Endorsed by the
International Parkinson and Movement Disorder Society

International Parkinson and
Movement Disorder Society

con il patrocinio di

Comune di Catania

UNIVERSITÀ degli STUDI di CATANIA

5° Congresso Accademia LIMPE-DISMOV

Accademia Italiana per lo Studio della Malattia di Parkinson e i Disordini del Movimento

CATANIA

22-24 MAGGIO 2019

Centro Congressi - Four Points by Sheraton Catania Hotel

ACCADEMIA ITALIANA
MALATTIA DI PARKINSON
E DISORDINI DEL MOVIMENTO

ACCADEMIA LIMPE-DISMOV

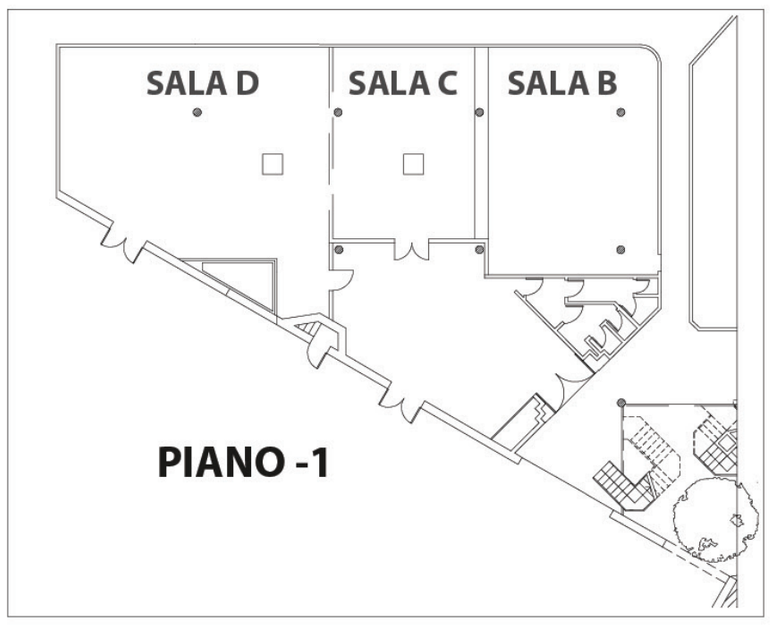
CONSULTA GLI ABSTRACT

PLANIMETRIA

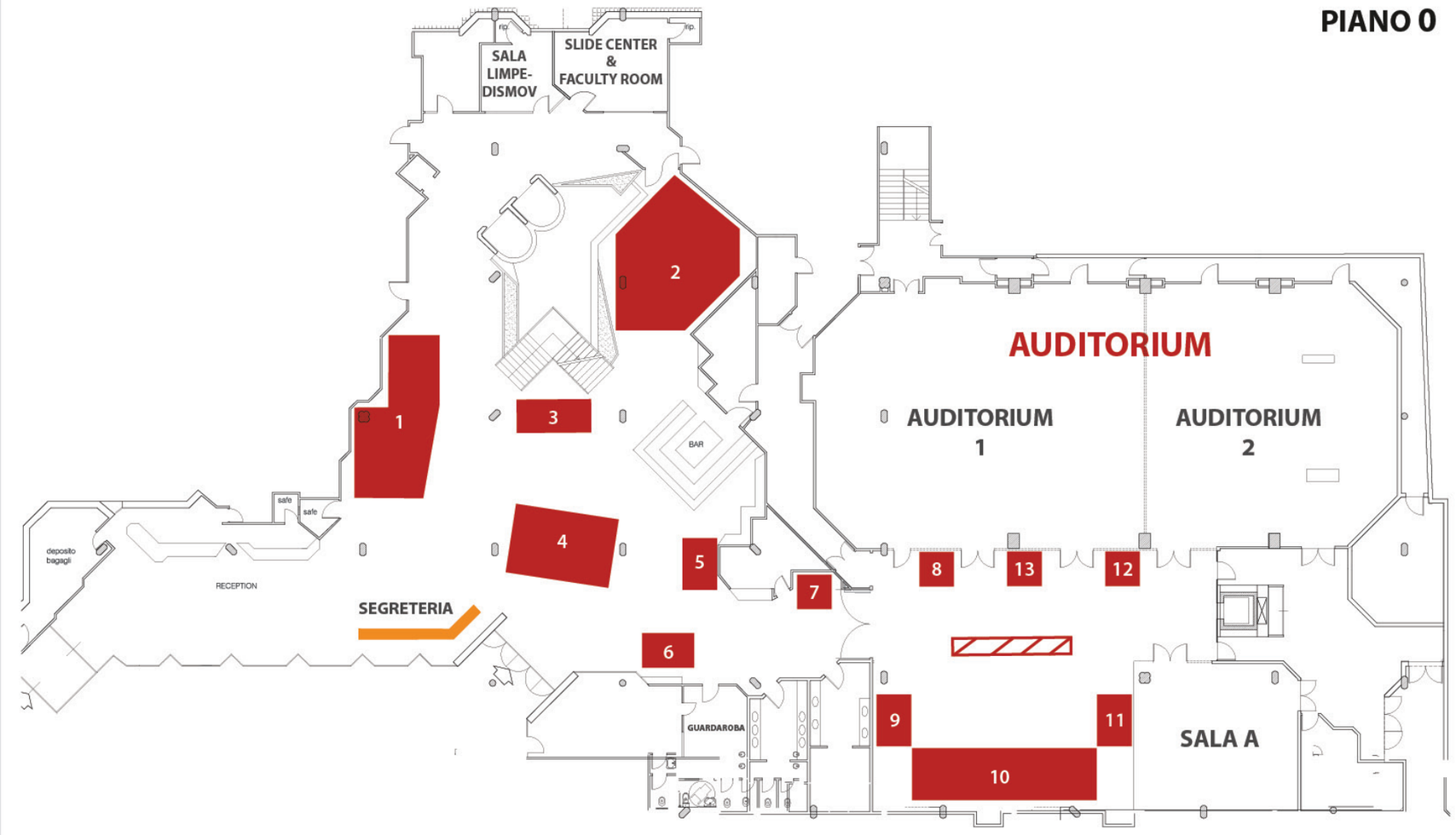
CENTRO CONGRESSI FOUR POINTS BY SHERATON CATANIA HOTEL

PIANO 1
AREA POSTER E RISTORAZIONE

PIANO 4
SALA E



PIANO 0



LEGENDA

Stand

1. Zambon Italia S.r.l.
2. AbbVie S.r.l.
3. UCB Pharma S.p.A.
4. Istituto Luso Farmaco d'Italia
5. Ecupharma S.r.l.
6. Chiesi Farmaceutici S.p.A.
7. Medtronic Italia S.p.A.
8. Piam Farmaceutici S.p.A.
9. Neuraxpharm Italy S.p.A
10. BIAL Italia S.r.l
11. GE Healthcare S.r.l.
12. Arcapharma S.r.l.
13. Careapt S.r.l.

Area Catering

Segreteria

CONSULTA GLI ABSTRACT

MERCOLEDÌ 22 MAGGIO 2019

PROGRAMMA SCIENTIFICO

CONGRESSO

15.10/15.50 **Cerimonia Inaugurale del Congresso**

L. Lopiano (Torino) - *G. Mancardi* (Genova) - *M. Zappia* (Catania)

15.50/17.50 SESSIONE PLENARIA **AUDITORIUM**

Aggiornamenti sui disturbi del movimento

Moderatori: *U. Bonuccelli* (Pisa) – *E. Costanzo* (Catania) – *A. Nicoletti* (Catania)

15.50 **Malattia di Parkinson** - *A. Nicoletti* (Catania)
16.20 **Parkinsonismi atipici** - *M.T. Pellecchia* (Salerno)
16.50 **Coree** - *A.R. Bentivoglio* (Roma)
17.20 **Tremore** - *G. Calandra Buonaura* (Bologna)

17.50/18.50 SESSIONE **AUDITORIUM**

I disturbi cognitivi nella malattia di Parkinson

con il contributo incondizionato di Istituto Luso Farmaco d'Italia S.p.A.
Moderatore: F. Stocchi (Roma)

17.50 **La diagnosi precoce dei disturbi cognitivi nella malattia di Parkinson** - *A. Padovani* (Brescia)
18.20 **Opzioni terapeutiche della fase iniziale** - *A. Tessitore* (Napoli)

18.50/19.50 SESSIONE **AUDITORIUM**

Continuous dopaminergic delivery and broad receptor profile: what is still to be learned?

con il contributo incondizionato di UCB Pharma S.p.A.

18.50 **The added value of a wide spectrum dopaminergic stimulation** - *K.R. Chaudhuri* (London, UK)
19.20 **Round Table**
The specific clinical relevance and outcome
K.R. Chaudhuri (London, UK), *L. Ferini Strambi* (Milano), *A. Stefani* (Roma), *F. Stocchi* (Roma)

CONSULTA GLI ABSTRACT

CONGRESSO

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

08.00/08.30 CONFERENZE DIDATTICHE

AUDITORIUM

08.00/08.30 **Neuroimaging strutturale e funzionale**
G. Arabia (Catanzaro)

08.40/09.00 **Flash news**
Diagnosi e terapie immunologiche nel Parkinson e parkinsonismi atipici
con il contributo incondizionato di Biogen Italia S.r.l.
R. Ceravolo (Pisa)

SALA A

08.00/08.30 **Come riconoscere i disturbi del movimento funzionali**
M. Tinazzi (Verona)

SALA B

08.00/08.30 **Tossina botulinica**
P. Girlanda (Messina)

08.40/09.00 **Flash news**
Verso una nuova indicazione della tossina botulinica di tipo A: la scialorrea
D. Restivo (Catania)

SALA C

08.00/08.30 **Terapie infusionali**
M. Sensi (Ferrara)

08.40/09.00 **Flash news**
I principi della DBS nella programmazione degli elettrocateteri direzionali
con il contributo incondizionato di Abbott Medical Italia S.p.A.
R. Eleopra (Milano)

SALA D

08.00/08.30 **Stimolazione cerebrale profonda**
M.G. Rizzone (Torino)

08.40/09.00 **Flash news**
Nuovi algoritmi di programmazione della DBS attraverso il neuroimaging e il calcolo del VTA
M. Pilleri (Arcugnano)

SALA E

08.00/08.30 **Stimolazione magnetica**
N.G. Pozzi (Pavia)

09.00/10.30 SESSIONE PLENARIA — AUDITORIUM

Modalità di funzionamento delle terapie nei disordini del movimento
Moderatori: P. Calabresi (Perugia) – *R. Ceravolo* (Pisa) – *G. Pennisi* (Catania)

09.00 **Meccanismi dell'effetto placebo nella malattia di Parkinson** - *L. Lopiano* (Torino)
09.30 **Meccanismi dopaminergici e non dopaminergici** - *A. Berardelli* (Roma)
10.00 **L'integrazione cognitivo-motoria nella riabilitazione** - *L. Avanzino* (Genova)

10.30/11.30 PAUSA CAFFÈ E SESSIONI POSTER — AREA POSTER

Distonie - *Moderatore: A. Castagna* (Milano)
Neurofisiologia 1 - *Moderatore: M. Bologna* (Roma)
Terapie avanzate - *Moderatore: F. Valzania* (Reggio Emilia)
Disordini del movimento 1 - *Moderatore: M.C. Altavista* (Roma)
Parkinson 1 - *Moderatore: C.E. Cicero* (Catania)
Riabilitazione 1 - *Moderatore: M. Rizzo* (Palermo)
Neuroimmagini 1 - *Moderatore: G. Arabia* (Catanzaro)
Disordini del movimento 2 - *Moderatore: V. Fetoni* (Milano)
Terapia - *Moderatore: T.P. Avarello* (Palermo)

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

11.30/13.00 SESSIONE PARALLELE — AUDITORIUM 1

Comunicazioni Libere

*M*oderatori : *G. Meco* (Roma) – *A. Pisani* (Roma)

11.30 **Proiezioni extrastriatali dopaminergiche e serotoninergiche nella malattia di Parkinson e demenza a corpi di Lewy: uno studio 123I-FP-CIT**
A. Pilotto, F. Schiano Di Cola, E. Premi, R. Grasso, R. Turrone, S. Gipponi, A. Scalvini, E. Cottini, B. Paghera, V. Garibotto, M.C. Rizzetti, L. Bonanni, B. Borroni, S. Morbelli, F. Nobili, U.P. Guerra, D. Perani, A. Padovani

11.40 **Attivazione sistemica del pathway Nrf-2 nei pazienti con malattia di Parkinson**
T. Schirinzi, S. Petrillo, G. Di Lazzaro, E. Bertini, N.B. Mercuri, F. Piemonte, A. Pisani

11.50 **Variazioni pressorie ortostatiche iniziali nella malattia di Parkinson: associazione con cadute, sincope e sintomi ortostatici**
N. Campese, A. Fanciulli, G. Göbel, J.P. Ndayisaba, S. Eschlboeck, C. Kaindlstorfer, C. Raccagni, R. Granata, U. Bonuccelli, R. Ceravolo, W. Poewe, G.K. Wenning

12.00 **Studio longitudinale su 6 anni di una coorte di soggetti portatori di mutazione del gene GBA: studio di markers prodromici di malattia di Parkinson**
M. Avenali, M. Toffoli, S. Mullin, A. McNeill, D. Hughes, A. Mehta, F. Blandini, A.H.V. Schapira

12.10 **Esistono differenti pattern di attivazione cerebrale in pazienti con malattia di Parkinson con e senza freezing of gait durante l'esecuzione di un task motorio?**
N. Piramide, F. Agosta, E. Sarasso, E. Canu, S. Galantucci, A. Tettamanti, M.A. Volontè, M. Filippi

12.20 **Le alterazioni della postura nella malattia di Parkinson: uno studio multicentrico clinico epidemiologico**
C. Geroin, M. Gandolfi, R. Ceravolo, M. Capecci, E. Andrenelli, M.G. Ceravolo, L. Bonanni, M. Onofrj, M. Vitale, M. Catalan, P. Polverino, C. Bertolotti, S. Mazzucchi, S. Giannoni, N. Smania, S. Tamburin, L. Vacca, F. Stocchi, F.G. Radicati, C.A. Artusi, M. Zibetti, L. Lopiano, A. Fasano, M. Tinazzi

12.30 **Patologia limbica da aggregati di sinucleina (tipo Lewy Bodies/Neurites) e sintomi del cluster psicotico in pazienti con demenza: risultati preliminari dalla Brain Bank di Abbiategrasso**
T.E. Poloni, V. Medici, G. Negro, A. Davin, E. Fogato, E. Riva, R. Vaccaro, S. Abbondanza, E. Galbiati, R. Castoldi, M. Ceroni, T. Suardi, A. Guaita

12.40 **Fattori di rischio vascolari e WMLs come fattori di rischio di deficit cognitivo nella malattia di Parkinson. Uno studio longitudinale dalla coorte PaCoS**
A. Luca, R. Monastero, G. Donzuso, R. Baschi, C.E. Cicero, C. Terravecchia, A. Salerno, M. Zuccarello, M. Davì, V. Restivo, G. Mostile, M. Zappia, A. Nicoletti

12.50 **Infusione intestinale di levodopa: analisi di sopravvivenza in pazienti trattati per oltre 10 anni**
C.A. Artusi, R. Balestrino, G. Imbalzano, S. Bortolani, E. Montanaro, M. Zibetti, L. Lopiano

11.30/13.00 SESSIONE PARALLELE — AUDITORIUM 2

Comunicazioni Libere

*M*oderatori: *A. Conte* (Roma) – *C. Pacchetti* (Pavia)

11.30 **L'alterazione della plasticità cerebrale di tipo LTP nella malattia di Parkinson può essere normalizzata dalla stimolazione transcranica a corrente alternata a frequenza gamma**
A. Guerra, A. Suppa, F. Asci, V. D'Onofrio, V. Sveva, A. Berardelli

11.40 **Connettoma funzionale in pazienti con malattia di Parkinson drug-naïve: correlazione con fenotipi motori e non motori e predizione della necessità di levodopa**
R. De Micco, F. Agosta, S. Basaia, M. Siciliano, C. Cividini, G. Tedeschi, A. Tessitore, M. Filippi

11.50 **Fattori determinanti la risposta alla stimolazione cerebrale profonda nella malattia di Parkinson**
M. Sarchioto, M. Zibetti, L. Ricciardi, E. Montanaro, M.J. Edwards, L. Lopiano, F. Morgante

12.00 **Biomarcatori del disturbo del comportamento in sonno REM idiopatico e associato a narcolessia**
E. Antelmi, F. Pizza, V. Donadio, Y.L. Sosero, R. Liguori, G. Plazzi

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

12.10 **Atrofia cerebellare in pazienti con distonia cervicale**
F. Silvestre, S. Peluso, S. Cocozza, G. Pontillo, C. Russo, F. Baglio, A. Macerollo, A. Brunetti, F. Manganelli, A. Castagna, M. Esposito

12.20 **La risposta alla terapia con levodopa negli stadi tardivi di malattia: studio caso-controllo**
M. Fabbri, M. Coelho, D. Abreu, L. Correia Guedes, M.M. Rosa, A. Antonini, J.J. Ferreira

12.30 **Sindrome da sospensione di dopamino-agonisti in pazienti sardi affetti da malattia di Parkinson**
P. Solla, R. Pau, G. Orofino, T. Ercoli, V. Melas, V. Pierri, D. Fonti, G. Defazio

12.40 **La memoria prospettica nella malattia di Parkinson: il ruolo dei sottotipi motori**
A. D'Iorio, G. Maggi, C. Vitale, D. Di Meglio, L. Trojano, G. Santangelo

12.50 **Discinesie indotte da levodopa e disturbo del controllo degli impulsi: due facce della stessa medaglia?**
F. Paolini Paoletti, N. Tambasco, G. Cappelletti, P. Eusebi, S. Simoni, P. Nigro, E. Brahimi, M. Filidei, P. Calabresi

13.00/14.00 COLAZIONE DI LAVORO E SESSIONI POSTER — AREA POSTER

Neurofisiologia 2 - *Moderatore: L.M. Romito* (Milano)

Parkinson 2 - *Moderatore: L. Vacca* (Roma)

Parkinson 3 - *Moderatore: R. Cilia* (Milano)

Disturbi Cognitivi 1 - *Moderatore: R. Colao* (Catanzaro)

Neuroimmagini 2 - *Moderatore: N. Tambasco* (Perugia)

Disturbi Cognitivi 2 - *Moderatore: M. Amboni* (Salerno)

Genetica - *Moderatore: C. Vitale* (Napoli)

Riabilitazione 2 - *Moderatore: E. Pelosin* (Genova)

14.00/16.40 SESSIONE INTERNAZIONALE — AUDITORIUM

Joint Session

Accademia LIMPE-DISMOV & German Parkinson Association

Parkinsonisms

14.00 **Introduction -** *G.U. Höglinger* (München, Germania) - *L. Lopiano* (Torino)

