheimer's Disease. PLOS ONE. 2016;11:e0149587.
[4] Fiorenzato E, Strafella AP, Kim J, Schifano R, Weis L, Antonini A, et al. Dynamic functional connectivity changes associated with dementia in Parkinson's disease. Brain. 2019;142:2860–72.

**P180**

## Occipital atrophy signature in prodromal Lewy bodies disease

*Alice Galli*[1], A. Pilotto[1], B. Chiarini[1], M. Giunta[1], D. Corbo[2], C. Tirloni[1], E. Premi[3], A. Lupini[1], C. Zatti[1], R. Gasparotti[2], A. Padovani[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Department of Molecular and Translational Medicine, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy
[3]Stroke Unit, ASST Spedali Civili of Brescia, Brescia, Italy

*Introduction:* Dementia with Lewy Bodies (DLB) is characterized by prominent parieto-temporo-occipital brain atrophy but less is known about structural brain alterations in the newly defined prodromal phases [1,2].

*Objective:* Objective of the study was to evaluate gray matter volume and cortical thickness changes in prodromal DLB (p-DLB) and compare them with matched controls and full-blown dementia (DLB-DEM).

*Methods:* The study included 69 subjects, namely 42 DLB patients (n=20 p-DLB and n=22 DLB-DEM) and 27 age-matched Healthy Controls (HC). Each subject underwent an extensive cognitive and behavioral assessment and structural 3-tesla MRI. T1-MRI images were pre-processed to obtain gray matter (GM) and surface segmentation. Univariate analyses using Voxel-Based Morphometry (VBM) on GM and cortical thickness were implemented to evaluate the differences between p-DLB, DLB-DEM and HC in an age – sex and education-adjusted model.

*Results:* p-DLB showed reduced GM volume and thickness in occipital and posterior lateral parieto-temporal regions compared to HC. DLB-DEM exhibited prominent reduction in cortical volume and thickness in posterior lateral occipito-temporal regions, together with a frontal thinning when compared to HC. Covariate analyses covariance analysis using occipital lobe as the seed point showed a related pattern of atrophy in temporal and frontal lobe increasing from prodromal to dementia stage, at variance with HC.

*Conclusions:* Occipital atrophy signature is detectable since the prodromal phases of DLB and correlated with long-distance pattern of atrophy in related regions. Further longitudinal studies are warranted to confirm and extend these findings.

**References:**

[1] McKeith IG, Ferman TJ, Thomas AJ, et al. Research criteria for the diagnosis of prodromal dementia with Lewy bodies. Neurology 2020;94:743–55.
[2] Sarro L, Senjem ML, Lundt ES, et al. Amyloid-β deposition and regional grey matter atrophy rates in dementia with Lewy bodies. Brain 2016;139:2740–50.

**P181**

## Hypothalamic involvement in multiple system atrophy: a structural MRI study

*Jacopo Pasquini*[1,2], M. Firbank[3], L. Best[2], V. Foster[2], G. Petrides[4], R. Ceravolo[1,5], K.N. Anderson[4], D.J. Brooks[3,6], N. Pavese[2,6]

[1]Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa, Italia
[2]Clinical Ageing Research Unit, Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK
[3]Positron Emission Tomography Centre, Newcastle University, Newcastle upon Tyne, UK
[4]The Newcastle Upon Tyne NHS Foundation Trust, Newcastle upon Tyne, UK
[5]Neurodegenerative Diseases Center, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy
[6]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, Aarhus, Denmark

*Introduction:* MSA is characterized by autonomic dysfunction and cerebellar/parkinsonian manifestations. The hypothalamus regulates autonomic and homeostatic functions and may also be involved in memory and learning. Pathological studies have identified hypothalamic neuronal loss and alpha synuclein glial and neuronal inclusions in MSA [1,2,3,4,5].

*Objective:* To investigate hypothalamic atrophy and its clinical correlates in multiple system atrophy (MSA) through MRI.