14.10 **Lectures** *Chairmen: A. Berardelli* (Roma) - *L. Lopiano* (Torino)
Update on PSP/CBD - *G.U. Höglinger* (München, Germania)
Update on MSA/DLB - *P. Cortelli* (Bologna)

15.10 **Oral Presentations** *Chairmen*: *A. Antonini* (Padova) - *M. Zappia* (Catania)
Prospective PSP cohort study - *G. Respondek* (München, Germania)
MSA: prospective MSA cohort study - *J. Levin* (München, Germania)
Digital biomarkers - *J. Klucken* (Erlangen, Germania)
MR Imaging - *J. Kassubek* (Ulm, Germania)
PET Imaging - *T. van Eimeren* (Köln, Germania)
Automated MRI biomarkers in parkinsonisms - *S. Nigro* (Catanzaro)
Susceptibility weighted MRI in atypical parkinsonisms - *S. Mazzucchi* (Pisa)
Cognitive impairment in MSA and PSP - *R. Biundo* (Venezia Lido)
MSA - *G. Giannini* (Bologna)
Clinical and radiological characterization of MDS subtypes in the Italian PSP population
M. Picillo (Salerno)

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

10.30/11.30 PAUSA CAFFÈ E SESSIONI POSTER — AREA POSTER

Sessione Poster "Distonie"

Moderatore: A. Castagna (Milano)

01 **Distonia focale della mano e riabilitazione: revisione sistematica di studi randomizzati controllati**
M. Tofani, G. Galeoto, E. Castelli, A. Berardi, G. Fabbrini

02 **Analisi vocale in pazienti affetti da disfonia laringea**
F. Asci, A. Suppa, L. Marsili, G. Ruoppolo, G. Costantini, G. Saggio, A. Berardelli

03 **RGS9-2 ripristina i livelli e il signaling dei recettori D2 della dopamina in modelli murini di distonia DYT1**
A. Pisani, G. Ponterio, P. Imbriani, A. Tassone, G. Sciamanna, S. Migliarini, G. Martella, M. Meringolo, R.E. Goodchild, N.B. Mercuri, M. Pasqualetti, E. Bezard, P. Bonsi

04 **Il dolore nella distonia cervicale dell'adulto: frequenza e caratteristiche clinico/demografiche associate**
M.M. Mascia, , R. Erro, T. Ercoli, M. Esposito, A. Berardelli, G. Ferrazzano, G. Abbruzzese, L. Avanzino, R. Pellicciari, R. Eleopra, F. Bono, L. Bertolasi, P. Barone, R. Liguori, C. Scaglione, A. Pisani, M. Turla, M.S. Cotelli, G. Cossu, R. Ceravolo, M. Coletti Moja, L. Lopiano, M. Zibetti, P. Girlanda, F. Morgante, A. Albanese, R. Piredda, A.R. Bentivoglio, M. Petracca, R. Cantello, L. Magistrelli, M.C. Altavista, S. Misceo, M. Romano, M. Aguggia, B. Minafra, L. Madema, N. Modugno, F. Di Biasio, D. Imperiale, D. Cassano, G. Defazio, M. Tinazzi

05 **Sintomi motori e non motori nei pazienti affetti da blefarospasmo: implicazioni cliniche e fisiopatologiche**
V. Baione, G. Ferrazzano, I. Berardelli, A. Conte, C. Concolato, D. Belvisi, G. Fabbrini, G. Defazio, A. Berardelli

06 **Sviluppo di un questionario per la valutazione del gesto antagonista in pazienti con distonia**
G. Bonassi, N. Cothros, C. Cosentino, F. Di Biasio, E. Pelosin, R. Marchese, F. Morgante, D. Martino, L. Avanzino

07 **La teoria della mente affettiva e cognitiva è compromessa nei pazienti affetti da distonia cervicale e tremore**
G. Lagravinese, G. Santangelo, E. Pelosin, S. Cuoco, R. Marchese, F. Di Biasio, C. Serrati, P. Barone, G. Abbruzzese, L. Avanzino

08 **La memoria prospettica in pazienti con distonia: un confronto tra distonici cervicali, pazienti con blefarospasmo e soggetti sani**
G. Maggi, A. D'Iorio, G. Mautone, S. Peluso, F. Manganelli, M. Esposito, G. Santangelo

Sessione Poster "Neurofisiologia 1"

Moderatore: M. Bologna (Roma)

09 **Analisi cinematica della bradicinesia facciale, dell'arto superiore e inferiore nella malattia di Parkinson**
A. Cannavacciuolo, M. Bologna, A. Formica, D. Colella, G. Paparella, A. Guerra, A. Berardelli

10 **Modulazione dell'inibizione afferente a breve latenza durante l'osservazione di posture emotive**
A. Botta, G. Lagravinese, M. Bove, C. Cosentino, E. Pelosin, L. Avanzino

11 **Caratterizzazione neurofisiologica del tremore posturale e del tremore riemergente nella malattia di Parkinson**
A. Fabbrini, G. Leodori, D. Belvisi, M.I. De Bartolo, M. Costanzo, F.A.V. Undurraga, A. Conte, A. Berardelli

12 **Monitoraggio delle oscillazioni subtalamiche per 24 ore durante varie attività quotidiane in un paziente con malattia di Parkinson**
B. Minafra, M. Arlotti, C. Palmisano, M. Todisco, C. Pacchetti, A. Canessa, N.G. Pozzi, R. Cilia, M. Prenassi, S. Marceglia, A. Priori, P. Rampini, S. Barbieri, D. Servello, J. Volkmann, G. Pezzoli, I.U. Isaias

13 **Apprendimento motorio e risposta di lunga durata alla levodopa nella malattia di Parkinson**
G. Sciacca, G. Mostile, I. Disilvestro, G. Donzuso, R. Manna, G. Portaro, C. Rascunà, S. Salomone, F. Drago, A. Nicoletti, M. Zappia

14 **Analisi del blink rate come tool diagnostico nella malattia di Parkinson**
M.L. Caminiti, A. Di Santo, A. Fallacara, M. Marano, P. Falco, V. Di Lazzaro, L. Di Biase

CONSULTA GLI ABSTRACT

15 **Studio di fattibilità di un protocollo per la valutazione della motor imagery del cammino dual task tramite EEG ad alta densità**
M. Putzolu, C. Ogliastro, G. Bonassi, R. Marchese, C. Serrati, G. Abbruzzese, L. Avanzino, D. Mantini, E. Pelosin

16 **Effetti della somministrazione in acuto di levodopa sulla motilità oculare nei pazienti affetti da malattia di Parkinson**
C.G. Chisari, G. Mostile, A. Luca, G. Donzuso, G. Sciacca, R. Bonomo, C. Rascunà, G. Portaro, F. Patti, A. Nicoletti, M. Zappia

Sessione Poster "Terapie avanzate"

Moderatore: F. Valzania (Reggio Emilia)

17 **Studio prospettico di 24 mesi su pazienti affetti da malattia di Parkinson in fase avanzata in terapia con infusione intestinale di levodopa-carbidopa gel (LCIG)**
S. Scalise, R. Cerroni, P. Imbriani, T. Schirinzi, M. Pierantozzi, A. Stefani, N.B. Mercuri, A. Pisani

18 **Infusione sottocutanea continua di apomorfina nella malattia di Parkinson: cause di interruzione e successive strategie terapeutiche**
C. Femiano, E. Olivola, A. Fasano, S. Varanese, F. Lena, M. Santilli, D. Centonze, N. Modugno

19 **Discinesie bifasiche in pazienti trattati con infusione intestinale di levodopa-carbidopa gel: studio multicentrico retrospettivo**
M. Marano, T. Naranian, L. Di Biase, G. Cossu, A. Di Santo, R. Arca, P. Marano, V. Di Lazzaro, A. Fasano

20 **Stimolazione cerebrale profonda del nucleo subtalamico nella malattia di Parkinson: uno studio sui sintomi neuropsichiatrici**
E. Montanaro, C.A. Artusi, M. Lopez, R. Balestrino, M. Fabbri, A. Romagnolo, M.G. Rizzone, M. Zibetti, L. Lopiano

21 **Trattamento con levodopa-carbidopa gel intestinale nella malattia di Parkinson in fase avanzata: effetti a lungo termine sui sintomi assiali e fattori prognostici correlati**
M. Fabbri, M. Zibetti, C. Pongmala, C.A. Artusi, A. Romagnolo, L. Lopiano

22 **L'impatto della stimolazione cerebrale profonda sui tratti di personalità nei pazienti con malattia di Parkinson**
F. Ruggiero, F. Mameli, M. Reitano, E. Gianoli, D. Tedino, L. Borellini, F. Cogiamanian, S. Barbieri, A. Priori, R. Ferrucci

Sessione Poster "Disordini del movimento 1"

Moderatore: M.C. Altavista (Roma)

23 **Unire o separare la degenerazione cortico-basale dalla paralisi sopranucleare progressiva: questo è il problema**
S. Cuoco, A. Cappiello, R. Erro, M.T. Pellecchia, P. Barone, M. Picillo

24 **Validazione della versione italiana del questionario sulla qualità della vita in pazienti con paralisi sopranucleare progressiva**
M. Picillo, S. Cuoco, M. Amboni, F.P. Bonifacio, B. Borroni, A. Bruno, F. Bruschi, I. Carotenuto, R. Ceravolo, R. De Micco, A. De Rosa, F. Di Blasio, A.B. Di Fonzo, F. Elifani, R. Erro, M. Fabbri, M. Falla, G. Franco, D. Frosini, S. Galantucci, G. Lazzeri, L. Magistrelli, M. Malaguti, N.B. Mercuri, A.V. Milner, B. Minafra, N. Modugno, A. Nicoletti, R. Marchese, E. Olivola, A. Padovani, A. Pilotto, C. Rascunà, M.C. Rizzetti, G. Santangelo, T. Schirinzi, A. Stefani, A. Tessitore, M.A. Volontè, R. Zangaglia, M. Zappia, M. Zibetti, P. Barone

25 **Un caso di emergenza ipercinetica**
A. Novelli, I.A. Di Vico, F. Terenzi, S. Sorbi, S. Ramat

26 **Trattamento con BonT-A del tremore di Holmes secondario ad emorragia talamica: follow-up in due pazienti**
T. De Santis, P. Latino, F.E.Pontieri, M. Giovannelli

27 **Caratterizzazione clinica, genetica e radiologica di pazienti con disturbi del movimento e calcificazioni dei gangli della base**
F. Arienti, G. Franco, E. Monfrini, A. Seresini, A.B. Di Fonzo

CONSULTA GLI ABSTRACT

28 **Valutazione dello schema motorio della deambulazione nei pazienti con paraparesi spastica ereditaria trattati con tossina botulinica**
M. Sansone, M. Costanzo, B. Corrado, S. Peluso, C. Criscuolo, A. Antenora, E. Raiano, F. Iorillo, F. Manganelli, M. Esposito

29 **Una rara causa di atassia della marcia: la sindrome CLIPPERS (infiammazione linfocitica cronica con enhancement perivascolare pontino responsiva agli steroidi) complicata da stroke**
F. Di Biasio, D. Sassos, C. Baglini Rolla, L. Saitta, C. Serrati

30 **Studio del recettore metabotropico del glutammato mGlu3 nei meccanismi di neurodegenerazione e neuroprotezione nel modello di parkinsonismo tossicologico da MPTP**
M. Alborghetti, L. Di Menna, A. Traficante, F.E. Pontieri, F. Nicoletti, V. Bruno, G. Battaglia

31 **Differenze nei parametri 3D spazio-temporali e cinematici della marcia tra pazienti con idrocefalo normoteso idiopatico associato a parkinsonismo e pazienti con malattia di Parkinson**
G. Portaro, G. Mostile, V. Dibilio, F. Contrafatto, P. Cunsolo, G. Raudino, F. Certo, A. Nicoletti, G.M. Barbagallo, M. Zappia

32 **Risposta clinica al drenaggio liquorale lombare nelle 72 ore nell'idrocefalo normoteso idiopatico associato a parkinsonismo: tempistiche e correlati**
G. Mostile, G. Raudino, G. Portaro, F. Certo, A. Nicoletti, G.M. Barbagallo, M. Zappia

Sessione Poster "Parkinson 1"

Moderatore: C.E. Cicero (Catania)

33 **Vitamina E nella dieta come fattore protettivo per la malattia di Parkinson: evidenze cliniche e sperimentali**
P. Imbriani, T. Schirinzi, G. Martella, G. Di Lazzaro, M. Alwardat, P. Sinibaldi Salimei, N.B. Mercuri, M. Pierantozzi, A. Pisani

34 **Relazione tra fluttuazioni motorie e non motorie nella malattia di Parkinson: prospettiva del paziente, valutazione clinica e misure oggettive da un dispositivo indossabile**
A. De Angelis, M. Horne, D. Paviour, A. Leake, J. Coebergh, M. Edwards, F. Morgante, L. Ricciardi

35 **La validazione del questionario DYMUS per lo screening della disfagia nella malattia di Parkinson e parkinsonismi**
A. Putortì, M. Avenali, C. Dagna, R. De Icco, M.L. Gandolfi, C. Solaro, D.A. Restivo, M. Bartolo, F. Meneghello, G. Sandrini, C. Tassorelli, DYPAK SIRN Group

36 **La fatica nella malattia di Parkinson: una revisione sistematica e metanalisi**
M. Siciliano, L. Trojano, G. Santangelo, R. De Micco, G. Tedeschi, A. Tessitore

37 **Alterazioni circadiane della pressione arteriosa nelle alfa-sinucleinopatie**
A. Romagnolo, F. Vallelonga, A. Merola, C. Di Stefano, G. Sobrero, V. Milazzo, M. Zibetti, C.A. Artusi, M. Fabbri, M.G. Rizzone, S. Maule, L. Lopiano

38 **Validazione internazionale della Parkinson's Disease Composite Scale**
F. Stocchi, F.G. Radicati, P. Martinez-Martin, C. Rodriguez Blazquez, J. Wetmore, N. Kovacs

39 **L'assetto infiammatorio liquorale correla con umore e qualità della vita in pazienti con malattia di Parkinson in fase iniziale**
E. Olivola, M. Stampanoni Bassi, L. Giglio, C. Femiano, G. Ricciardo Rizzo, R. Furlan, A. Finardi, D. Centonze, N. Modugno

40 **Disfunzioni visive nella malattia di Parkinson: un protocollo standardizzato per la valutazione delle condizioni visive. Dati preliminari**
M. Meglio, E. Olivola, C. Femiano, L. Belli, G. Fioretto, D. Centonze, N. Modugno

41 **Frequenza dei sintomi non motori in un gruppo di pazienti con malattia di Parkinson suddivisi per stadio di malattia**
M. Sforza, D. Rinaldi, T. De Santis, E. Bianchini, M. Alborghetti, M. Giovannelli, F.E. Pontieri

42 **Effetto acuto sul cammino di un ritmo basato sulla Golden Ratio in pazienti con malattia di Parkinson: dati preliminari**
A. Peppe, F. Ferretti, S. Bottino, M. Iosa, G. Vannozzi

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

Sessione Poster "Riabilitazione 1"

Moderatore: M. Rizzo (Palermo)

43 **Effetti di un training combinato Action Observation e Motor Imagery in pazienti con malattia di Parkinson con instabilità posturale e disordini del cammino durante l'esecuzione di un dual-task: studio clinico e di risonanza magnetica funzionale**
E. Sarasso, F. Agosta, N. Piramide, E. Canu, M. Chiesi, I. Ravani, S. Galantucci, A. Tettamanti, M.A. Volontè, M. Filippi

44 **Dual-task in pazienti con malattia di Parkinson: studio combinato di gait analysis e risonanza magnetica funzionale**
E. Sarasso, F. Agosta, A. Gardoni, S. Galantucci, A. Tettamanti, M.A. Volontè, M. Filippi

45 **Un programma riabilitativo specifico per il tronco di quattro settimane riduce la flessione anteriore nei pazienti affetti da malattia di Parkinson: uno studio clinico, singolo cieco, randomizzato controllato**
C. Geroin, M. Gandolfi, M. Tinazzi, F. Magrinelli, G. Busselli, E. Dimitrova, N. Polo, P. Manganotti, A. Fasano, N. Smania

46 **Controllo posturale e cammino nei pazienti con malattia di Parkinson: studio pilota sull'uso promettente dell'ambientazione virtuale assistita da sistema computerizzato**
V. Cimino, G. Di Lorenzo, C. Sorbera, S. Marino, R.S. Calabrò, A. Buda, G. Paladina, A. Naro, A. Manuli, D. Milardi, P. Bramanti, A. Bramanti

47 **Efficacia di un programma neuroriabilitativo multidisciplinare e intensivo sui pazienti affetti da malattia di Parkinson**
V. Lo Buono, L. Bonanno, R. Palmeri, M. Berenati, C. Sorbera, V. Cimino, P. Bramanti, G. Di Lorenzo, S. Marino

48 **Stimolazione a corrente diretta (tDCS) cerebellare associata a riabilitazione nel trattamento della paralisi sopranucleare progressiva: studio doppio cieco randomizzato controllato**
A. Pilotto, M.C. Rizzetti, R. Serughetti, D. Locatelli, B. Cavaletti, A. Pedrini, W. Maetzler, C. Hansen, B. Borroni, A. Padovani

Sessione Poster "Neuroimmagini 1"

Moderatore: G. Arabia (Catanzaro)

49 **Cambiamenti longitudinali dello spessore corticale associati ad apatia in pazienti affetti da malattia di Parkinson**
F. Imperiale, F. Agosta, E. Canu, T. Stojković, I. Stankovic, S. Basaia, A. Fontana, V. Markovic, I. Petrović, E. Stefanova, V. Kostic, M. Filippi

50 **Studio dei pattern corticali FDG-PET come predittori di disability milestones e progressione motoria nella malattia di Parkinson**
A. Imarisio, A. Pilotto, E. Premi, S.P. Caminiti, L. Presotto, A. Sala, R. Turrone, R. Grasso, A. Alberici, B. Paghera, M.C. Rizzetti, B. Borroni, D. Perani, A. Padovani

51 **L'influenza dell'età sul trasportatore della dopamina: evidenze da uno studio SPECT su pazienti con malattia di Parkinson a esordio precoce e tardivo, confrontati separatamente con soggetti controllo di pari età**
G. Palermo, D. Frosini, S. Giannoni, M. Giuntini, D. Volterrani, U. Bonuccelli, R. Ceravolo

52 **Studio della connettività cerebellare tramite resting state nella malattia di Parkinson in fase precoce e drug-naïve**
S. Marino, L. Bonanno, V. Lo Buono, C. Sorbera, V. Cimino, P. Bramanti, G. Di Lorenzo

53 **Correlati neuroanatomici della risposta di lunga durata nei pazienti con malattia di Parkinson *de novo***
G. Donzuso, G. Sciacca, G. Mostile, A. Nicoletti, M. Zappia

54 **Le alterazioni dei trasportatori dopaminergici presinaptici nell'idrocefalo normoteso e nella malattia di Parkinson *de novo*: studio con [123I]Ioflupane e SPECT**
N.G. Pozzi, J. Brumberg, M. Todisco, B. Minafra, R. Zangaglia, G.R. Trifirò, R. Ceravolo, I.U. Isaias, C. Pacchetti

55 **Le alterazioni dello SPECT 123I-FP-CIT nell'idrocefalo normoteso sono sempre indicative di degenerazione? Evidenze da due casi clinici**
C. Del Gamba, A. Bruno, D. Frosini, D. Volterrani, G. Migaleddu, N. Benedetto, P. Perrini, M. Cosottini, U. Bonuccelli, R. Ceravolo

CONSULTA GLI ABSTRACT

Sessione Poster "Disordini del movimento 2"

Moderatore: V. Fetoni (Milano)

56 **C'è evidenza di bradicinesia in pazienti con tremore essenziale?**
D. Colella, M. Bologna, G. Paparella, A. Cannavacciuolo, S. Pietracupa, A. Guerra, A. Berardelli

57 **L'eterogeneità del tremore essenziale**
G. Ferrazzano, G. Paparella, M. Bologna, I. Berardelli, P. Giustini, D. Alunni-Fegatelli, A. Berardelli

58 **L'effetto dell'ossitocina intranasale in pazienti affetti da sintomi motori funzionali: uno studio pilota**
B. Demartini, D. Goeta, A. Priori, O. Gambini

59 **Corea e disturbi respiratori potenzialmente fatali nella malattia da anticorpi anti-IgLON5**
M. Filidei, N. Tambasco, F. Paolini Paoletti, S. Simoni, E. Brahimi, G. Cappelletti, P. Nigro, P. Calabresi

60 **Disfonia spasmodica come sintomo d'esordio di atassia spinocerebellare tipo 12**
F. Cavallieri, J. Rossi, G. Giovannini, C. Budriesi, A. Gessani, M. Carecchio, D. Di Bella, E. Sarto, J. Mandrioli, S. Contardi, S. Meletti

61 **Analisi delle caratteristiche clinico-strumentali prima e dopo shunt ventricolo-peritoneale nell'idrocefalo normoteso: uno studio prospettico osservazionale**
G. Giannini, G. Palandri, A. Ferrari, F. Oppi, D. Milletti, L. Albini-Riccioli, P. Mantovani, S. Magnoni, L. Chiari, P. Cortelli, S. Cevoli

62 **Disturbo del movimento nei pazienti con mutazione GNAO1: analisi retrospettiva**
T. Schirinzi, G. Garone, F. Graziola, G. Vasco, S. Galosi, D. Battaglia, E. Bertini, A. Capuano, V. Leuzzi

63 **Correlazione tra il punteggio della scala UPDRS e le misurazioni accelerometriche rilevate durante il monitoraggio continuo dei disordini del movimento**
L. Battista, A. Romaniello, E. Ferrante

64 **Disturbi del linguaggio nella paralisi sopranucleare progressiva: una condizione sottostimata?**
E. Del Prete, L. Tommasini, D. Frosini, S. Mazzucchi, E. Belli, U. Bonuccelli, R. Ceravolo

65 **Mioritmia craniocervicale post-ictus responsiva al trattamento con tossina botulinica. Un caso clinico**
V. Oppo, M. Melis, G. Cossu

66 **Differenze cliniche nei sottotipi di paralisi sopranucleare progressiva in accordo con i criteri MDS**
A. Cappiello, M. Picillo, S. Cuoco, M.F. Tepedino, G. Volpe, R. Erro, G. Santangelo, M.T. Pellecchia, P. Barone

67 **Stiff-Person Syndrome paraneoplastica con positività anticorpi anti-amfifisina e anti-recettore della glicina: caso clinico**
M. Mainardi, M. Carecchio, A. Antonini

Sessione Poster "Terapia"

Moderatore: T.P. Avarello (Palermo)

68 **Gestione terapeutica della malattia di Parkinson complicata: applicazione clinica dei Motor Fluctuation Indices**
R. Bonomo, G. Mostile, A. Nicoletti, M. Zappia

69 **Efficacia e sicurezza del 5-idrossitriptofano nel trattamento delle complicazioni motorie indotte dalla levodopa nella malattia di Parkinson**
M. Meloni, M. Puligheddu, A. Cannas, R. Farris, M. Figorilli, G. Defazio, M. Carta

70 **Efficacia e sicurezza del 5-idrossitriptofano nel trattamento della depressione e dell'apatia nella malattia di Parkinson**
M. Meloni, M. Puligheddu, M. Carta, A. Cannas, M. Figorilli, R. Farris, G. Defazio

71 **Effetti della safinamide sui sintomi cognitivi e comportamentali in pazienti con malattia di Parkinson con fluttuazioni: uno studio longitudinale prospettico**
S. Satolli, R. De Micco, M. Siciliano, F.P. Bonifacio, A. De Mase, A. Giordano, G. Tedeschi, A. Tessitore

72 **Sicurezza e tollerabilità della safinamide in pazienti anziani con malattia di Parkinson**
D. Rinaldi, M. Sforza, T. De Santis, S. Tagliente, M. Giovannelli, M. Alborghetti, F.E. Pontieri

73 **Studio di sicurezza e tollerabilità sul cambio immediato (overnight) tra rasagilina e safinamide in pazienti fluttuanti con malattia di Parkinson**
L. Vacca, G. Caminiti, M. Casali, C. Coletti, P. Grassini, F.G. Radicati, M. Torti, F. Stocchi

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

13.00/14.00 COLAZIONE DI LAVORO E SESSIONI POSTER — AREA POSTER

Sessione Poster "Neurofisiologia 2"

Moderatore: L.M. Romito (Milano)

74 **Stimolazione transcranica a corrente diretta su pazienti affetti da malattia di Parkinson con freezing della marcia: risultati preliminari**
S. Scalise, G. Di Lazzaro, M. Alwardat, N.B. Mercuri, M. Patera, L. Pietrosanto, G. Saggio, A. Pisani

75 **Correlati EEG durante un compito di working memory in soggetti sani e in pazienti con malattia di Huntington**
G. Bonassi, M. Semprini, M. Chiappalone, F. Barban, E. Pelosin, G. Lagravinese, R. Marchese, L. Trevisan, P. Mandich, D. Mantini, L. Avanzino

76 **Incremento unilaterale del ciclo di recupero del blink reflex nell'emiparkinsonismo *de novo***
G. Sciacca, G. Mostile, I. Disilvestro, G. Donzuso, R. Manna, G. Portaro, C. Rascunà, S. Salomone, F. Drago, A. Nicoletti, M. Zappia

77 **Effetti della somministrazione acuta di levodopa sulla motilità oculare in pazienti affetti da parkinsonismi atipici**
C.G. Chisari, G. Mostile, G. Donzuso, G. Sciacca, G. Portaro, C. Rascunà, F. Patti, A. Nicoletti, M. Zappia

78 **Analisi esplorativa della complessità di segnale elettrocorticale in pazienti con paralisi sopranucleare progressiva e degenerazione corticobasale**
G. Mostile, L. Giuliano, R. Terranova, A. Luca, G. Donzuso, G. Portaro, C. Rascunà, V. Sofia, A. Nicoletti, M. Zappia

79 **Prima l'uovo o la gallina? Effetto del propofol e del curaro su rigidità e ritmo beta subtalamico nella malattia di Parkinson**
T. Bocci, F. Cortese, M. Arlotti, S. Marceglia, F. Cogiamanian, G. Ardolino, M. Locatelli, P. Rampini, S. Barbieri, A. Priori

Sessione Poster "Parkinson 2"

Moderatore: L. Vacca (Roma)

80 **Terapia dopaminergica e disturbi della parola nella malattia di Parkinson: analisi acustica e correlazioni con aspetti motori e discinesie**
F. Cavallieri, C. Budriesi, A. Gessani, E. Menozzi, S. Contardi, F. Valzania, F. Antonelli

81 **Valutazione cinematica di bradicinesia, marcia e riflessi posturali in una popolazione di pazienti con neodiagnosi di malattia di Parkinson**
G. Di Lazzaro, M. Ricci, T. Schirinzi, M. Alwardat, A. Pallotti, F. Giannini, N.B. Mercuri, G. Saggio, A. Pisani

82 **Identificazione cinematica precoce di pazienti affetti da malattia di Parkinson in stadio iniziale e differenti fenotipi**
G. Di Lazzaro, M. Ricci, T. Schirinzi, M. Alwardat, A. Pallotti, F. Giannini, N.B. Mercuri, G. Saggio, A. Pisani

83 **Validazione della versione italiana del questionario di valutazione della qualità di vita dei caregivers di pazienti con parkinsonismo**
M. Picillo, S. Cuoco, M. Amboni, F.P. Bonifacio, B. Borroni, A. Bruno, F. Bruschi, I. Carotenuto, R. Ceravolo, R. De Micco, A. De Rosa, F. Di Blasio, A.B. Di Fonzo, F. Elifani, R. Erro, M. Fabbri, M. Falla, G. Franco, D. Frosini, S. Galantucci, G. Lazzeri, L. Lopiano, L. Magistrelli, M. Malaguti, N.B. Mercuri, A.V. Milner, B. Minafra, N. Modugno, A. Nicoletti, R. Marchese, E. Olivola, A. Padovani, A. Pilotto, C. Rascunà, M.C. Rizzetti, G. Santangelo, T. Schirinzi, A. Stefani, A. Tessitore, M.A. Volontè, R. Zangaglia, M. Zappia, P. Barone

84 **Tremore riemergente nella malattia di Parkinson: il ruolo della corteccia motoria**
G. Leodori, D. Belvisi, A. Fabbrini, M.I. De Bartolo, M. Costanzo, F.A.V. Undurraga, A. Conte, A.Berardelli

85 **Sintomi non motori nei sottotipi motori di malattia di Parkinson**
T. Ercoli, M.M. Mascia, A. Cannas, G. Defazio, P. Solla

86 **Malattia di Parkinson senile benigna: un nuovo fenotipo clinico?**
A. Pilotto, V. Dell'Era, A. Lupini, S. Gipponi, E. Cottini, A. Scalvini, A. Imarisio, R. Turrone, B. Borroni, M.C. Rizzetti, A. Padovani

CONSULTA GLI ABSTRACT

87 **Spessore retinico e pattern microvascolare in paziente con malattia di Parkinson in fase iniziale**
C. Rascunà, C. Terravecchia, A. Russo, G. Mostile, C.E. Cicero, A. Luca, N. Castellino, S. Tripodi, A. Longo, T. Avitabile, M. Reibaldi, M. Zappia, A. Nicoletti

88 **I pazienti parkinsoniani allo stadio Hoehn and Yahr 1 presentano un deficit del controllo inibitorio reattivo ma non di quello proattivo**
G. Mirabella, V. Di Caprio, N. Modugno, C. Mancini, E. Olivola

89 **Rilevazione del freezing del cammino nella malattia di Parkinson tramite smartphone**
G. Imbalzano, L. Borzì, C.A. Artusi, A. Romagnolo, M. Fabbri, M.G. Rizzone, M. Zibetti, S. Sibile, M. Varrecchia, G. Olmo, L. Lopiano

Sessione Poster "Parkinson 3"

Moderatore: R. Cilia (Milano)

90 **Malattia di Parkinson: esiste una correlazione tra discinesie e discontrollo degli impulsi?**
D. Goeta, A. De Angelis, C. Siri, M. Horne, A. Leake, D. Paviour, M. Edwards, F. Morgante, L. Ricciardi

91 **Malattia di Parkinson e microbiota in una popolazione selezionata dell'Italia centrale**
R. Cerroni, M. Conti, M. Pierantozzi, N.B. Mercuri, A. Stefani, D. Pietrucci, V. Unida, S. Biocca, A. Desideri

92 **Microbioma intestinale: correlazione con il fenotipo clinico e terapie nella malattia di Parkinson**
M. Melis, S. Vascellari, V. Palmas, V. Oppo, M. Sarchioto, A. Manzin, G. Cossu

93 **Studio delle cause dei ridotti livelli di caffeina nella malattia di Parkinson**
M.I. De Bartolo, G. Leodori, A. Fabbrini, M. Costanzo, D. Belvisi, A. Conte, S. Manetto, A. Ciogli, C. Villani, A. Berardelli, G. Fabbrini

94 **Valutazione delle proprietà psicometriche della Barthel Index in un campione di individui con malattia di Parkinson**
G. Galeoto, M. Tofani, G. Fabbrini, P. Massai, A. Berardi, E. Pelosin, D. Valente

95 **Correlati clinici dell'ideazione suicidaria nella malattia di Parkinson**
M. Costanzo, D. Belvisi, I. Berardelli, G. Ferrazzano, V. Corigliano, G. Fabbrini, M. Pompili, A. Berardelli

96 **Berg Balance Scale modificata: validazione italiana in una popolazione con malattia di Parkinson**
M. Tofani, G. Galeoto, A. Berardi, G. Fabbrini

97 **Il dolore nella malattia di Parkinson: studio clinico e neurofisiologico in pazienti con fluttuazioni motorie in add on terapia con levodopa**
C. Geroin, S. Ottaviani, G.M. Squintani, A. Segatti, T. Bovi, M. Tinazzi

98 **Alterazione della percezione dei disturbi del linguaggio nei vari stadi della malattia di Parkinson**
D. Melchionda, D. Perfetto, R. Goffredo, C. Avolio

Sessione Poster "Disturbi Cognitivi 1"

Moderatore: R. Colao (Catanzaro)

99 **Funzione autonomica cardiovascolare e MCI nella malattia di Parkinson**
C.E. Cicero, L. Raciti, R. Monastero, G. Mostile, G. Sciacca, A. Luca, C. Terravecchia, L. Giuliano, R. Baschi, M. Davì, M. Zappia, A. Nicoletti

100 **Influenza del sistema immunitario periferico sul profilo cognitivo in pazienti con malattia di Parkinson**
L. Magistrelli, E. Storelli, A.V. Milner, E. Rasini, F. Marino, M. Cosentino, C. Comi

101 **Le basi neurali del disturbo del controllo degli impulsi nella malattia di Parkinson: una meta-analisi**
G. Santangelo, S. Raimo, M. Cropano, C. Vitale, P. Barone, L. Trojano, G. Santangelo

102 **Il declino cognitivo nella malattia di Parkinson: una revisione sistematica e meta-analisi**
C. Baiano, P. Barone, G. Santangelo

103 **Atrofia corticale e networks elettrocorticali del segnale elettroencefalografico nei pazienti con malattia di Parkinson e deterioramento cognitivo lieve. Lo studio PaCoS**
G. Donzuso, L. Giuliano, R. Monastero, R. Baschi, G. Mostile, A. Luca, C.E. Cicero, M. Zappia, A. Nicoletti

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

104 **Alterazioni di connettività funzionale intrinseca in paziente con malattia di Parkinson drug-naïve con decadimento cognitivo lieve**
F.P. Bonifacio, R. De Micco, M. Siciliano, F. Di Nardo, S. Satolli, G. Caiazzo, F. Esposito, G. Tedeschi, A. Tessitore

105 **Prevalenza e fattori di rischio per lo sviluppo di comportamenti impulsivi-compulsivi in una coorte di pazienti affetti da malattia di Parkinson**
S. Simoni, N. Tambasco, P. Eusebi, P. Nigro, E. Brahimi, F. Paolini Paoletti, M. Filidei, G. Cappelletti, P. Calabresi

Sessione Poster "Neuroimmagini 2"

Moderatore: N. Tambasco (Perugia)

106 **L'atrofia del bulbo è il singolo maggiore predittore RMN dei segni non motori in pazienti con atrofia multisistemica**
M. Todisco, I.U. Isaias, P. Vitali, E. Alfonsi, R. Zangaglia, B. Minafra, M. Terzaghi, R. Manni, C. Pacchetti

107 **L'uso fuori indicazione dello studio per il trasportatore della dopamina nella pratica clinica**
A. Landolfi, S. Scannapieco, M. Picillo, M.T. Pellecchia, L. Pace, P. Barone, R. Erro

108 **Tremore d'azione e a riposo isolato e asimmetrico: valutazione della degenerazione nigro-striatale tramite [123]I-ioflupane SPECT**
M. Turazzini, G. Salomone, P. Tocco, L. Ferigo, R. Del Colle, S. Rossetto, A. Polo

109 **Valutazioni morfometriche del tronco encefalico in risonanza magnetica in pazienti paralisi sopranucleare progressiva tipizzati secondo i criteri MDS**
F. Abate, M. Picillo, S. Ponticorvo, M.F. Tepedino, R. Erro, M.T. Pellecchia, D. Frosini, P. Cecchi, M. Cosottini, R. Ceravolo, R. Manara, P. Barone

110 **Atrofia e perfusione nell'ambito delle sinucleinopatie**
S. Scannapieco, R. Erro, M. Picillo, S. Ponticorvo, F. Esposito, R. Manara, P. Barone, M.T. Pellecchia

111 **Studio di trattografia probabilistica della via nigro-striatale nella malattia di Parkinson**
S. Tagliente, H. Wilson, Z. Chappell, T. Yousaf, E. De Natale, G. Pagano, M. Politis

112 **Immagini di suscettibilità magnetica nel tremore essenziale**
S. Pietracupa, M. Bologna, S. Tommasin, F. Elifani, F. Vasselli, G. Paparella, N. Petsas, A. Berardelli, P. Pantano

Sessione Poster "Disturbi Cognitivi 2"

Moderatore: M. Amboni (Salerno)

113 **Il disturbo ossessivo-compulsivo di personalità come fattore di rischio di disfunzione esecutiva nella malattia di Parkinson**
A. Luca, A. Nicoletti, G. Mostile, C. Rascunà, C. Terravecchia, C. D'Agate, G. Donzuso, C.E. Cicero, G. Portaro, G. Sciacca, M. Zappia

114 **Mild Behavioral Impairment nella malattia di Parkinson: dati dal Parkinson's Disease Cognitive Impairment Study**
R. Baschi, V. Restivo, A. Nicoletti, C.E. Cicero, A. Luca, D. Recca, M. Zappia, R. Monastero

115 **Il ruolo dei sottotipi motori nella relazione tra ansia e disfunzioni cognitive nella malattia di Parkinson**
G. Maggi, A. D'Iorio, M. Amboni, D. Di Meglio, P. Barone, C. Vitale, G. Santangelo

116 **Punteggi qualitativi nella Figura di Rey-Osterrieth: confronto tra pazienti con paralisi sopranucleare progressiva e demenza fronto-temporale a variante comportamentale**
L. Tommasini, C. Pagni, E. Del Prete, J. Bonaccorsi, C. Radicchi, S. Cintoli, G. Tognoni, U. Bonuccelli, R. Ceravolo

117 **Olfatto e gusto nella malattia di Parkinson: relazione con il decadimento cognitivo minimo e il coinvolgimento dei singoli domini cognitivi**
S. Tamburin, M.P. Cecchini, A. Federico, A. Zanini, E. Mantovani, C. Masala, M. Tinazzi

CONSULTA GLI ABSTRACT

118 **L'osservazione delle azioni con doppio compito nel miglioramento delle abilità cognitive nella malattia di Parkinson: uno studio pilota**
E. Bianchini, A. Fineschi, T. De Santis, M. Sforza, D. Rinaldi, M. Giovannelli, F.E. Pontieri