*Methods:* 11 MSA, 18 Parkinson's disease (PD) and 18 Healthy Controls (HC) were included. T1-weighted images were acquired on a 3T-MRI scanner. Images were pre-processed prior to applying a previously validated automated hypothalamic segmentation tool (https://github.com/BBillot/hypothalamus_seg). Whole hypothalamus volumes and 5 subregions were generated and adjusted for total intracranial volume. Hypothalamic volumes in MSA were compared with HC and PD volumes. Associations with clinical scales of autonomic dysfunction, depression, sleep problems and cognitive function were also tested.

*Results:* Age and sex were not different across groups. Total hypothalamus showed a trend towards a significant reduction in MSA vs HC ($t=1.937$, $p=0.065$) and posterior hypothalamus was significantly lower in MSA ($t=2.578$, $p=0.016$). A trend toward reduced posterior hypothalamus was also found in MSA compared to PD ($t=1.768$, $p=0.088$). Total hypothalamus volume was not associated with age or disease duration. In the parkinsonism (MSA+PD) group, total hypothalamus volume was associated with MoCA scores ($rho=0.425$, $p=0.022$), but not with autonomic (SCOPA-AUT), sleep (SCOPA-SLEEP), or depression (HADS-D) scores. Among hypothalamic subregions, only posterior hypothalamus volume was associated with MoCA scores ($rho=0.718$, $p<0.001$).

*Conclusions:* Total hypothalamus and posterior hypothalamus volumes are reduced in MSA compared with HCs. General cognitive functioning scores are associated with total hypothalamus and posterior hypothalamus volumes. The posterior hypothalamus volume includes the mammillary bodies and the lateral hypothalamus, regions associated with memory and learning functions. Further studies are needed to characterize the central correlates of autonomic dysfunction in MSA.

**References:**

[1]Cykowski MD, Coon EA, Powell SZ, et al (2015) Expanding the spectrum of neuronal pathology in multiple system atrophy. Brain 138:2293–2309. https://doi.org/10.1093/brain/awv114.
[2]Ozawa T (2007) Morphological substrate of autonomic failure and neurohormonal dysfunction in multiple system atrophy: Impact on determining phenotype spectrum. Acta Neuropathol 114:201–211. https://doi.org/10.1007/s00401-007-0254-1.

[3]Benarroch EE, Schmeichel AM, Parisi JE, Low PA (2015) Histaminergic tuberomammillary neuron loss in multiple system atrophy and dementia with Lewy bodies. Mov Disord 30:1133–1139. https://doi.org/10.1002/mds.26287.
[4]Burdakov D, Peleg-Raibstein D (2020) The hypothalamus as a primary coordinator of memory updating. Physiol Behav 223:112988. https://doi.org/10.1016/j.physbeh.2020.112988.
[5]Chen S, He L, Huang AJY, et al (2020) A hypothalamic novelty signal modulates hippocampal memory. Nature 586:270–274. https://doi.org/10.1038/s41586-020-2771-1.

**P182**

## Age at onset and functional striatal connectivity in drug-naïve patients with Parkinson's disease

*Emilia Norma Mosca*[1], R. De Micco[1], N. Piramide[1], F. Di Nardo[1], G. Caiazzo[1], M. Siciliano[1,2], G. Tedeschi[1], F. Esposito[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

*Introduction:* Compelling evidence suggests that age at onset may significantly affect the clinical picture of Parkinson's disease (PD), in terms of motor and nonmotor symptoms as well as rate of disease progression and development of complications.

*Objective:* We investigated the potential effect of age on the regional striatal functional connectivity (FC) in a cohort of early PD patients using resting-state functional MRI (rs-fMRI) data.

*Methods:* 147 drug-naïve PD patients and 38 healthy controls were enrolled. Non-hierarchical cluster were applied to stratify PD patients according to age at onset in 3 subgroups: 32 "early/young", 69 "early/intermediate" and 46 "early/old". "Early/old" PD were presenting with more severe motor and cognitive impairment relative to "early/young" patients. No differences were detected in terms of disease duration between the study groups. Clinical assessments as well as rs-fMRI were performed at baseline. Longitudinal clinical data were also collected at 4-year follow-up. Using connectivity-based parcellation, we obtained three regions-of-interest (ROIs) for different striatal functional subregions: sensorimotor, limbic and cognitive.

*Results:* The sensorimotor ROI showed increased FC with the left superior frontal gyrus, precuneus and cerebellum, and decreased FC with right lingual gyrus, paracentral lobule and left inferior frontal gyrus in "early/young" compared to "early/old" PD. The limbic ROI showed increased FC with the right temporal gyrus and decreased FC with the posterior cingulate cortex (PCC) in "early/young" compared to "early/old" PD. The cognitive ROI showed increased FC with the cerebellum and decreased FC with PCC in "early/young" compared to "early/old" PD. "Early-young" PD presented a higher risk to develop treatment-related motor complications after 4 years.

*Conclusions:* Specific changes in the striatal FC are associated with age at onset in PD patients. This pattern is related with better motor outcome at baseline and increased vulnerability to develop treatment-related motor complications overtime, suggesting the presence of striatal compensatory mechanisms.

**P183**

## Neuroimaging correlates of postural instability in motor subtypes of Parkinson's disease

*Andrea Quattrone*[1], C. Calomino[2], A. Sarica[2], M.E. Caligiuri[2], M.G. Bianco[2], B. Vescio[3], J. Buonocore[1], M.G. Vaccaro[2], A. Quattrone[2,3]

[1]Institute of Neurology, Department of Medical and Surgical Sciences, Magna Graecia University, Catanzaro, Italy
[2]Neuroscience Research Center, Department of Medical and Surgical Sciences, University "Magna Graecia", Catanzaro, Italy
[3]Neuroimaging Research Unit, Institute of Molecular Bioimaging and Physiology, National Research Council, Catanzaro, Italy

*Objective:* Neuroimaging correlates of postural instability (PI) in Parkinson's disease (PD) are largely unknown. We aimed to identify the brain structures associated with PI in PD subtypes using different MRI approaches.

*Methods:* We consecutively enrolled 142 PD patients (postural-instability-and-gait-difficulty [PIGD], n=66; tremor-dominant [TD], n=76) and 45 control subjects. PI was assessed using MDS-UPDRS-III pull-test item (PT). A whole-brain multi-regression analysis identified brain areas where grey matter (GM) volume correlated with the PT score in PD. Voxel-based morphometry (VBM) and Tract-Based Spatial Statistics (TBSS) were used to compare unsteady (PT³1) and steady (PT=0) PD patients. Associations between GM volume in regions of interest and several clinical features were then investigated using a multivariate regression analysis.

*Results:* PI was present in 65.1% of PIGD and 26.3% of TD patients. The whole-brain multi-regression analysis identified bilateral inferior frontal gyrus (IFG) and superior temporal gyrus (STG) as the only regions associated with the PT score. VBM showed reduced GM volume in fronto-temporal areas (superior, middle, medial and inferior frontal gyrus, and STG) in unsteady compared with steady PD patients, while TBSS did not show any difference between groups. GM volume in these fronto-temporal areas was significantly associated with the PT score, after correcting for confounding factors.

*Conclusions:* This study demonstrates a significant atrophy of the IFG and STG in unsteady PD patients, suggesting that these brain areas may play a role in the pathophysiological mechanisms underlying postural instability in PD. This result paves the way for further studies on postural instability in parkinsonism.

## P184

### White and gray matter alterations in de novo PD patients: which matter most?

*Matteo Costanzo*[1], S. Pietracupa[1], D. Belvisi[1,2], C. Piervincenzi[2], S. Tommasin[2], G. Pasqua[2], N. Petsas[1], M.I. De Bartolo[1], A. Fabbrini[2], N. Manzo[3], A. Berardelli[1,2], P. Pantano[1,2]

[1]IRCSS Neuromed, Pozzilli, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]IRCCS San Camillo Hospital, Lido di Venezia, Venice, Italy

*Background:* Only one study has investigated white matter (WM) and gray matter (GM) alterations in the same sample of patients [1]. The sample size of patients studied in this paper was small, there was no correlation between motor and nonmotor features, and the results were not corrected for multiple comparisons. An evaluation of GM and WM abnormalities in the same sample of early PD patients may provide a better understanding of early brain damage.

*Objectives:* This paper aimed to identify WM and GM abnormalities in a sample of early PD patients, and their correlations with motor and non-motor symptom severity.