Sessione Poster "Genetica"

Moderatore: C. Vitale (Napoli)

119 **Risposta a breve termine alla stimolazione cerebrale profonda del GPi bilaterale in paziente con neurodegenerazione associata a mutazione del gene PLA2G6**
N. Golfrè Andreasi, M.C. Malaguti, L.M. Romito, A.E. Elia, G. Devigili, P. Soliveri, A. Novelli, S. Rinaldo, A.B. Di Fonzo, R. Eleopra

120 **Sequenziamento di RNA leucocitario per identificare nuovi biomarcatori della malattia di Parkinson**
V. Tommasini, M. Catalan, M. Romano, G. Mazzon, T. Cattaruzza, L. Antonutti, P. Polverino, C. Bertolotti, E. Buratti, P. Manganotti

121 **L'identificazione di alleli ricombinanti di GBA incrementa la resa diagnostica nella malattia di Parkinson e nella demenza a corpi di Lewy**
E. Monfrini, G. Franco, L. Straniero, A. Pilotto, A. Padovani, S. Duga, A.B. Di Fonzo

122 **Angiopatia amiloidea cerebrale correlata a mutazione del gene ITM2B e parkinsonismo atipico**
P. Tocco, F. Rossi, L. Ferigo, A. Lupato, G. Salomone, G.M. Fabrizi, A. Polo

123 **Un caso di parkinsonismo giovanile associato a mutazione del gene RLIM**
D. Frosini, B. Toschi, C. Congregati, A. Provenzano, A. La Barbera, S. Giglio, V. Nicoletti, R. Ceravolo

124 **Nuova mutazione in PEO1 causa malattia di Parkinson familiare e ptosi senza oftalmoplegia**
E. Monfrini, G. Franco, F. Arienti, M. Percetti, A.B. Di Fonzo

125 **Mutazioni di TARDBP e CHMB2P in casi di parkinsonismo atipico familiare**
G. Bitetto, F. Morgante, C. Sorbera, C. Fenoglio, R. Del Bo, A.B. Di Fonzo

Sessione Poster "Riabilitazione 2"

Moderatore: E. Pelosin (Genova)

126 **Utilizzo delle onde d'urto extracorporee nel freezing della marcia: studio pilota**
P. Polverino, C. Bertolotti, M. Catalan, G. Mazzon, P. Manganotti

127 **L'efficacia del trattamento fisioterapico nei pazienti con distonia cervicale: revisione sistematica e meta-analisi**
G. Galeoto, M. Tofani, A. Berardi, J. Sansoni, G. Fabbrini

128 **Studio retrospettivo su un gruppo di pazienti con malattia di Parkinson trattati con fisioterapia motoria da sola o in associazione a stimolazione focale meccanica-vibratoria. Follow up di almeno 1 anno**
A. Peppe, F. Serio, C. Minosa, M. De Luca, P.G. Conte, G. Albani

129 **La deambulazione nelle persone con malattia di Parkinson: strategie riabilitative**
G.P. Salvi, S. Mazzoleni, E. Battini, E. Ancona, M. Simonini, A. Quarenghi,

130 **Efficacia della fisioterapia sul sintomo del freezing del cammino nella malattia di Parkinson: revisione sistematica e meta-analisi su studi randomizzati controllati**
C. Cosentino, M. Putzolu, G. Lagravinese, R. Marchese, M. Baccini, L. Avanzino, E. Pelosin

131 **Esiste un ruolo per la riabilitazione nelle distonie oro-mandibolari? Una case-series su un disturbo del movimento raro**
M. Marano, V. Deidda, F. Motolese, J. Lanzone, L. Di Biase, V. Luccarelli, V. Di Lazzaro

CONSULTA GLI ABSTRACT

VENERDÌ 24 MAGGIO 2019

PROGRAMMA SCIENTIFICO

08.00/09.00 SESSIONE PLENARIA — **AUDITORIUM**

Ipercinesie

Moderatori: G. Fabbrini (Roma) - *V. Sofia* (Catania) - *A. Tessitore* (Napoli)

08.00 **Discinesie tardive** - *D. Martino* (Calgary, Canada)
08.20 **Discinesie parossistiche** - *R. Erro* (Salerno)
08.40 **Le ipercinesie nei disturbi della glicosilazione** - *G. Mostile* (Catania)

09.00/10.00 SESSIONE — **AUDITORIUM**

Infusione intestinale di levodopa e carbidopa: oltre 10 anni di esperienza. Cosa abbiamo imparato

con il contributo incondizionato di AbbVie S.r.l.
Moderatore: L. Lopiano (Torino)

09.00 **Come riconoscere la fase avanzata della malattia di Parkinson** - *A. Antonini* (Padova)
09.30 **Follow-up e gestione del paziente** - *M. Zibetti* (Torino)

10.00/10.15 PAUSA CAFFÈ

10.15/11.45 SESSIONE PLENARIA — **AUDITORIUM**

Ipotesi patogenetiche nella malattia di Parkinson

Moderatori: G. Defazio (Cagliari) - *L. Morgante* (Messina)

10.15 **Sinucleinopatie e ipotesi prionica** - *P. Cortelli* (Bologna)
10.45 **La malattia di Parkinson inizia nell'intestino?** - *F. Stocchi* (Roma)
11.15 **LRRK2 e GBA** - *E.M. Valente* (Pavia)

11.45/12.45 SESSIONE — **AUDITORIUM**

Ruolo degli IMAO B nella gestione dei sintomi non motori: esiste un effetto di classe?

con il contributo incondizionato di Zambon Italia S.r.l.
Moderatori: P. Barone (Salerno) - *M. Zappia* (Catania)

11.45 **IMAO B e dolore** - *M. Tinazzi* (Verona)
12.05 **IMAO B e funzioni cognitive** - *F.E. Pontieri* (Roma)
12.25 **Gli IMAO B sono tutti uguali?** - *F. Nicoletti* (Roma)

12.45/13.30 **ASSEMBLEA ACCADEMIA LIMPE-DISMOV E PREMIAZIONI** — **AUDITORIUM**

13.30/14.00 COLAZIONE DI LAVORO

CONSULTA GLI ABSTRACT

VENERDÌ 24 MAGGIO 2019

PROGRAMMA SCIENTIFICO

14.00/15.00 SESSIONE **AUDITORIUM**

Inibizione COMT: nuovi dati ed esperienze cliniche

con il contributo incondizionato di Bial Italia S.r.l.
Moderatore: G. Cossu (Cagliari)

14.00 **Introduzione e nuove pubblicazioni** - *G. Cossu* (Cagliari)
14.20 **Esperienza clinica in U.K. -** *F. Morgante* (London, UK - Messina)
14.40 **Casi clinici in Italia -** *M. Sensi* (Ferrara)

15.00/16.30 SESSIONE VIDEO **AUDITORIUM**

con il contributo incondizionato di Roche S.p.A.

Moderatori: A.B. Di Fonzo (Milano) – *R. Marconi* (Grosseto) - *P. Martinelli* (Bologna) - *F. Patti* (Catania)

S. Satolli (Napoli)

G. Ricciardo Rizzo (Pozzilli)

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CONSULTA GLI ABSTRACT

CORSI DI FORMAZIONE PER MEDICI

MERCOLEDÌ 22 MAGGIO 2019

PROGRAMMA SCIENTIFICO

13.00/15.00 **AUDITORIUM**

Semeiotica dei disturbi del movimento

Moderatore: M. Esposito (Napoli)

12.45 Registrazione ECM
13.00 **Disturbi ipocinetici**- *B. Minafra* (Pavia)
13.40 **Disturbi ipercinetici 1: coree, distonie e tic** - *M. Carecchio* (Padova)
14.20 **Disturbi ipercinetici 2: Mioclono, tremori e altri** - *M. Esposito* (Napoli)

13.00/15.00 **SALA A**

Urgenze ed emergenze nei disturbi del movimento

Moderatore: R. Marchese (Genova)

12.45 Registrazione ECM
13.00 I **disturbi ipocinetici** - *D. Frosini* (Pisa)
13.40 I **disturbi ipercinetici** - *C. Dallocchio* (Voghera)
14.20 **Gestione del paziente in regime di ricovero** - *R. Marchese* (Genova)

13.00/15.00 **SALA B**

Psichiatria e disturbi del movimento

Moderatore: M. Pasquini (Roma)

12.45 Registrazione ECM
13.00 **Temperamento e personalità nei disturbi del movimento** - *A. Luca* (Catania)
13.40 **Aspetti psichiatrici nei disturbi del movimento** - *M. Pasquini* (Roma)
14.20 **Disturbi del movimento in pazienti psichiatrici** - *R. De Micco* (Napoli)

13.00/15.00 **SALA C**

Disturbi della deambulazione e della postura

Moderatore: D. Volpe (Arcugnano)

12.45 Registrazione ECM
13.00 **Deambulazione** - *M.F. De Pandis* (Cassino)
13.40 **Postura** - *C. Geroin* (Verona)
14.20 **Trattamento riabilitativo** - *E. Pelosin* (Genova)

13.00/15.00 **SALA D**

Tic e Tourette

Moderatore: N. Nardocci (Milano)

12.45 Registrazione ECM
13.00 **Inquadramento clinico -** *R. Rizzo* (Catania)
13.40 **Fisiopatologia -** *A. Suppa* (Roma)
14.20 **Terapia -** *N. Nardocci* (Milano)

13.00/15.00 **SALA E**

Distonie

Moderatore: A. Albanese (Milano)

12.45 Registrazione ECM
13.00 **Genetica -** *S. Petrucci* (Roma)
13.40 **Fisiopatologia -** *G. Abbruzzese* (Genova)
14.20 **Clinica e terapia** - *A. Albanese* (Milano)

CONSULTA GLI ABSTRACT

GIOVEDÌ 23 MAGGIO 2019

PROGRAMMA SCIENTIFICO

16.45/18.45 **AUDITORIUM**

Disturbi del movimento rari ma trattabili

Moderatore: G. De Michele (Napoli)

16.30 Registrazione ECM
16.45 **Parkinsonismi** - *F. Morgante* (London, UK - Messina)
17.25 **Disturbi del movimento ipercinetici** - *G. De Michele* (Napoli)
18.05 **Atassie** - *A. Elia* (Milano)

16.45/18.45 **SALA A**

Terapie innovative

Moderatore: A. Priori (Milano)

16.30 Registrazione ECM
16.45 **tDCS** - *A. Priori* (Milano)
17.25 **Nuove tecniche di stimolazione cerebrale profonda** - *M.F. Contarino* (Amsterdam, Paesi Bassi)
18.05 **Talamotomia mediante ultrasuoni focalizzati (MRgFUS)** - *S. Tamburin* (Verona)

16.45/18.45 **SALA B**

Sintomi non motori nella malattia di Parkinson

Moderatore: M. Amboni (Salerno)

16.30 Registrazione ECM
16.45 **Disturbi cognitivi** - *R. Monastero* (Palermo)
17.25 **Disturbi psichiatrici** - *M. Amboni* (Salerno)
18.05 **Disturbi del sonno** - *R. Savica* (Rochester, USA)

16.45/18.45 **SALA C**

Disautonomie

Moderatore: A. Merola (Cincinnati, USA)

16.30 Registrazione ECM
16.45 **Disturbi cardiovascolari** - *A. Merola* (Cincinnati, USA)
17.25 **Disturbi urogenitali** - *L. Brusa* (Roma)
18.05 **Disturbi gastroenterici** - *M. Torti* (Roma)

16.45/18.45 **SALA D**

Sex, drugs and rock 'n' roll

Moderatore: L. Ricciardi (London, UK)

16.30 Registrazione ECM
16.45 **La sessualità nel Parkinson** - *L. Ricciardi* (London, UK)
17.25 **Cannabis terapeutica?** - *G. Rizzo* (Bologna)
18.05 **Musica, teatro e altro** - *N. Modugno* (Pozzilli)

16.45/18.45 **SALA E**

Aspetti etici e medico-legali

Moderatore: R. Quatrale (Mestre)

16.30 Registrazione ECM
16.45 **La capacità di intendere e volere del paziente parkinsoniano** - *C. Pomara* (Catania)
17.25 **Tematiche di fine vita** - *R. Quatrale* (Mestre)
18.05 **Il rapporto medico-paziente** - *F. Rodolico* (Giarre)

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ACCADEMIA LIMPE-DISMOV
Viale Somalia, 133 - 00199 Roma
Tel. +39.06.96046753 - Fax+39.06.98380233
info@accademialimpedismov.it
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5° CONGRESSO
ACCADEMIA LIMPE-DISMOV
ACCADEMIA ITALIANA PER LO STUDIO DELLA MALATTIA DI PARKINSON E I DISORDINI DEL MOVIMENTO

CATANIA

22-24 MAGGIO 2019

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C1

Extrastriatal dopaminergic and serotonergic pathways in Parkinson's disease and in dementia with Lewy bodies: a 123I-FP-CIT study

Andrea Pilotto[1,2], *F. Schiano Di Cola*[1], *E. Premi*[1,3], *R. Grasso*[1], *R. Turrone*[1], *S. Gipponi*[1], *A. Scalvini*[1], *E. Cottini*[1], *B. Paghera*[4], *V. Garibotto*[5], *M.C. Rizzetti*[2], *L. Bonanni*[6], *B. Borroni*[1], *S. Morbelli*[7,8], *F. Nobili*[8,9], *U.P. Guerra*[10], *D. Perani*[11], *A. Padovani*[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Parkinson's Disease Rehabilitation Centre, FERB ONLUS, S. Isidoro Hospital, Trescore Balneario, Italy
[3]Stroke Unit, Azienda Socio Sanitaria Territoriale Spedali Civili, Spedali Civili Hospital, Brescia, Italy
[4]Nuclear Medicine Unit, University of Brescia, Brescia, Italy
[5]Department of Medical Imaging, Geneva University Hospital, Geneva, Switzerland
[6]Department of Neuroscience Imaging and Clinical Sciences, University "G. D'Annunzio" of Chieti-Pescara, Chieti, Italy
[7]Nuclear Medicine Unit, Department of Health Sciences, University of Genoa, Genoa, Italy
[8]IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[9]Dept. of Neuroscience (DINOGMI), University of Genoa, Genoa, Italy
[10]Nuclear Medicine Unit, Poliambulanza Hospital, Brescia, Italy
[11]Nuclear Medicine Unit San Raffaele Hospital, Division of Neuroscience San Raffaele Scientific Institute, Milan, Italy

Background: Aim of the study is to evaluate extrastriatal dopaminergic and serotonergic pathways in patients with Parkinson's disease (PD) and dementia with Lewy bodies (DLB) by using a [123I]-FP-CIT SPECT imaging.

Methods: Fifty-six PD patients without dementia, 41 DLB patients and 54 controls entered the study. Each patient underwent a standardized neurological examination and [123I]-FP-CIT SPECT. For each subject, bindings of nigrostriatal and extrastriatal regions of interest were calculated from spatially normalized images. The occipital- adjusted specific to non-displaceable binding (SBR) in the different regions was compared among PD, DLB and controls adjusting for the effect of age, sex, disease duration and serotonergic/dopaminergic treatment. A covariance analysis provided the correlates of local and long-distance regions with extrastriatal [123I]-FP-CIT deficits.

Results: Both PD and DLB patients showed lower [123I]-FP-CIT SPECT SBR in several regions beyond the nigrostriatal system, especially the insula, cingulate and thalamus. DLB patients showed significant lower [123I]-FP-CIT SBR in thalamus compared to controls and PD patients. Thalamic and cingulate [123I]-FP-CIT SBR deficits correlated, respectively, with limbic serotonergic and widespread cortical dopaminergic projections only in DLB patients while exhibited only local correlations in PD patients and controls.

Conclusions: PD and DLB share insular dopamine deficits, whereas impairment of thalamic serotonergic pathways was specifically associated with DLB. Longitudinal studies will be necessary in order to evaluate the clinical value of extrastriatal [123I]-FP-CIT SPECT assessment.

C2

Systemic activation of Nrf-2 pathway in patients with Parkinson's disease

Tommaso Schirinzi[1,2], *S. Petrillo*[2], *G. Di Lazzaro*[1], *E. Bertini*[2], *N.B. Mercuri*[1], *F. Piemonte*[2], *A. Pisani*[1]

[1]Department of Systems Medicine, University of Roma Tor Vergata, Rome, Italy
[2]Department of Neurosciences, Bambino Gesù Children's Hospital, Rome, Italy

Introduction: Nuclear factor erythroid-2-related factor 2 (Nrf-2) – activated pathway has been shown to be deeply involved in the pathogenesis of Parkinson's disease (PD). Accordingly, it has been proposed as a candidate target for disease-modifying treatments. However, to date such preclinical evidence has not been translated on a clinical ground.

Objectives: To demonstrate the activation of Nrf-2 pathway in PD patients.

Methods: 32 PD patients and 32 sex/age-matched healthy controls were enrolled. Blood samples were collected and standardized clinical assessment performed. Evaluation of Nrf-2 pathway included the measurement of Nrf-2 levels in leukocytes and the assay of both the upstream activators (mitochondrial complex I activity; glutathione oxidized/reduced ratio) and the downstream effectors (the phase II enzyme NQO1; the glutathione metabolism enzymes GCL and GR). In addition, leukocyte content of alpha-synuclein oligomers was measured as a peripheral marker of synucleinopathy. ELISA, western blotting and qRT-PCR were used. Mean and regression statistical analysis were performed.

Results: In blood leukocytes of PD patients, alpha-synuclein oligomers and complex I activity were reduced, whereas glutathione oxidized/reduced ratio was increased, suggesting systemic mitochondrial impairment and major oxidative stress, in combination with an ongoing synucleinopathy. Nrf-2 levels were increased, as well as NQO1, GCL and GR, demonstrating a significant activation of the whole pathway. Levels of Nrf-2 and alpha-synuclein oligomer were associated to disease duration, directly and inversely respectively.

Conclusions: The study provides evidence in vivo of the systemic activation of Nrf-2 pathway in PD, also disclosing some interesting interactions with both the pathological and clinical features of the disease. Our findings confirm preclinical data, encouraging the development of therapies targeting Nrf-2. Moreover, it further suggests that accurate analysis of blood leukocytes may offer a novel set of biomarkers, which may reflect remote pathogenic mechanisms of PD.

C3

Transient orthostatic blood pressure changes in Parkinson's Disease: impact on falls, syncope and orthostatic intolerance

A. Fanciulli[1], *Nicole Campese*[2], *G. Göbel*[3], *J.P. Ndayisaba*[1], *S. Eschlboeck*[1], *C. Kaindlstorfer*[1], *C. Raccagni*[1], *R. Granata*[1], *U. Bonuccelli*[2], *R. Ceravolo*[2], *W. Poewe*[1], *G.K. Wenning*[1]

[1]Department of Neurology, Innsbruck Medical University, Innsbruck, Austria
[2]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[3]Department of Statistics, Informatics and Health Economics, Innsbruck Medical University, Innsbruck, Austria

Background: Orthostatic hypotension (OH) is a common, disabling non- motor feature in Parkinson's Disease (PD), defined as a sustained blood pressure (BP) fall after 3 minutes standing. Transient BP falls within the first minute upon standing negatively influence morbidity and mortality in the geriatric population. [1] However, their prevalence and impact on major clinical outcomes in PD is unknown.

Objective: To assess the prevalence of transient orthostatic BP changes and their influence on falls, syncope and orthostatic symptoms in PD.

Methods: 167 patients with PD who underwent cardiovascular autonomic function tests under continuous non-invasive heart rate and BP monitoring at the Innsbruck Medical University between 2007 and 2016 were retrospectively studied.

Results: OH occurred in 16% of patients, while transient orthostatic BP changes within the first minute of standing in 20%, the combination of both was present in 6% of patients. Neither OH, nor transient orthostatic BP changes or the combination of both were associated with an increased frequency of falls (p: 0.082), syncope (p: 0.473) or orthostatic symptoms (p: 0.235) in the 6 months preceding or following cardiovascular autonomic function testing. At multivariate analysis, history of falls was associated with a more advanced H&Y stage (OR: 2.6, p: 0.001) and history of syncope (OR: 61,6, $p<0.001$). History of syncope was associated with a greater systolic ($p<0.001$) and diastolic ($p=0.05$) BP fall within 30s standing. History of orthostatic symptoms was associated with a greater systolic BP fall (p: 0.015) 15s after standing.

Conclusions: Transient orthostatic BP falls are more frequent than OH in PD. Lower BP values within 30s upon standing indirectly increase the risk of falls, by increasing the risk of syncope. A standing test under continuous HR and BP monitoring contributes to the identification of a modifiable riskfactor for syncope and falls in PD.

References

[1] Van Wijnen VK et al., Journal of Internal Medicine 2017

C4

A 6-year longitudinal study on a cohort of individuals bearing mutations in the glucocerebrosidase gene: evolution of prodromal parkinsonian features

Micol Avenali[*1,2], *M. Toffoli*[*3], *S. Mullin*[3], *A. McNeill*[3], *D. Hughes*[4], *A. Mehta*[4], *F. Blandini*[5], *A.H.V. Schapira*[3]

*These authors contributed equally to this work

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]Department of Neurology and Neurorehabilitation, IRCCS Mondino Foundation, Pavia, Italy
[3]Department of Clinical and Movement Neurosciences, University College London Institute of Neurology, London, UK
[4]Lysosomal Storage Disorders Unit, Department of Haematology, Royal Free Hospital, London, UK

[5]Laboratory of Functional Neurochemistry, IRCCS Mondino Foundation, Pavia, Italy

Objectives: GBA mutations are the most frequent risk factor for Parkinson disease (PD). The aim of this study is to evaluate clinical features in a group of GBA mutation positive individuals (GD and Het GBA carriers) at risk of developing PD over 6-years follow-up.

Methods: This is a longitudinal study on a cohort of GBA positive carriers. At baseline, we enrolled 30 GD Type1 patients (mean age 52.4 years), 30 Het GBA (mean age 59 years) carriers and 30 mutation negative controls (HC). We assessed motor and non-motor prodromal signs of PD in all subjects, by means of clinical questionnaires and scales (MoCA, UPSIT, RBDsq, UPDRS-III, UMSARS, and BDI). At 6 years, we repeated the assessment and collected venous blood samples to measure GCase activity.

Results: After 6 years, 1 GD patient developed a clinically defined PD syndrome. Over the 6-year follow-up, we observed a significant worsening in UMSARS, RBDsq, UPDRS-III and BDI scores compared to baseline scores in both the GD and HetGBA groups. Intergroup comparisons showed that GD subjects had significantly worse scores in UPSIT, UMSARS, MoCA and UPDRS-III than HC, while Het GBA displayed worse outcomes in UPSIT and UPDRS-III compared to HC. In GBA mutation positive individuals (Het GBA and GD), an UPSIT score of 23 at baseline was correlated with worse outcome at 6 years in UPSIT, MoCA, UPDRS-III and BDI. GCase enzymatic activity in Het GBA carriers was lower than HC and higher than GD.

Conclusions: Our study includes a long period of observation in a unique cohort of GBA positive individuals carefully evaluated for the presence of prodromal features over time. In this 6-year longitudinal study, we were able to confirm the biological effect of GBA mutations in determining motor and non-motor prodromal PD features.

C5

Different patterns of brain activity during lower limb movements in Parkinson's disease patients with and without freezing of gait

Noemi Piramide[1], *F. Agosta*[1], *E. Sarasso*[1,3], *E. Canu*[1], *S. Galantucci*[2], *A. Tettamanti*[3], *M.A. Volontè*[2], *M. Filippi*[1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy
[3]Laboratory of Movement Analysis, San Raffaele Scientific Institute, Milan, Italy

Introduction: To date, few studies have investigated task-based fMRI alterations underlying gait difficulties in PD-FoG patients, suggesting an abnormal interplay between motor, basal ganglia, pedunculopontine and cognitive control networks. However, the mechanisms underlying FoG pathophysiology are still debated.

Objective: To assess brain functional MRI (fMRI) activity during a feet movement task in Parkinson's disease patients with (PD-FoG) and without freezing of gait (PD-noFoG) and healthy controls.

Methods: 10 PD-noFoG, 17 PD-FoG patients and 18 matched healthy controls were recruited. PD-FoG were divided into 9 with mild and 8 with moderate FoG according to the New FoG-Questionnaire (NFoG-Q). Patients underwent motor (Timed Up and Go test, 10-meters-walking test, UPDRSIII) and neuropsychological evaluations (executive-attentive, visuo-spatial and memory domains). Both patients and controls performed an fMRI task consisting of alternate dorsal/plantar feet flexion movements according to an auditory stimulus of 0.5 Hz.

Results: PD-FoG and PD-noFoG patients were similar for all motor variables except for the presence of FoG. Only PD-FoG patients performed worse in executive-attentive, visuo-spatial and memory functions relative to healthy controls. fMRI results showed decreased activity in sensorimotor areas in PD-FoG and PD-noFoG patients relative to healthy controls. PD-noFoG patients showed an increased activation of frontal-striatal network while PD-FoG subjects had an increased parieto-occipital and cerebellar cortices recruitment compared to healthy subjects. PD-FoG showed a decreased basal ganglia activity relative to PD-noFoG. Analysing PD-FoG subgroups, mild PD-FoG subjects revealed an increased fronto-parietal activation relative to moderate PD-FoG patients.

Conclusions: All PD subjects showed a decrease recruitment of sensorimotor areas during feet movements relative to healthy controls. Despite this common feature, this study revealed the presence of two different patterns of brain activity during feet movements in PD-FoG and PD-noFoG patients, suggesting a compensatory role of parieto-occipital network to overcome the fronto-striatal failure in PD-FoG subjects.

C6

Postural abnormalities in Parkinson's disease: an epidemiological and clinical multicenter study

Christian Geroin[1], *M. Gandolfi*[2,3], *R. Ceravolo*[4], *M. Capecci*[5], *E. Andrenelli*[5], *M. G. Ceravolo*[5], *L. Bonanni*[6], *M. Onofrj*[6], *M. Vitale*[6], *M. Catalan*[7], *P. Polverino*[7], *C. Bertolotti*[7], *S. Mazzucchi*[4], *S. Giannoni*[4], *N. Smania*[2,3], *S. Tamburin*[1], *L. Vacca*[8], *F. Stocchi*[8], *F.G. Radicati*[8], *C.A. Artusi*[9], *M. Zibetti*[9], *L. Lopiano*[9], *A. Fasano*[10,11], *M. Tinazzi*[1]

[1]Neurology Unit, Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Neuromotor and Cognitive Rehabilitation Research Center (CRRNC), Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]Neurorehabilitation Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[4]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[5]Department of Experimental and Clinical Medicine, Neurorehabilitation Clinic, "Politecnica delle Marche" University, Ancona, Italy
[6]Department of Neuroscience, Imaging and Clinical Sciences, University "G.D'Annunzio" of Chieti-Pescara, Chieti, Italy
[7]Clinical Neurology Unit, Department of Medical, Surgical and Health Services, University of Trieste, Trieste, Italy
[8]University and Institute for Research and Medical Care IRCCS, San Raffaele, Rome, Italy
[9]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Italy
[10]Edmond J. Safra Program in Parkinson's Disease and the Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, UHN, Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[11]Krembil Brain Institute, Toronto, Ontario, Canada

Objective: To evaluate the overall prevalence of postural abnormalities (PA) in patients with Parkinson's disease (PD) and to assess their association with demographic and clinical variables.

Background: In PD the overall frequency of PA is unknown. Previous studies have investigated the prevalence of each isolated PA reporting variable results [1,2,3].

Methods: We performed a multicenter cross-sectional study enrolling consecutive PD outpatients attending 7 tertiary Italian centers. Patients underwent evaluations and were compared according to the presence of isolated PA including camptocormia (CC), Pisa syndrome (PS) and anterocollis (AC) and of combined forms (i.e CC+PS, CC+AC, etc.) for several demographic and clinical variables.

Results: Among 811 PD patients enrolled, PA were detected in 174 patients (21.5%, 95% CI 18.6%-24.3%). Isolated PA were 144 whilst the combined were 30. The prevalence of CC was 11.2% (95% CI 9%-13.3%), of PS was 8% (CI 6.2%-9.9%) and of AC was 6.5% (CI 4.9%-8.3%). PA patients were more frequent male, older, with longer disease duration, had a more advanced disease stage, more severe PD symptoms, bradykinetic/rigid phenotype, and poorer quality of life. They were initially treated with L-dopa, took higher daily L-dopa equivalent daily dose, and had more comorbidities. Falls and back pain were more frequent in PD with PA than in PD without PA. Multiple logistic regression models confirmed an association of PA with male gender, Hoehn & Yahr stage, and total score of UPDRS. Combined PA were

associated with a more advanced PD stage and severity of symptoms than isolated PA.

Conclusions: PA are frequent and disabling complications in PD. Early detection and treatment of PA may prevent the development of fixed and irreversible deformities.

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C7

Is limbic Lewy Type Synucleinopathy (LTS) associated with psychotic symptoms in patients with dementia? Preliminary results from the Abbiategrasso Brain Bank (Milan)

Tino Emanuele Poloni[1,2], *V. Medici*[1], *G. Negro*[1,3], *A. Davin*[1], *E. Fogato*[1,2], *E.* Riva[2], *R. Vaccaro*[1], *S. Abbondanza*[1], *E. Galbiati*[2], *R. Castoldi*[2], *M. Ceroni*[1,3], *T. Suardi*[2], *A. Guaita*[1]

[1]Golgi-Cenci Foundation, Abbiategrasso, Italy
[2]ASP Golgi-Redaelli, Milan, Italy
[3]National Neurological Institute "C. Mondino", Pavia, Italy

Background: Limbic system is strictly related to behavior and frequently affected by LTS in patients with Dementia due to Lewy Bodies (LBD/PDD) or other etiologies. Psychotic symptoms are the most considerable problem for caregivers and pose therapeutic challenges. Nevertheless, their mechanisms and pathologic basis remain poorly investigated.

Aims: To verify the correlation between limbic LTS and psychotic symptoms in a series of pathologically definite demented patients.

Methods: Sixteen brain donors (6 males and 10 females), belonging to the Abbiategrasso Brain Bank, had previously been characterized through serial clinical evaluations. At death, they were aged between 71 and 104 years (average: 82.8). Brain sections were stained using HE, Nissl, Luxol, Gallyas, and antibodies against beta-amiloid, TAU, TDP43, alpha- synuclein to obtain a complete characterization of the vascular and degenerative lesions. Fisher's exact test was used for statistical analysis.

Results: Clinical diagnosis was Alzheimer's Disease (AD) in 7 cases, mixed etiologies in five, LBD in two, Vascular dementia (VaD) in one and FTLD in the remaining case. At neuropathological examination, additional unexpected pathology was found in 9 out of 16 cases, including LTS, TDP43 pathology, Small Vessel Disease (SVD), Primary Age Related TAUopathy (PART). Particularly, 4 cases had AD/LBD, two had AD/LBD/SVD, two had AD/SVD and one had TDP/LTS. Nine cases had behavioral symptoms, all of them showed additional limbic lesions (4 LTS/TDP43; 4 TDP43; 1 LTS). Five out of the 7 subjects without behavioral symptoms did not show any additional limbic pathology, whereas the remaining 2 cases had moderate limbic lesions: (1 LTS; 1 TDP43).

Conclusions: In this series, the presence of limbic LTS and/or TDP-43 pathology is significantly associated with pervasive psychotic symptoms during the clinical course (Fisher test: P:0.0048). Frequently, limbic LTS and TDP43 lesions are concomitant suggesting a possible synergistic role of these proteinopathies, causing limbic dysfunction and influencing the clinical phenotype.

C8

Vascular risk factors and WMLs as risk factors for cognitive impairment in Parkinson's disease. A longitudinal study from the PaCoS cohort

Antonina Luca[1], *R. Monastero*[2], *G. Donzuso*[1], *R. Baschi*[2], *C.E. Cicero*[1], *C. Terravecchia*[1], *A. Salerno*[1], *M. Zuccarello*[1], M. Davì[2], *V. Restivo*[3], *G. Mostile*[1], *M. Zappia*[1], *A. Nicoletti*[1]

[1]Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[2]Department of Experimental Biomedicine and Clinical Neurosciences, Section of Neurology, University of Palermo, Palermo, Italy
[3]Department of Sciences for Health Promotion and Mother-Child Care, University of Palermo, Palermo, Italy

Background: Vascular risk factors (VRFs) may be associated with cognitive decline in early Parkinson disease (PD) and identification of modifiable factors is essential.

Methods: PD patients of the PaCoS cohort who underwent a baseline and follow-up neuropsychological evaluations were enrolled in the study. PD-MCI and PDD were diagnosed according to the MDS criteria. Baseline brain MRI was used to calculate the white matter lesions (WMLs) burden using a visual scale. Laboratory data, presence of hypertension, diabetes and use of anti-hypertensive drugs were collected and the Framingham cardiovascular disease Risk Score (FRS) was calculated. VRFs predicting MCI and PDD were evaluated using Cox proportional hazard regression model.

Results: Out of 139 enrolled PD patients, 84 were classified as normal cognition (NC), 55 (39.6%) as MCI at baseline. At follow-up 28 (33.3%) PD-NC developed MCI and 4 (4.8%) PDD. Out of 55 PD-MCI patients at baseline, 14 (25.4%) converted to PDD at follow-up. Among PD-NC the presence of a higher systolic blood pressure (>135 mmHg) and use of anti-hypertensive were the stronger predictors of MCI at follow-up (adjHR 5.12; 95%CI 1.48-17.76; p-value 0.01 and adjHR 7.13; 95%CI 2.11-24.13: p-value 0.002 respectively). For PDD the risk was associated with MCI at baseline (adj HR 11.4; 95%CI 2.39-54.64; p-value 0.002), and a higher WML burden (adj HR 4.50 1.20-16.8 p-value 0.02).

Conclusions: in our sample presence of hypertension at baseline represent the most important modifiable risk factors increasing of about 6 times the risk of MCI.

C9

Levodopa intestinal gel infusion: survival analysis in patients treated over 10 years

Carlo Alberto Artusi, R. Balestrino, G. Imbalzano, S. Bortolani, E. Montanaro, M. Zibetti, L. Lopiano

Dipartimento di Neuroscienze "Rita Levi Montalcini", Università di Turin, Turin, Italy

Introduction: Levodopa/carbidopa intestinal gel (LCIG) infusion for Parkinson's disease (PD) demonstrated a sustained efficacy on PD symptoms and motor fluctuations. However, survival analyses of LCIG cohorts are lacking.

Objective: We sought to analyze the survival rate and death causes of 105 PD patients treated with LCIG for over 10 years.

Materials and Methods: We retrospectively analyzed data of 105 PD patients treated with LCIG in time-frame 2005-2018. Inclusion criteria: PD diagnosis and LCIG treatment. We analyzed the death rate, the mean survival time and the causes of death. To verify the influence on the mortality rate of LCIG we used a control group of 86 patients with advanced PD, evaluated as potential candidates to advanced therapy (LCIG or DBS) but maintained on standard dopaminergic therapy.

Results: According to data availability, we enrolled 98 LCIG patients. The mean age at LCIG start was 67.9±7.3 years, and disease duration 13.0±4.3 years. The mean follow-up time since LCIG infusion start was 5.3±2.7 years. During follow-up, 34.7% of patients died. The mean survival time since LCIG start was 4.6±2.6 years. The causes of death were pneumonia in 17.1% of patients, cardio-circulatory/cerebrovascular disease in 14.3%, general condition deterioration in 31.4%, sepsis in 5.7%, other in 14.3%, and unknown in 14.3%. The Cox regression model based on the entire cohort of 184 advanced PD patients showed a not-significant association between mortality and LCIG infusion therapy (HR: 0.748, 95% CI 0.287- 1.948; p: 0.552), and a significant association with MMSE score (HR: 0.900, 95% CI 0.825-0.983; p: 0.019).

Conclusions and discussion: We analyzed the death rate and death causes of LCIG patients. Our findings did not support the hypothesis of an influence of LCIG therapy on mortality.

C10

Impaired LTP-like plasticity in Parkinson's Disease can be restored by gamma-transcranial alternating current stimulation

Andrea Guerra[1,2], *A. Suppa*[1,2], *F. Asci*[2], *V. D'Onofrio*[2], *V. Sveva*[2], *A. Berardelli*[1,2]

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

Introduction: In patients with Parkinson's disease (PD) there is an impaired long-term potentiation (LTP)-like plasticity in the primary motor cortex (M1). Indeed, previous transcranial magnetic stimulation studies have shown that intermittent theta burst stimulation (iTBS) fails to induce long-lasting changes in motor evoked potentials (MEPs). We have recently introduced a neurophysiological approach allowing to boost LTP-like plasticity in healthy subjects. It consists in the combined stimulation of M1 by transcranial alternating current stimulation (tACS), delivered at the gamma frequency, and iTBS.

Objective: To test whether the co-stimulation gamma-tACS-iTBS is effective in improving the impaired LTP-like plasticity of M1 in patients with PD.

Methods: We designed a single-blinded placebo-controlled study in which patients ('OFF' dopaminergic therapy) underwent iTBS during 'real' gamma-tACS and during 'sham' gamma-tACS in two different randomized sessions. MEPs were recorded before (T0) and after 5 (T1), 15 (T2) and 30 (T3) minutes after the intervention to measure the after-effects produced by the stimulation. A group of age- and sex- matched healthy subjects (HS) was used to compare the effect of 'sham' gamma- tACS-iTBS with that obtained in patients.

Results: In HS, 'sham' gamma-tACS-iTBS produced a significant MEPs facilitation at T1 and T2. By contrast, the same stimulation did not induce long-lasting changes of MEPs in patients. When the effect of 'sham' gamma-tACS-iTBS was compared with that produced by 'real' gamma-tACS-iTBS, the analysis demonstrated that in the 'real' session MEPs amplitude increased at all the time-points after the stimulation. The amount of facilitation was comparable with that induced by 'sham' gamma-tACS- iTBS in HS.