*Methods:* We enrolled 62 *de novo* PD patients and 31 healthy subjects. Disease severity and non-motor symptom burden were assessed by the UPDRS part III and the Non-Motor Symptoms Scale, respectively. Cognitive performance was assessed using MoCA and Frontal Assessment Battery. All subjects underwent a 3-Tesla MRI protocol. MRI analyses included tract-based spatial statistics, cortical thickness, and subcortical and cerebellar volumetry.

*Results:* In comparison to control subjects, PD patients exhibited lower fractional anisotropy and higher mean, axial, and radial diffusivity in most WM bundles, including corticospinal tracts, the internal and external capsule, the anterior and posterior thalamic radiations, the genu and body of the corpus callosum, cerebellar peduncles, and superior and inferior longitudinal and fronto-occipital fasciculi. Correlations between MoCA scores and fractional anisotropy values in the right posterior thalamic radiation, left superior corona radiata, right inferior-fronto-occipital fasciculus, left inferior longitudinal fasciculus, bilateral anterior thalamic radiations, and bilateral superior longitudinal fasciculi were found. Smaller cerebellar volumes in early PD patients in the left and right crus I were also found. No GM changes were present in subcortical or cortical regions.

*Conclusions:* The combined evaluation of WM and GM in the same patient sample demonstrates that WM microstructural abnormalities precede GM structural changes in early PD patients.

**References:**

[1] Lee E, Lee JE, Yoo K, et al (2014) Neural correlates of progressive reduction of bradykinesia in de novo Parkinson's disease. Parkinsonism Relat Disord 20:1376–1381. https://doi.org/10.1016/j.parkreldis.2014.09.027.

**P185**

## Distinct striatal connectivity patterns in patients with Parkinson's disease with and without urinary symptoms

*Noemi Piramide*[1], R. De Micco[1], F. Di Nardo[1], M. Siciliano[1,2], G. Caiazzo[1], G. Tedeschi[1], F. Esposito[1], A. Tessitore[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Neuropsychology Laboratory, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

*Introduction:* Urinary symptoms are frequent in patients with Parkinson's disease (PD) and may severely affect quality of life. The pathophysiological mechanisms potentially underpinning their presence are still unclear.

*Objective:* We aimed at investigating the potential effect of urinary symptoms on the regional striatal functional connectivity (FC) in a cohort of drug-naïve PD patients applying a region-of-interests-(ROIs)-based approach to resting-state functional MRI data.

*Methods:* Seventy-nine drug-naive PD patients (45 PD-urinary+/34 PD-urinary-) and 38 healthy controls (HC) were consecutively enrolled. Motor, nonmotor and cognitive assessments were performed. Using connectivity-based parcellation, we obtained three ROIs for different striatal functional subregions: sensorimotor, limbic and cognitive.

*Results:* No demographical/clinical differences were found between PD-urinary+ and PD-urinary- patients. PD-urinary+ showed increased FC between the sensorimotor ROI and the bilateral fusiform gyri compared to HC. The limbic ROI showed increased FC with the right superior temporal gyrus, and decreased FC with left insula, left anterior cingulate cortex and right anterior PFC in PD-urinary+ patients compared to HC. The right cognitive ROI showed increased FC with the left insula in PD-urinary+ patients compared to HC.
PD-urinary- showed decreased FC between the sensorimotor ROI and the bilateral substantia nigra as well as decreased FC between the limbic ROI and the right anterior PFC and left dorsal PFC compared to HC. Compared to PD-urinary-, PD-urinary+ showed increased FC between the sensorimotor ROI and the right premotor/supplementary as well as the primary motor areas, and decreased FC between the sensorimotor ROI and the right angular gyrus. The limbic ROI showed also decreased FC with the left anterior PFC in PD-urinary- patients compared to PD-urinary+.

*Conclusions:* Our findings revealed that the presence of a specific pattern of striatal FC may be potentially associated to altered urge perception and motor control in early PD patients, eventually leading to high micturition frequency and urgency.