Conclusions: iTBS-induced LTP-like plasticity is impaired in PD. However, by synchronizing the neuronal elements of M1 at the gamma rhythm by using tACS, the mechanisms responsible for altered LTP-like plasticity can be restored. Thus, gamma oscillations of M1 have a pathophysiological role in LTP-like plasticity in PD.

C11

Functional brain connectome in drug-naïve Parkinson's disease patients: correlation with motor and non-motor phenotypes and prediction of levodopa requirement

Rosa De Micco[1], *F. Agosta*[2], *S. Basaia*[2], *M. Siciliano*[1], *C. Cividini*[2], *G. Tedeschi*[1], *A. Tessitore*[1], *M. Filippi*[2]

[1]Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy

Introduction: Graph analysis and connectomics may be applied to characterize functional architecture changes related to Parkinson'disease (PD) development and progression.

Objective: To investigate whole-brain network topologic organization in a large cohort of drug-naïve PD patients using resting-state functional MRI (rs-fMRI); and to determine whether early functional connectivity measures may predict disease progression overtime.

Methods: 147 drug-naïve PD patients underwent motor, non-motor and neuropsychological assessments as well as rs-fMRI at baseline. 38 age- and sex-matched controls were also enrolled. Non-hierarchical cluster analysis using clinical data were applied to stratify PD patients in two subtypes: 77 patients were grouped as "early/mild" and 70 as "early/severe". Graph analysis and connectomics assessed global and local topological network properties and regional functional connectivity (FC) at baseline in both PD patients and controls. Multivariate linear and logistic regressions investigated whether functional imaging data at baseline were predictors of motor impairment and levodopa requirement over a 2-year period.

Results: At baseline, "early/mild" PD patients showed a preserved global functional brain architecture compared to controls. "Early/severe" PD patients showed altered functional topological properties within the basal ganglia network compared to "early/mild" PD patients. Widespread FC abnormalities were detected in several networks encompassing basal ganglia, sensorimotor and occipital areas in PD patients compared to controls. Decreased FC involving mainly striato-frontal, striato-temporal and limbic connections differentiated "early-mild" from "early-severe" PD patients. FC abnormalities at baseline were found to be an independent predictor of levodopa requirement over 2-years.

Conclusions and discussion: Our findings revealed that a specific subtype of PD patients, characterized by severe motor and non-motor burden as well as widespread FC abnormalities, may be identified at the time of diagnosis. We hypothesize that this FC pattern may reflect the presence of more diffuse neuropathological changes. Combined clinical and neuroimaging tools are promising to stratify risk of PD progression overtime.

C12

Poor responders to STN DBS in Parkinson's disease: 1 year follow-up study

Marianna Sarchioto[1,2], *M. Zibetti*[1], *L. Ricciardi*[2], *E. Montanaro*[1], *M. Edwards*[2], *L. Lopiano*[1], *F. Morgante*[2]

[1]Center for the Study of Movement Disorders, Department of Neuroscience, University of Turin, Turin, Italy
[2]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute St George's University of London, London, UK

Despite Subthalamic Nucleus (STN) Deep Brain Stimulation (DBS) proven safety and efficacy in Parkinson's Disease (PD), postoperative impact on patients' quality of life and activities of daily living is difficult to predict. Aim of this study is to determine which factors contribute to a poor outcome at 12 months after surgery. We retrospectively analyzed prospectively acquired data at University of Turin DBS center and we defined as "Poor DBS Responders" those who had less than 20% of improvement at UPDRS-II OFF MED/ON STIM at 12 months. "Poor" and "Good" responders were compared for demographical, clinical, cognitive and affective variables collected during the pre-surgery DBS assessment (T0) and at 1-year follow-up (T1). Out of 203 consecutive PD patients treated with STN-DBS, we identified 126 suitable subjects. According to our criteria, out of this sample 35 were "Poor-DBS responders" and 91 "Good-DBS responders". Poor-DBS and Good-DBS patients did not differ for age at PD onset, age at STN-DBS and disease duration. Similarly, both categories had a significant improvement of UPDRSIII, dyskinesia and a significant reduction of dopaminergic drugs at T1. In contrast, Poor-DBS responders had a non- significant improvement of UPDRS Axial score and OFF score at 12 months. Furthermore, Poor-DBS responders had significantly less impaired motor functions and daily life activities at T0 when compared with Good-DBS responders. In conclusion, despite STN-DBS efficacy on motor symptoms and fluctuations, our study indicates that major determinants of poor DBS outcome are non-significant improvement of axial symptoms and time spent in OFF condition. Moreover, our data suggest that Poor-DBS responders are significantly less impaired at the time of DBS selection. Further studies are needed in order to better understand the possible mechanisms determining this last finding.

C13

Biomarkers of idiopathic REM sleep behavior disorder versus RBD within narcolepsy

Elena Antelmi[1,2], *F. Pizza*[1,2], *V. Donadio*[1,2], *Y.L. Sosero*[1,2] *R. Liguori*[1,2], *G. eoewe*[1,2]

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

Background: REM sleep behavior disorder (RBD) may be idiopathic (iRBD) or linked to other diseases. The second most common cause of RBD in narcolepsy. The pathophysiology of RBD within narcolepsy is still a vexing issue.

Objective: We aimed at comparing iRBD and RBD due to narcolepsy, searching for discriminating clinical, neurophysiological and pathological biomarkers.

Methods: Seventeen adults' patients with NT1 and RBD were compared with 30 age and sex-matched patients with iRBD. Both groups underwent extensive examinations, including neuropsychological investigations, neuroimaging and skin biopsy looking for phosphorylated alpha-synuclein (p-alpha-syn) deposits. Whole-night video-polysomnography (v-PSG) was analyzed for identifying simple and complex motor episodes during all sleep stages.

Results: Patients with iRBD reported more frequently an every-day occurrence of RBD episodes, which more often were reported to be violent in pattern. NT1 patients had more frequently simple motor episodes which occurred through all the night, in all sleep stages and showed an "intra-individual" stereotypic patter, when compared to iRBD. IRBD patients instead had episodes largely confined to REM sleep and occurring predominantly in the second half of the night. Skin biopsy was positive for p-alpha-syn deposits in almost 87% of iRBD patients and in none of NT1 patients. IRBD patients showed more frequently abnormities at neuropsychological investigations, when compared to NT1 patients.

Conclusions: iRBD and RBD due to NT1 do have different clinical and pathological findings, confirming a completely different pathophysiology.

C14

Cerebellar atrophy in patients with cervical dystonia

Francesco Silvestre[1], *S. Peluso*[1], *S. Cocozza*[2], *G. Pontillo*[2], *C. Russo*[2], *F. Baglio*[3], *A. Macerollo*[4], *A. Brunetti*[2], *F. Manganelli*[1], *A. Castagna*[3], *M. Esposito*[1]

[1]Department of Neurosciences, Reproductive and Odontostomatological Sciences, University of Naples "Federico II", Naples, Italy
[2]Department of Advanced Biomedical Sciences, University of Naples "Federico II", Naples, Italy
[3]IRCCS Santa Maria Nascente - Don Carlo Gnocchi Foundation ONLUS, Milan, Italy
[4]Sobell Department of Motor Neuroscience and Movement Disorders University College London, London, UK

Background: Cervical dystonia (CD) is a focal dystonia caused by the involuntary contraction of neck muscles and clinically characterized by abnormal movements and postures of the head and neck. Dystonia has been considered a disorder of the basal ganglia but experimental clinical and neuroimaging data suggest the involvement of cerebellum.

Material and methods: Volumetric T1w images from 22 CD patients (mean age: 50.9±12.2, M/F: 11/12) and 23 healthy controls (HC) (mean age: 49.5±10.5, M/F: 11/12) were acquired on two different MR scanners as part of a conjunct project. Images were segmented using the Spatially Unbiased Infratentorial Tooblox implemented in the Statistical Parametric Mapping (SPM v.12) software, and cerebellar lobes (anterior, as the sum of Lobules I-V, and posterior, as the sum of Lobule VI-X) and single lobule volumes were automatically extracted for each subject, along with the respective intracranial volume for normalization purposes. Between group differences were probed via Generalized Linear Model, correcting for age and sex, while possible correlations with clinical variables (disease duration and TSUI score) were tested via Spearman correlation analysis, with statistical significance set at $p<0.05$ Bonferroni corrected for multiple comparisons.

Results: Patients with CD proved to have a significant reduction of the anterior cerebellum ($p=0.002$) compared to HC (mean values: 17.1ml ± 2.0ml vs 18.3ml ± 1.8ml, respectively), while no significant differences emerged for the posterior cerebellum. A significant volume reduction was found for lobule V ($p=0.002$) and VI ($p=0.002$), suggesting their possible specific involvement. A significant correlation between Lobule V volume and disease duration was also found ($\rho=-0.57$, $p=0.005$).

Conclusions: Our study confirm the involvement of cerebellum in dystonia. Its anterior lobules could have a relevant role into the pathophysiological mechanisms underlying CD. A deeper knowledge of cerebellar dysfunctions in CD pathogenesis could open new scenarios on the therapeutic use of cerebellar stimulation techniques.

C15

Levodopa response in later stages of Parkinson's disease: a case-control study

Margherita Fabbri[1,2], *M. Coelho*[1,3], *D. Abreu*[1], *L. Correia Guedes*[1,3], *M.M. Rosa*[1,3,4], *A. Antonini*[5], *J.J. Ferreira*[1,3,4]

[1]Instituto de Medicina Molecular, Lisbon, Portugal
[2]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[3]Neurology Service, Department of Neurosciences, Hospital Santa Maria, Lisbon, Portugal
[4]Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, University of Lisbon, Portugal
[5]Fondazione Ospedale San Camillo"-I.R.C.C.S., Parkinson and Movement Disorders Unit, Venice, Italy

Background: L-dopa efficacy on Parkinson's disease (PD) cardinal motor symptoms may decrease with disease progression. If so, a simplification of drug regimen in later disease stages may be beneficial.

Objective: To compare the response of motor and non-motor symptoms (NMS) to a L-dopa challenge test between late stage (LS) and advanced stage (AD) PD patients.

Methods: A case-control study on 17 LSPD patients (Schwab and England ADL Scale <50 or Hoehn Yahr Stage >3 in MED ON) and 17 advanced ADPD (presence of L-dopa induced motor complications) patients matched for age at disease onset underwent an acute levodopa challenge test and an extensive cross-sectional clinical assessment for motor, NMS, namely blood pression (BP), pain and fatigue. Probable PD dementia (PDD) was diagnosed according to the Level I recommendation of the MDS Task Force.

Results: Fourteen LSPD patients (82%) had probable PDD. L-dopa improved 14% the MDS-UPDRS-III score ($p<0.001$) of LSPD patients, but had no effect on NMS, except a lowering of orthostatic BP. Conversely, the MDS-UPDRS-III score of ADPD patients improved 51% ($p<0.001$) with L-dopa, including most axial signs. L-dopa improved fatigue and pain of ADOD patients, despite worsening orthostatic BP. In LSPD, ΔMDS-UPDRS-III had a positive correlation with MDS-UPDRS-IV, item 4.2 and ΔAIMS (R=0.536/0.730/0.535), while no significant correlations were found for ADPD patients. Multiple regression analysis showed that PDD was the only variable that independently predicted a worse L-dopa response (β=-14.4; p=0.011; R2:0.691).

Conclusions: The L-dopa response on motor and non-motor symptoms is worse in LSPD compared to ADPD patients, despite similar age, age at PD onset and disease duration Dementia is highly predictive of a worse response to L-dopa, probably reflecting more disease progression. Identification of clinical markers of L-dopa responsiveness could help clinicians in the management of these patients and in the education of patients and families.

C16

Dopamine agonist withdrawal syndrome in Sardinian patients affected by Parkinson's Disease

Paolo Solla, R. Pau, G. Orofino, T. Ercoli, V. Melas, V. Pierri, D. Fonti, L. Fadda, F. Marrosu, G. Defazio

Movement Disorders Center, AOU Cagliari, University of Cagliari, Cagliari, Italy

Background: Dopamine agonist (DA) withdrawal syndrome (DAWS) is a complication that affects patients affected by Parkinson' disease (PD). DAWS is defined as a severe, stereotyped cluster of physical and psychological symptoms related to DA tapering, causing clinically significant distress or social/occupational dysfunction and is scarcely investigated. Currently there are no standard treatments for this disorder, whilst early recognition of risk factors appears significant for prevention.

Objective: The aim of this study was to determine the frequency of DAWS in a sample of Sardinian patients with Parkinson's disease.

Methods: 278 (169 male) PD patients outpatients on DA treatment from the Movement Disorders Center of the University of Cagliari were included in the study. DAWS diagnosis was made according with proposed criteria of Rabinak et Niremberg [1]. Causes of DA reduction/suspension were registered. Presence of impulse control disorders (ICD), dopamine dysregulation syndrome, and other behavioral/neuropsychiatric disorders was also investigated. Levodopa Equivalent Daily Dose (LEDD) was registered.

Results: Mean age of the sample was 69.4±8.6 years. Mean disease duration was 8.9 ± 5.5. Among different DAs, 165 patients (59.3%) were on pramipexole, 73 patients (26.3%) were on rotigotine, and 64 patients (23.0%) were receiving ropinirole. 22 patients (7.9%) were on treatment with more DAs. Of these 278 subjects treated with a DA, 111 underwent subsequent DA reduction/suspension (39,93%). Among causes of DA reduction/suspension, the most important was the presence of ICD (26.1%), followed by psychoses (22,5%). Of these 111 subjects, 10 (9%) developed DAWS. Only 4 subjects with DAWS had baseline DA-related impulse control disorders, while the remaining six patients did not have a history of ICD. DAWS development was mainly related to DA dosage before the suspension (280,5 ± 84 mg in patients with DAWS vs 109,2 ± 113 mg in patients without DAWS, $p<0,001$).

Conclusions: DAWS represents a possible psychiatric behavioral complication in PD patient, although often not adequately investigated. Physicians should control patients closely when tapering DAs to prevent this disabling syndrome.

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C17

Prospective memory in Parkinson's disease: the role of the motor subtypes

Alfonsina D'Iorio[1], G. Maggi[1], *C. Vitale*[2,3], *D. Di Meglio*[1], *L. Trojano*[1,4], *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 Health, IDC-Hermitage Capodimonte, Naples, Italy
[4]Salvatore Maugeri Foundation, Scientific Institute of Telese, Telese Terme, Italy

Introduction: Prospective memory (PM) is defined as memory for future intentions and it is typically divided into time-based and event-based. Deficit of PM has been reported in patients with Parkinson's Disease (PD) but, until now, no study has yet explored the association between motor subtypes (TD, tremor dominant and PIGD, rigidity/bradykinesia dominant) and performance on PM tasks.

Objectives: In the present study, we evaluated whether deficits in PM abilities were present to the same extent in TD-PD and PIGD-PD subtypes and whether the putative PM defects could be associated with specific neuropsychological features, and also with reduced functional autonomy in the two different motor subtypes.

Methods: Consecutive PD outpatients were screened and placed into the two groups according to Jankovic et al.'s criteria [1]. In addition, we enrolled healthy controls (HCs) matched with PD patients for demographic features. All participants underwent a neuropsychological battery to assess PM functioning, verbal memory, executive functions, the frequency of prospective and retrospective memory failures, the subjective memory complaints and the apathetic symptoms. In PD patients we also evaluated the functional impact of cognitive impairment.

Results: We enrolled 28 patients with TD-PD, 28 patients with PIGD-PD and 50 HCs. The three groups did not differ on demographic and cognitive variables. Patients with TD-PD performed worse on time-based PM tasks than patients with PIGD-PD and HCs, while no significant difference was found among the three groups on event-based PM tasks. Executive dysfunctions contributed to reduced time-based PM scores in TD-PD. Moreover, more severe deficit of time-based PM and more frequency of perceived failures of PM contributed to reduced functional autonomy in TD-PD.

Conclusions: Our finding of a poorer performance of patients with TD-PD on time-based tasks suggests that this might be considered as a distinctive non-motor symptom of TD-PD and it might affect the functional autonomy in this subtype of PD.

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C18

Levodopa-induced dyskinesias and impulse disorders in Parkinson's disease: two sides of the same coin?

Federico Paolini Paoletti[1], *N. Tambasco*[1], *G. Cappelletti*[1], *P. Eusebi*[1], *S. Simoni*[1], *P. Nigro*[1], *E. Brahimi*[1], *M. Filidei*[1], *P. Calabresi*[1,2]

[1]Neurology Clinic, S. Maria della Misericordia Hospital, University of Perugia, Perugia, Italy
[2]IRCCS "Santa Lucia", Rome, Italy

Introduction: Dopaminergic replacement therapy is the mainstay of treatment in Parkinson's disease (PD). However, its chronic use is associated with the development of motor and behavior complications, represented by levodopa-induced dyskinesias (LID) and impulse control and repetitive behavior disorders (ICRB), respectively [1]. Several studies have demonstrated an increasing risk of LID and IRCB co-occurrence in PD patients.

Objective: We aimed to evaluate the prevalence of ICRB in PD patients with and without LID.

Methods: 117 non-demented PD patients with a disease duration higher than 5 years were consecutively recruited from our Movement Disorders Centre. Motor disability and disease severity were evaluated by using MDS-UPDRS-III and H&Y scores. For each patient Levodopa Equivalent Daily Dose (LEDD) was calculated. LID and ICRB were tested by means of Rush Dyskinesia Rating Scale and Impulsive-Compulsive Disorders Questionnaire-Rating Scale (QUIP-RS), respectively. PDQ-39 was used to assess health-related quality of life. Statistical analysis was performed by using Spearman coefficient for associations between continuous variable and Chi-square test for categorical variables.

Results: In our cohort, 55 patients were affected by LID. The overall prevalence of ICRB was 41% (95% CI = 32% to 50%). Prevalence of ICRB was higher in patients with LID compared to those without LID (58% vs 26%, $p<0.001$). QUIP-RS was positively correlated with PDQ-39 ($rs = 0.19$, $p=0.039$). We did not find any correlations between QUIP-RS and disease duration, MDS-UPDRS-III and LEDD.

Conclusions: In line with previous literature [2], our study confirms that ICRB are more frequent in PD patients with LID. Findings such these strengthen the idea that motor and behavior complications of dopaminergic replacement therapy are linked by a common susceptibility and that LID and IRCB share underlying pathophysiological mechanisms.

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Poster

**CONSULTA
IL
PROGRAMMA**

P1

Focal hand dystonia and rehabilitation: systematic review of randomized control trials

Marco Tofani[1], *G. Galeoto*[2], *E. Castelli*[1], *A. Berardi*[3], *G. Fabbrini*[4,5]

[1]Neurorehabilitation Unit, Department of Neurosciences and Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy
[2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
[3]Sapienza University of Rome, Rome, Italy
[4]Department of Human Neurosciences Sapienza University of Rome, Rome, Italy
[5]IRCCS Neuromed, Pozzili, Italy

Introduction: Focal Hand Dystonia (FHD) is an enigmatic disorder typically characterized by muscles spasms, involuntary movements, and abnormal posturing. Different rehabilitation approaches are used: sensory-motor training, neurorehabilitation, task- specific rehabilitation, splinting techniques, or the use of different apparatus associated with rehabilitation. However, in international literature, there is no unanimous consent on which intervention may be useful to improve people's performance and quality of life.

Objective: To evaluate the evidences on FHD rehabilitation through a systematic review of randomized control trials (RCT).

Methods: Search terms included "Hand Dystonia" and "Rehabilitation" [MEshTerms]. All randomized control trials published between January 1997 and December 2018 which referred to FHD rehabilitation were included. The search strategies was performed in seven databases, namely Pubmed, Medline, Embase, Cinahl, Scopus, PEDro and OTseeker.

Results: The database search yielded 7 articles which met inclusion criteria: 2 focused the intervention on motor re-training, 1 on the use of kinesiotaping, 4 on rehabilitation associated with repetitive transcranial magnetic stimulation (rTMS). Caused to the heterogeneity of the intervention and especially for the different outcome measures investigated, it was not possible to perform a meta-analysis study.

Conclusions: Kinesiotaping may be useful in treating pain, rehabilitation is not necessarily task-specific and the use of rTMS can increase therapy effectiveness in rehabilitation. However, evidences produced do not make possible formulating strong recommendations. To confirm the usefulness of a specific rehabilitation intervention in FHD, further works are needed.

P2

Voice analysis in spasmodic dysphonia

Francesco Asci[1], *A. Suppa*[1,2], *L. Marsili*[1,2], *G. Ruoppolo*[4], *G. Costantini*[3], *G. Saggio*[3], *A. Berardelli*[1,2]

[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]Department of Sensorial Organs, Otorhinolaryngology Section, Sapienza University of Rome, Rome, Italy

Objective: To investigate differences in voice parameters between patients affected by different variants of spasmodic dysphonia (SD) and healthy subjects (HS).

Background: SD is a task-specific focal dystonia manifesting with involuntary laryngeal muscle spasms leading to intermittent strained/strangled voice. The lack of diagnostic criteria and validated severity scales makes the diagnosis of SD rather challenging. In the present study, we examined voice instrumentally in SD patients by means of acoustic analysis and compared a number of voice parameters in SD patients and HS.

Methods: we investigated 50 right-handed non-demented, non-depressed native Italian speakers SD patients and 50 age and sex-matched healthy subjects. 25 SD patients were studied also during the effect of Botulinum Neurotoxin-A (BoNT-A) therapy. Phoniatric evaluation included laryngoscopy, voice spectrogram and voice cepstral analysis of a "standardized sentence repetition" and a "sustained vowel (A, E, IU, IAMM). We collected voice samples using a high-definition audio recorder. Cepstral peak prominence (CPP) together with other spectral features, such as CPPS (smoothed CPP), Hi/Low frequencies rate, harmonics-to-noise ratio, shimmer and jitter were extracted. Finally, in order to differentiate automatically voice in SD and HS, we used a classification procedure with Support Vector Machine (SVM), Naïve Bayes and Multilayer Perceptron Neural Network (ANN) using Weka software.

Results: Voice analysis discriminates HS and SD, with a sensitivity of 76% by using SVM, Naïve Bayes and ANN; and a specificity of 100%, 87% and 83% by using respectively SVM, Naïve Bayes and ANN. Positive predictive value is 100%, 84%, 80% by using respectively SVM, Naïve Bayes and ANN. Negative predictive value is 83%, 81%, 80% by using respectively SVM, Naïve Bayes and ANN. Accuracy increased significantly after Feature selection and Discretization. Good performances of the algorithm were obtained also in the differentiation of 25 SD patients examined under- and not-under BoNT-A therapy.

Conclusions: Voice analysis discriminates SD patients from HS, representing a new helpful tool to better characterize voice abnormalities in SD. These results suggest the idea that voice features extraction and classification are important instruments to support clinicians in the correct diagnosis of SD, among different voice disorders.

P3

RGS9-2 rescues dopamine D2 receptor levels and signaling in DYT1 dystonia mouse models

Antonio Pisani[1,2], *G. Ponterio*[1,2], *P. Imbriani*[1,2], *A. Tassone*[1,2], *G. Sciamanna*[1,2], *S. Migliarini*[1], *G. Martella*[1,2], *M. Meringolo*[1,2], *R.E. Goodchild*[4], *N.B. Mercuri*[1,2], *M. Pasqualetti*[3,5], *E. Bezard*[6], *P. Bonsi*[1]

[1]Santa Lucia Foundation IRCCS, Rome, Italy
[2]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[3]Department of Biology, University of Pisa, Pisa, Italy
[4]Department of Neurosciences, VIB-KU Leuven Center for Brain and Disease Research, KU Leuven, Leuven, Belgium
[5]Center for Neuroscience and Cognitive Systems @UniTn, Istituto Italiano di Tecnologia, Rovereto, Italy
[6]Institut des Maladies Neurodégénératives, UMR 5293, Bordeaux, France

Introduction: Striatal dopaminergic transmission is central to movement control and several disease conditions. Multiple lines of evidence demonstrated an altered dopamine D2 receptor (DRD2) signaling in some neurological disorders, including the severe early-onset generalized DYT1-TOR1A dystonia. Nevertheless, the mechanisms that regulate D2 receptor signaling in health and disease remain poorly understood.

Objective: To investigate the molecular mechanisms underlying DRD2 reduced levels and altered signaling in the striatum of DYT1 dystonia animal models, specifically Tor1a$^{+/-}$ - knock-out and Tor1a$^{\Delta gag/+}$ knock-in mice.

Methods: Age- and sex-matched wild-type and mutant mice were randomly allocated to experimental groups. We used a combined approach, based on immunoblotting, receptor autoradiography, stereotactic injections of viral particles and electrophysiological patch-clamp recordings on striatal cholinergic interneurons.

Results: We investigated the molecular mechanisms of striatal DRD2 dysfunction in multiple mouse models of DYT1 dystonia, finding reduced striatal levels of D2 receptor, and of its regulatory proteins spinophilin and RGS9-2. We showed that D2 receptor downregulation is mediated by an abnormal, selective trafficking to lysosomal degradation. Further, we presented evidence that genetic depletion of RGS9-2 mimics the D2 receptor loss of DYT1 dystonia striatum, whereas RGS9-2 overexpression rescues both receptor levels and electrophysiological responses in DYT1 striatal neurons.

Conclusions: This work uncovers the molecular mechanism underlying D2 receptor downregulation in DYT1 mice and in turn provides an explanation for the lack of effectiveness of dopaminergic drugs in DYT1 patients, despite significant evidence for striatal D2 receptor dysfunction in disease pathophysiology. Our data also open up novel avenues for disease-modifying therapeutics to this incurable neurological disorder.

P4

Pain in adult-onset cervical dystonia: frequency and associated clinical/demographic features.

Marcello Mario Mascia[1], *R. Erro*[12], *T. Ercoli*[1], *M. Esposito*[2], *A. Berardelli*[3,4], *G. Ferrazzano*[4], *G. Abbruzzese*[5,6], *L. Avanzino*[6,7], *R. Pellicciari*[8], *R. Eleopra*[9], *F. Bono*[10], *L. Bertolasi*[11], *P. Barone*[12], *R. Liguori*[13,14], *C. Scaglione*[14], *A. Pisani*[15], *M. Turla*[16], *M.S. Cotelli*[16], *G. Cossu*[17], *R. Ceravolo*[18], *M. Coletti Moja*[19], *L. Lopiano*[20], *M. Zibetti*[20], *P. Girlanda*[21], *F. Morgante*[21]*A. Albanese*[22], *R. Piredda*[22], *A.R. Bentivoglio*[23], *M. Petracca*[23], *R. Cantello*[24], *L. Magistrelli*[24], *M.C. Altavista*[25], *S. Misceo*[26], *M. Romano*[27], *M. Aguggia*[28], *B. Minafra*[29], *L. Madema*[30], *N. Modugno*[4], *F. Di Biasio*[6], *D. Imperiale*[31], *D. Cassano*[31], *G. Defazio*[1], *M. Tinazzi*[11]

[1]Department of Medical Science and Public Health, Neurology Unit, University of Cagliari, Italy
[2]Department of Neurosciences, Reproductive Science and Dentistry, Federico II University of Naples, Naples, Italy
[3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy [4]IRCSS Neuromed, Pozzilli, IS, Italy
[5]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genoa, Genoa, Italy
[6]Ospedale Policlinico San Martino IRCSS, Genoa, Italy
[7] Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, Genoa, Italy
[8]Department of Basic Science, Neuroscience and Sense Organs, Aldo Moro University of Bari, Bari, Italy
[9]Neurological Unit 1, Fondazione IRCCS. Istituto Neurologico "Carlo Besta", Milan, Italy
[10]Neurology Unit, Department of Medical and Surgical Sciences, Magna Graecia University of Catanzaro, Catanzaro, Italy
[11]Neurology Unit, Department of Neuroscience, University Hospital, University of Verona, Verona, Italy
[12]Center for Neurodegenerative Diseases (CEMAND), Neuroscience Section, University of Salerno, Salerno, Italy
[13]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[14]IRCCS Istituto delle Scienze Neurologiche, Bologna, Italy
[15]Neurology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[16]Neurology Unit, Valle Camonica Hospital, Brescia, Italy
[17]Department of Neurology, AOB "G. Brotzu" General Hospital, Cagliari, Italy
[18]Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[19]Neurology Unit, Umberto I Hospital, Turin, Italy
[20]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[21]Department of Neuroscience, University of Messina, Messina, Italy
[22]Department of Neurology, Istituto Clinico Humanitas, Rozzano, Milan, Italy
[23]Movement Disorders Unit, Center for Parkinson's Disease and Extrapyramidal Disorders, Institute of Neurology, Catholic University, Rome, Italy
[24]Section of Neurology, Department of Translational Medicine, University of Eastern Piedmont "Amedeo Avogadro", Novara, Italy
[25]San Filippo Neri Hospital, ASL Roma 1, Rome, Italy
[26]Neurologic Unit, San Paolo Hospital, Bari, Italy

[27]Neurology Unit, Villa Sofia Hospital, Palermo, Italy
[28]Neurology Department, Asti Hospital, Asti, Italy
[29]Parkinson's Disease and Movement Disorders Unit, C. Mondino National Neurological Institute, IRCCS, Pavia, Italy
[30]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milan, Italy
[31]Unit of Neurology, Ospedale Maria Vittoria, ASL "Città di Torino", Turin, Italy

Introduction/objectives: Neck pain of cramping or arthralgic quality is a frequent non motor symptom in cervical dystonia (CD), the most common form of adult-onset dystonia. This study was aimed to identify the main clinical and demographic features associated with pain in CD, an issue that has received little attention so far.

Methods: date were obtained from the Italian Dystonia Registry (IDR). Patients were stratified into two groups according to the presence of neck pain. Among the clinical and demographic features collected and analysed, there were working activities, level of education, phenomenology of dystonia, age at dystonia onset, dystonia associated features, family history of dystonia, aetiology of dystonia, neck/trunk injury, medical conditions associated with or predisposing participants to painful symptoms, geographical distribution of pain.

Results: Pain was reported by 446/802 CD patients (55.6 %). On multivariable logistic regression analysis neck pain was associated with lower education and presence of sensory trick. With regard to geographical distribution, the frequency of pain significantly decreased from Southern Italy to Central and Northern Italy. This relationship was not affected by potentially confounding variables.

Discussion/conclusions: The association between neck pain and education confirmed a similar finding already observed in other painful conditions. The association of pain and sensory trick would suggest a relationship between pain and impaired processing and integration of nociceptive stimuli at least in a proportion of CD patients. The greater frequency of pain in Southern Italy remains to be clarified.

P5

Motor and non-motor symptoms in blepharospasm: clinical and pathophysiological implications

Viola Baione[1], *G. Ferrazzano*[2], *I. Berardelli*[3], *A. Conte*[1,2], *C. Concolato*[1], *D. Belvisi*[2], *G. Fabbrini*[1,2], *G. Defazio*[4], *A. Berardelli*[1,2]

[1]Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy
[4]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy

Introduction: Blepharospasm (BSP) is a focal dystonia characterized by an increased activity of the orbicularis oculi muscles, increased blinking and apraxia of eyelid opening. BSP patients have been classified according to three clinical phenotypes, associated with varying degrees of brainstem interneuron hyperexcitability. BSP patients may have non-motor features, including psychiatric, sleep, cognitive and ocular symptoms.

Objective: The aim of the study was to investigate the presence of non- motor symptoms in BSP patients and whether they correlate with the clinical motor phenotypes of BSP or with specific demographic features. To assess whether different clinical features are accompanied by varying degrees of brainstem excitability, we also investigated the blink reflex recovery cycle. Results were compared with those of age- and sex- matched healthy controls.

Methods: We consecutively enrolled 60 patients with BSP and 40 age-matched healthy controls. The severity of BSP was assessed by means of the Blepharospasm Severity Rating Scale. All the participants underwent a psychiatric evaluation using the SCID I and II, a sleep evaluation using the PSQI and ESS, a cognitive evaluation using the MoCA, and an evaluation of ocular symptoms using a standardized questionnaire. The blink reflex recovery cycle was studied in all the subjects. Finally, we investigated the correlations between motor, non-motor symptoms and patients' clinical, demographic and neurophysiological features.

Results: The frequency of psychiatric, sleep and cognitive disorders and ocular symptoms was higher in BSP patients than in healthy controls. The total burden of non-motor symptoms was associated with age though not with the disease severity, clinical motor phenotypes or R2 recovery index of BSP. R2 recovery index abnormalities instead correlated with the various motor phenotypes of BSP.

Conclusions: Non-motor symptoms are independent of motor features and belong to the clinical spectrum of BSP. The presence of non-motor symptoms possibly reflect the network disorder of BSP.

P6

Development of a questionnaire to assess sensory trick in patients with dystonia

Gaia Bonassi[1], *N. Cothros*[2], *C. Cosentino*[3], *F. Di Biasio*[4], *E. Pelosin*[3,4], *R. Marchese*[4], *F. Morgante*[5], *D. Martino*[2,6], *L. Avanzino*[1,4]

[1]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[2]Department of Clinical Neurosciences, University of Calgary, Calgary, Canada
[3]Department of Neuroscience, University of Genoa, Genoa, Italy
[4]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[5]St George's, University of London, London, UK
[6]Hotchkiss Brain Institute, Calgary, Canada

Introduction: The sensory trick (ST) is a voluntary manoeuvre that temporarily improves dystonic postures and movements. Although self-induced application of sensory stimuli is the most common and effective category of ST, clinical experience suggests that the phenomenon is more diverse, to include purely motor and cognitive tricks. However, there are no systematic instruments to evaluate type and frequency of ST in idiopathic dystonia.

Objective: We developed an ad hoc questionnaire detailing ST information, in order to classify the most used tricks, their frequency and their efficacy to temporarily relieve dystonia in a sample of patients with cervical dystonia (CD).

Methods: CD patients were included in the study if they fulfilled following criteria: diagnosis of adult-onset idiopathic CD according to standard criteria, age >18 years, time elapsing from the previous botulinum toxin injection 3 months or more. We collected patients' demographic and clinical features. Severity of CD was assessed with TWSTRS. The questionnaire screened for different types of STs (sensorimotor, purely motor, purely sensory or cognitive), selected through consultation within a panel of experts and literature review. Patients were asked to describe, for each of them, the frequency of use and the relief induced by the ST on a 0-10 visual analogue scale.

Results: During this preliminary study, a total of 43 patients met eligibility criteria (32 females, 62.5±12.4 years). Mean disease duration was 15.3 years, with a mean TWSTRS scoring of 20.5. Thirty-three of them reported to frequently use STs. 72% out of 33 reported to use STs more than once in a day, with a mean relief of 7.2 out of 10. Most participants reported similar actions as resting chin on hand and pushing back of the head.

Conclusions: ST is a relevant clinical characteristic in CD and can be assessed by the use of a specific questionnaire.

P7

Affective and cognitive theory of mind is impaired in patients with cervical dystonia and tremor

Giovanna Lagravinese[1], *G. Santangelo*[2], *E. Pelosin*[1,3], *S. Cuoco*[4], *R. Marchese*[3], *F. Di Biasio*[3], *C. Serrati*[3], *P. Barone*[4], *G. Abbruzzese*[1], *L. Avanzino*[3,5]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[3]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[4]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine and Surgery, Neuroscience Section, University of Salerno, Salerno, Italy
[5]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy

Background: Cervical dystonia (CD) is characterized by recurrent or continuous involuntary muscle contractions and subsequent abnormal postures of head and neck [1]. Recently, evidence is accumulating for a range of non-motor symptoms accompanying this disease. In particular, difficulties in theory of mind (ToM), such as inferring mental states on both cognitive and affective levels were also observed [2].

Aim: To assess the ability to infer others' beliefs and intentions (cognitive ToM) and to infer other people's emotions and feelings (affective ToM) in patients with CD with and without tremor.

Methods: We evaluated affective ToM by means of the modified Italian version of the Emotion Attribution Task (EAT [3]) and cognitive ToM by means of the Italian version of the Advanced Test of ToM (AT [3]) in 23 patients with CD and tremor (CD-T), 14 patients without tremor (CD-NT), and 50 healthy subjects (HS). All groups were matched for age and education level.

Results: Results confirmed that both cognitive and affective ToM abilities were impaired in CD patients. In particular, regarding affective ToM, CD-T and CD-NT showed a worse performance compared to HS in recognizing others' people emotions (p always <0.05). Regarding cognitive ToM, both CD-T and CD-NT performed worse than HS in the AT task (CD-T: $p<0.001$; CD-NT: $p=0.039$). Moreover, CD-T were more impaired in inferring others' people mental states than CD-NT ($p=0.045$).

Discussion: Our study showed that the ability to recognize other people's emotions and feelings is abnormal in patients with cervical dystonia with and without tremor. Patients with tremor showed a worse performance at the cognitive ToM respect to CD without tremor. These findings support the hypothesis that dystonia may be a "network disorder" which involves basal ganglia and their connections with other brain structures, such as cerebellum (probably involved in tremor) and areas involved in cognitive and affective states' recognition.

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P8

Prospective memory in patients with dystonia: a comparison between cervical dystonia, blepharospasm patients and healthy subjects

Gianpaolo Maggi[1], *A. D'Iorio*[1], *G. Mautone*[1], *S. Peluso*[2], *F. Manganelli*[2], *M. Esposito**[2], *G. Santangelo**[1]

**These authors equally contributed to the article*

[1]Neuropsychology and Memory Clinic, Department of Psychology, University of Campania Luigi Vanvitelli, Caserta, Italy
[2]Department of Neuroscience, Reproductive Science and Dentistry, Federico II University of Naples, Naples, Italy

Introduction: The most prevalent forms of dystonia are those that affect a relatively isolated region of the body (focal dystonias, FD), as blepharospasm (BSP) and cervical dystonia (CD) [1]. Although previous studies revealed slight difference in executive function domain between patients with dystonia and healthy subjects (HCs) [2], until now, no study has yet investigated the prospective memory (PM) abilities, that is the memory for future intentions which is typically divided into time-based (TMPM) and event-based (EBPM) and it is mediated by frontal-striatal circuits, in patients with different forms of focal dystonia.