**P186**

## Conventional and iron-sensitive MRI brain imaging in the differential diagnosis of 4RTauopathies

*Eleonora Del Prete*[1], G. Migaleddu[2], D. Frosini[1], E. Benevento[3], S. Barone[3], S. Mazzucchi[3], M. Cosottini[4], R. Ceravolo[3]

[1]Neurology Unit, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[2]Neuroradiology Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[3]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[4]Neuroradiology Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

*Background:* Progressive Sopranuclear Palsy (PSP) and Corticobasal Degeneration (CBD), are 4Rtaupathies presenting as atypical parkinsonisms. Although the clinical presentation is usually different between them sometimes the differential diagnosis could be challenging.
The research of radiological biomarkers to help the clinician to differentiate these disease is fervent. Susceptibility weighted imaging (SWI)is sensitive to iron accumulation and allows to identify micro-structural brain modificationsin substantia nigra pars compacta of subjects with neurodegenerative parkinsonism, moreover susceptibility abnormalities are detected in the cortex of CBD patients. This last sign, recently described, consists of a signal alteration on the frontoparietal cortex, expression of the ongoing neurodegeneration at this level.

*Objectives:* The aim of this study is to explore the accuracy of different radiological MRI imaging biomarkers in the differential diagnosis between PSP and Corticobasal Syndrome (CBS) and between CBS patients and a subgroup ofPSP patients with CBS phenotype (PSP-CBS).

*Materials and methods:* We recruited patients with clinical diagnosis of PSP and CBS. All patients underwent a neurological examination and 3T MRI imaging. Conventional and iron sensitive radiological biomarkers were investigated in our cohort.

*Results:* We found that signal alteration of substantia nigra pars compacta on SWI was present in 97% of PSP patients and 54% of CBS patients. Mesencephalic atrophy was detected in 66% of PSP patients and none of CBS, moreover in the 81% of CBS and 4% of PSP asymmetric frontoparietal atrophy was found. Our study also showed that cortical intensity abnormalities in SWI was present in all patients with CBS, it was also present in 60% of PSP-CBS patients and in 14% of PSP phenotypes other than CBS.

*Conclusions:* These results confirm the importance of brain MRI imaging in the differential diagnosis of 4RTauopathies, with interesting perspective regarding iron-sensitive imaging.

**P187**

## EEG-based sleep state functional connectivity in Parkinson's disease

*Valerio Ferrari*[1], M. Conti[1], M. Pierantozzi[1], N.B. Mercuri[2], A. Stefani[1], C. Liguori[2]

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

*Introduction:* Parkinson's disease (PD) is a neurodegenerative disorder characterized by a multisystem involvement, with heterogeneous complex of motor and non-motor symptoms. Among them, sleep disorders represent a common clinical feature in PD. Previous functional connectivity (FC) studies have shown an impairment in functional connectivity (FC) in PD patients in conscious state [1], while FC in sleep state has been scarcely examined. Thus, FC, based on electroencephalography (EEG) registration during polysomnography (PSG), may lead to a deeper understanding of the pathophysiology of this disorder.

*Objective:* To analyze the differences in FC during the different phases of sleep between PD patients and healthy controls by means of PSG.

*Methods:* 14 PD patients and 13 healthy controls (HC) were included in this study. The analyses used custom-written scripts on the Matlab platform, combined with high-level functions of Brainstorm toolbox [2]. Study subjects underwent PSG examination, with 8 EEG traces. Then, FC matrices of each subject were calculated in four frequencies (δ-θ-α-β), using weighted phase-lag index (wPLI) [3]. Finally, we compared FC matrices between healthy controls and de novo PD patients through two-samples T-test.

*Results:* We identified a significant bilateral reduction in FC between fronto-occipital and centro-temporal connections in δ band in slow-wave NREM sleep phase in PD patients compared to HC. On the contrary, a significant increasing in FC between bilateral fronto-temporal and fronto-central links was found in REM sleep in θ frequencies in PD patients compared to HC.

*Conclusion:* Our study showed that PD is associated with abnormal FC during different phases of sleep. In particular, the reduction in FC in δ band in NREM sleep may be linked to a widespread impairment of different cortical networks. Conversely, the increasing of connectivity in θ frequency band in REM sleep may be associated with REM sleep behavior disorder (RBD).

**References:**

[1] M. Conti et al., "Brain Functional Connectivity in de novo Parkinson's Disease Patients Based on Clinical EEG," Front. Neurol., vol. 13, no. March, 2022, doi: 10.3389/fneur.2022.844745.
[2] F. Tadel, S. Baillet, J. C. Mosher, D. Pantazis, and R. M. Leahy, "Brainstorm: A user-friendly application for MEG/EEG analysis," Comput. Intell. Neurosci., vol. 2011, 2011, doi: 10.1155/2011/879716.
[3] T. M. Lau, J. T. Gwin, K. G. McDowell, and D. P. Ferris, "Weighted phase lag index stability as an artifact resistant measure to detect cognitive EEG activity during locomotion," J. Neuroeng. Rehabil., vol. 9, no. 1, 2012, doi: 10.1186/1743-0003-9-47.

**P188**

## Transcranial sonography: a useful tool in patients affected by parkinsonism with normal dopaminergic functional imaging

*Valentina Floris*[1], C. Frau[2], S. Othmani[1], S. Nuvoli[3], A. Spanu[3], P. Solla[2], C.F. Bagella[2]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[2]Unit of Neurology, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
[3]Unit of Nuclear Medicine, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

*Introduction:* Scans without evidence of Dopaminergic Deficit (SWEDD) represent 10% of patients affected by parkinsonism resembling Parkinson's Disease (PD) [1]. According to new PD diagnostic criteria normal imaging result is defined as absolute exclusion criterium but the significance of DAT still remain unclear [2]. Recent findings argue that striatal dopamine transporter imaging may reflect dopaminergic activity rather than number of surviving neurons or their striatal projection axons [3]. Hyperechogenicity of Substantia Nigra (SN), detected by Transcranial sonography (TCS) could represent a useful tool to identify these patients [4].

*Objective:* To evaluate the TCS in the patients affected by SWEDD-parkinsonism.

*Methods:* 3 patients with a clinical diagnosis of tremor-dominant parkinsonism and normal [123] IFP-CIT SPECT scans were recruited. TCS was performed with a 2.5 MHz transducer using a transtemporal window. Hyperechogenicity of SN was defined as an echogenic area above of 0.20 cm2.

*Results:* Patient 1: female; 55 years old; age at motor symptoms onset: 47 years; disease duration at SPECT: 8 years; disease duration at TCS: 8 years; SN hyperechogenicity (right: 0,41 cm2, left 0,38 cm2);
Patient 2: female; 76 years old; age at motor symptoms: 74 years; disease duration at SPECT: 1 years; disease duration at TCS: 2 years; SN hyperechogenicity (right:0,46 cm2, left:0,33 cm2);
Patient 3: male; 70 years old; age at motor symptoms: 53 years; disease duration at SPECT: 14 years; disease duration at TCS: 17 years; SN hyperechogenicity (right: 0,28 cm2, left 0,22 cm2);
All patient respond to dopaminergic therapy.

*Conclusions:* Clinical diagnosis of SWEDD-parkinsonism with normal dopaminergic functional imaging is challenging and still debated, and maybe alternative diagnosis could be considered. TCS, which detects SN hyperechogenicity found in up to 90% of patients with PD, could be a useful tool in identify these patients, when presynaptic dopaminergic nerve terminals are still preserved.

**References:**

[1] Marek K, Seibyl J, Eberly S, et al. Parkinson Study Group PRECEPT Investigators. Longitudinal follow-up of SWEDD subjects in the PRE- CEPT Study. Neurology 2014;82:1791–1797.
[2] Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord 2015;30:1591–1601.
[3] Honkanen EA, Saari L, Orte K, Gardberg M, Noponen T, Joutsa J, Kaasinen V. No link between striatal dopaminergic axons and dopamine transporter imaging in Parkinson's disease. Mov Disord. 2019 Oct.
[4] Walter U, Behnke S, Eyding J, Niehaus L, Postert T, Seidel G, Berg D. Transcranial brain parenchyma sonography in movement disorders: state of the art. Ultrasound Med Biol. 2007 Jan.

# Indice Autori

# A

## B

## C

# D

## E

# F

## G

## H



## I



## J



## K



## L

# M

## N

## O



## P

# Q



# R

## S

# T

## U



## V

## W



## Y



## Z