Objectives: In the present study we explored PM functioning in CD and BSP patients compared with HCs using the Memory for Intentions Screening Test (MIST), a standardized tool which allows to evaluate TMPM and EBPM.

Methods: Consecutive dystonic patients and HCs matched for demographic features were enrolled. All participants underwent a neuropsychological battery assessing PM functioning, verbal memory, executive functions, the frequency of prospective memory and retrospective memory failures, the subjective memory complaints and apathy.

Results: Twenty-seven patients with BSP, 26 patients with CD and 30 HCs were included in the study. The three groups did not differ on demographic and cognitive variables. BSP and CD groups performed worse on time-based PM tasks than HCs while no significant difference was found on event-based PM tasks. Moreover, poor performance on time-based PM task was related to poor performance on Trail Making Test within BSP group and on Modified Card Sorting Test within CD.

Conclusions: Our finding of a time-based PM deficit in BSP and CD patients is in line with the fact that dystonic patients showed mild executive dysfunctions when compared to HCs because performance on time-based PM is stricty related to difficulty in managing two concurrent cognitive demands [3], which is an executive function and is mediated by prefrontal cortex.

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P9

Kinematic analysis of facial, upper and lower limb bradkinesia in Parkinson's disease

Antonio Cannavacciuolo[1], *M. Bologna*[1,2], *A. Formica*[1], *D. Colella*[1], *G. Paparella*[1], *A. Guerra*[2], *A. Berardelli*[1,2]

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

Introduction: Kinematic analysis allows objective evaluation of bradykinesia, one of the cardinal motor symptoms in patients with Parkinson's disease (PD). While upper-limb bradykinesia in PD has been characterized in a relatively high number of studies using kinematic techniques, little is known on facial- and lower-limb bradykinesia.

Objective: We aimed to verify the discriminative properties of facial-, upper- and lower-limb bradykinesia in patients with PD, as assessed by motion capture analysis.

Methods: We included 15 patients with PD patients (10M, 5F), mean age ± 1 S.D.= 65.8±6.59 (range 45-76) years and 10 (4 M, 6 F) healthy controls, mean age ± 1 S.D.= 64.3±6.23 (range 55-72) years. The clinical assessment of patients included the motor section (part III) of the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Repetitive voluntary blinking as well as the finger- and toe-tapping subtest of the MDS-UPDRS (part 3), were recorded using an optoelectronic 3D motion capture system. Number of movements, movement rhythm, amplitude (hypokinesia) and velocity (bradykinesia) and progressive amplitude and velocity reduction during movement repetition (sequence effect) were analysed. Receiver operating characteristic (ROC), its area under curve (AUC) and Hanley-McNeil's 95% AUC confidence intervals were computed.

Results: During voluntary blinking, velocity (bradykinesia) measures only differentiated between PD patients and controls (AUC = 0.80; P<0.01). During finger tapping, amplitude (hypokinesia) and velocity (bradykinesia) measures differentiated between PD patients and controls (both AUC = 0.78; both Ps<0.01). For the lower limb measurements similar values were observed for both amplitude (AUC = 0.73; P<0.05) and velocity (AUC = 0.78; P<0.01). In addition, among the toe tapping measurements the movement rhythm also differentiated PD patients and controls (AUC = 0.70; P<0.05)

Conclusions: Kinematic analysis of finger and toe tapping allowed an objective analysis of facial, upper and lower limb bradykinesia. The results provide evidence of a rostrocaudal motor impairment in PD, possibly reflecting distinct pathophysiological mechanisms in the various body segments. The data emphasize the importance of the lower limb assessment in differentiating between PD patients and controls.

P10

Short-latency afferent inhibition modulation during observation of emotional postures

Alessandro Botta[1,2], *G. Lagravinese*[2], *M. Bove*[1], *C. Cosentino*[2], *E. Pelosin*[2,3], *L. Avanzino*[1,3]

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

Introduction: Observation of emotional body language has been shown to modulate corticospinal excitability response of primary motor cortex (M1) [1]. Emotional and attentive processes are physiologically mediated by the activity of cholinergic interneurons. A valid and non-invasive technique to assess cholinergic activity is Short-Latency Afferent Inhibition (SAI) protocol.

Objective: The aim of our study was to assess sensorimotor modulation through SAI paradigm while participants were observing emotional body posture pictures.

Methods: Ten undergraduate students were enrolled in the experiment. A total of 45 emotional body posture pictures divided in three different clusters ('Fear', 'Happy' and 'Neutral') were shown to the subjects. SAI was tested by means of transcranial magnetic stimulation at 120, 300 and 400ms from picture onset. A behavioural experiment was also performed in order to estimate reaction times of the dominant hand [2] while recognizing emotional and non-emotional body postures.

Results: Results showed that the inhibition of the SAI protocol on M1 excitability significantly increased during observation of 'Fear' and 'Happy' body postures compared to 'Neutral' at 120ms. Interestingly, SAI significantly increased during the observation of 'Neutral' body postures at longer intervals (400ms). Behavioural data showed that reaction times were shorter when participants were asked to recognize 'Happy' postures.

Conclusions: Our results showed that the observation of emotional postures has a modulatory effect over the sensorimotor circuit underpinning SAI. We observed an increased inhibition of SAI protocol on M1 excitability in the early phase while watching postures with an emotional connotation, which decreases in time when cognitive processes are involved [3]. The behavioural experiment strengthened our results showing that emotional body postures have an effect also over reaction times, meaning that emotional body language induces both neurophysiological and behavioural modifications. This paradigm could be applied in neurodegenerative diseases involving the cholinergic system, such as Parkinson's disease.

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P11

Neurophysiological characterization of postural tremor and re-emergent tremor in Parkinson's disease

Andrea Fabbrini[1], *G. Leodori*[2], *D. Belvisi*[2], *M.I. De Bartolo*[1], *M. Costanzo*[1], *F.A.V. Undurraga*[3], *A. Conte*[1,2], *A. Berardelli*[1,2]

[1]Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Human Motor Control Section, NINDS, NIH, Bethesda, MD, USA

Introduction: Parkinsonian patients may show a tremor that occurs immediately after a posture is reached (i.e. postural tremor) or after a short period of time of maintaining a posture (re-emergent tremor) [1]. Little is known about the pathophysiological basis of tremors during posture in Parkinson's disease.

Objective: To investigate the neurophysiological differences between postural and re-emergent tremor (RET) in Parkinson's disease.

Methods: The study was performed with 9 patients with rest tremor and RET and 5 patients with rest tremor and postural tremor. EMG was recorded from the extensor digitorum communis on the more affected side and EEG was recorded from C3/C4 channels. Tremor frequency and power, and cortico-muscular coherence (CMC) between EMG and EEG where measured at rest and while maintaining a posture. Single-pulse TMS was delivered over M1 and its effect on the RET and postural tremor was evaluated by calculating the tremor-resetting index (RI) [2].

Results: In patients with RET, the tremor frequency at rest and during RET had a similar peak at 4.5 Hz. In patients with postural tremor, the frequency of tremor at rest was 5.5 Hz whereas tremor frequency during posture was 10 Hz. Patients with RET showed an higher CMC in the tremor frequency range during rest and posture in comparison to patients with postural tremor who had less CMC.

With single-pulse TMS over M1 the RI of rest tremor was similar in patients with RET and in patients with postural tremor. Conversely, there was a trend toward an higher RI on postural tremor in RET patients than in patients with postural tremor.

Conclusions: Differences in frequency of tremor, CMC and RI between RET and postural tremor suggest that RET and postural tremor have different physiological mechanisms.

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P12

Monitoring subthalamic oscillations for 24 hours in a freely-moving Parkinson's disease patient

Brigida Minafra[1], *M. Arlotti*[2], *C. Palmisano*[3,4], *M. Todisco*[1,3], *C. Pacchetti*[1], *A. Canessa*[5,6], *N.G. Pozzi*[3], *R. Cilia*[7], *M. Prenassi*[8], *S. Marceglia*[2,8], *A. Priori*[9], *P. Rampini*[2], *S. Barbieri*[2], *D. Servello*[10], *J. Volkmann*[3], *G. Pezzoli*[7], *I.U. Isaias*[3]

[1]Parkinson and Movement Disorder Unit, National Neurological Institute Foundation "C. Mondino" IRCCS, Pavia, Italy
[2]Clinical Center for Neurotechnologies, Neuromodulation, and Movement Disorders, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Department of Neurology, University Hospital and Julius Maximilian University of Wuerzburg, Wuerzburg Germany
[4]Department of Electronics, Information and Bioengineering, MBMC Lab, Politecnico di Milano, Milan, Italy
[5]Fondazione Europea di Ricerca Biomedica, Cernusco sul Naviglio, Italy
[6]Department of Informatics, Bioengineering, Robotics and System Engineering, University of Genoa, Genoa, Italy
[7]Centro Parkinson, ASST G. Pini-CTO, Milan, Italy
[8]Dipartimento di Ingegneria e Architettura, Università degli Studi di Trieste, Trieste, Italy
[9]"Aldo Ravelli" Research Center, Department of Health Sciences, University of Milan and Ospedale San Paolo, Milan, Italy
[10]Department of Neurosurgery and Neurology, IRCCS Galeazzi Hospital, Milan, Italy

Introduction: True advances in deep brain stimulation (DBS) should allow personalizing stimulation delivery by following the current state of symptom-specific neural signals and tuning the stimulation according to activities of daily living (e.g. walking, sleeping, etc.).

Objective: The first steps for establishing adaptive DBS comprise the capacity for measurements in chronically-implanted patients (to avoid the "stunning effect") and for prolonged recordings not corrupted by artifacts.

Methods: We recorded for twenty-four hours the bilateral subthalamic local field potentials in one patient chronically implanted for Parkinson's disease (PD). The recordings were performed with the externalized AlphaDBS device in a 55 year-old patient at the time of battery replacement. Recordings lasted for 24 hours continuously over two days, in which the patient freely performed everyday life activities and had approximately six hours of sleep at night. Recordings were performed during active stimulation (left: 3- C+, 4.8V, 60μsec, 170Hz; right: 11-C+, 5.5V, 60μsec, 170Hz) in a differential configuration (left: contacts 0-1; right: contacts 8-9) and stored on the device.

Results: Despite active stimulation, we showed clear modulation of the low β-frequency range (13-20 Hz) following levodopa intake. In this band, we recorded the highest interhemispheric subthalamic cross-frequency amplitude-amplitude coupling ($r=0.62$, $p<0.0001$) during the daytime, which significantly diminished during night sleep. The clinical efficacy of DBS was maintained throughout the experiment, with a stable improvement of 30-37%, which was similar to what experienced by the patient at the enrollment (36% improvement in stim-on and meds-off).

Conclusions: Our results prove the feasibility of prolonged recordings in freely-moving chronically-stimulated patients. We also showed preliminary evidence that interhemispheric subthalamic coupling changes between wakefulness and sleep could provide an additional behavior-specific biomarker. These findings pave the way for testing different adaptive stimulation paradigms for STN-DBS and prompt a more accurate definition of symptom-related and behavior- specific biomarkers in PD.

P13

Motor learning and long duration response to levodopa in Parkinson's disease

Giorgia Sciacca[1], *G. Mostile*[1], *I. Disilvestro*[1], *G. Donzuso*[1], *R. Manna*[1], *G. Portaro*[1], *C. Rascunà*[1], *S. Salomone*[2], *F. Drago*[2], *A. Nicoletti*[1], *M. Zappia*[1]

[1]Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, Catania, Italy
[2]Department of Biomedical and Biotechnological Sciences, Section of Pharmacology, University of Catania, Catania, Italy

Introduction: Long-duration response (LDR) derived from prolonged administration of levodopa in Parkinson's disease (PD) [1]. Animal models supported the hypothesis that LDR is implicated in motor learning [2]. P300, motor evoked potentials (MEPs) and Bereitschaftspotential (BP) are neurophysiological tools to quantify motor learning in humans. We aimed to define the role of LDR in motor learning, evaluating neurophysiological parameters of PD patients with and without LDR and undergone or not motor learning skills.

Methods: Drug-naïve PD patients were prospectively enrolled. Patients underwent a 15-day-treatment of levodopa/carbidopa 250/25 mg at 24 h interdose intervals and randomized to perform or not a 15-day motor-training skill. Achievement of LDR was assessed at 15th day of treatment. Patients underwent clinical (Unified Parkinson's Disease Rating Scale motor section and Hoehn and Yahr stage) and neurophysiological (P300, MEPs and BP) assessments at baseline (T0) and at 15th levodopa (T15) day of treatment, before taking.

Results: 30 PD patients were enrolled: 9 trained patients with a sustained LDR (Group 1), 8 untrained patients with a sustained LDR (Group 2), 7 trained patients without a stable LDR (Group 3) and 6 untrained patients without a stable LDR (Group 4). A statistically significant improvement of P300 latency, MEPs amplitude and early and late BP latencies was observed in Group 1 from T0 to T15 ($p<0.006$; $p<0.03$; $p< 0.02$; $p<0.002$). A statistically significant improvement of early and late BP latencies was observed in Group 2 from T0 to T15 ($p<0.001$; $p<0.005$). No significant differences of neurophysiological parameters were found in Group 3 and 4 from T0 to T15.

Conclusions: Our findings support the hypothesis that LDR promote motor learning in PD patients. This observation might change therapeutic approach for PD.

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P14

Blink rate analysis in Parkinson's disease as diagnostic tool

Maria Letizia Caminiti[1], *A. Di Santo*[1], *A. Fallacara*[1], *M. Marano*[1], *P. Falco*[2], *V. Di Lazzaro*[1], *L. Di Biase*[1]

[1]Neurology Unit, Campus Bio-Medico University, Rome, Italy
[2]Radiotherapy Unit, Campus Bio-Medico University, Rome, Italy

Introduction: Decrease blink rate is a motor feature of idiopathic Parkinson's disease and other parkinsonism. An objective evaluation of blink rate can be used as a diagnostic not invasive biomarker for Parkinson's disease.

Objective: The aim of the study is to compare blink rate in Parkinson disease patients on therapy with healthy controls.

Methods: We enrolled 12 patients (68±6,5 yo) diagnosed with PD according to UK Parkinson's Disease Society Brain Bank diagnostic criteria, and 9 healthy subject as controls (55±9 yo). All subjects were filmed under three different test conditions for 1 min for each task. The three test conditions were: (1) rest, (2) conversation and (3) reading. Digitally recorded video images focusing on the eyes were collected. The observer reviewed the videotapes and measured the number of blinks for 1 min during each segment.

Results: A paired-samples t-test was conducted to compare the blink rate in PD patients and in healthy controls for each task. There was a significant difference in the blink rate during rest between PD patients (M 10,83; SD 12,15) and healthy controls (M 22,11; SD 6,25); t(19)=-2,53, p = 0,020. There was a significant difference also during conversation, between patients (M 17,42, SD 12,57) and controls (M 32, SD13,58); t(19)=-2,54, p =0,020. Otherwise, there was a non significant difference in the blink rate between cases (M 7,25, SD 10,21) and controls (M 16,56, SD 10,45); t(19)=-2,04 p = 0,055 during the reading task. Combining the two diagnostic predictors (blink rate during rest and conversation), the ROC AUC was 0.852.

Conclusions: This study confirms the utility of an objective evaluation of the blink rate, as a quantitative tool for the diagnosis of Parkinson's disease.

P15

Evaluating motor imagery of gait under normal and dual task conditions through high density EEG: a feasibility study

Martina Putzolu[1], *C.* Ogliastro[1], *G. Bonassi*[2], *R. Marchese*[3], *C. Serrati*[3], *G. Abbruzzese*[1], *L. Avanzino*[2,3], *D. Mantini*[4], *E. Pelosin*[1,2]

[1]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health Unit, University of Genoa, Genoa, Italy
[2]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[3]Ospedale Policlinico San Martino-IRCCS, Genoa, Italy
[4]Research Center for Motor Control and Neuroplasticity, KU Leuven, Leuven, Belgium

Introduction: Motor imagery (MI) is defined as the mental simulation of an action without its real execution [1]. MI has been used to study the cerebral control of gait since actual and simulated walking recruit very similar cerebral structures [2]. Alpha and beta EEG bands have been found to be involved during MI showing the so-called "event-related desynchronizations" (ERD), which represent indicators of cortical activity.

Objective: Our primary aim was to test the feasibility of an EEG protocol for identifying the neural correlates of gait MI and exploring the potential differences of imagined walking under normal (NW) and dual task (DT) conditions (obstacle crossing performance).

Methods: 19 healthy subjects (HS) were recruited to participate in the study. MI of gait was assessed by using high-density EEG (Brain Products, 128 electrodes). Participants were asked to imagine walking (through visual MI) in two different straight pathways: (i) path with no obstacles; (ii) pathway with a hurdle. A press button was used by participants in order to signal the starting and the ending moment of MI performances.

Results: Statistically significant ERD were found both in alpha and beta band during MI of NW in motor-related areas (i.e. primary, premotor cortices and supplementary motor areas); moreover, in alpha band we found significant cortical activity in occipital brain areas. MI of DT performance revealed similar ERD to NW task, with a greater involvement of planning regions

Conclusions: This EEG protocol was able to detect gait-related cortical areas and significant differences were found in brain regions among motor imagery conditions (Normal vs DT walking). These results support future application for assess MI ability and brain plasticity induced by MI training in PD population.

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P16

Effect of acute L-Dopa administration on eye movement parameters in Parkinson disease

Clara Grazia Chisari, G. Mostile, A. Luca, G. Donzuso, G. Sciacca, R. Bonomo, C. Rascunà, G. Portaro, F. Patti, A. Nicoletti, M. Zappia

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

Introduction: Previous studies on the effect of dopaminergic treatment on eye movements of patients with Parkinson disease (PD) have given inconsistent results.

Objective: To evaluate the eye movement parameters in patients with PD before and after acute L-Dopa administration.

Methods: We enrolled patients with diagnosis of PD, diagnosed to curretly accepted criteria. Eye movements were recorded at baseline (T0) and 120 min after the administration of carbidopa-levodopa 250+50 mg per os (T1) using an infrared-emitting videobased eye tracker (EyeLink 1000 Plus®). We evaluated: saccades (mean peak-velocity [pvel], mean latency, percentage of hypometric saccades); smooth pursuit (number of catch-up saccades [CUS] during pursuit and the mean of total amplitude of catch-up saccades [Amp CUS]); up- and downgaze limitation (the maximum range of amplitude [MaxAmp]); fixation task (square wave intrusion [SWI]).

Results: Twenty-two patients (mean age 66.3±10.9, 60.6% men) were enrolled. At T1, in the PD group we found, for saccadic task, an improvement in pvel (758.6±35.7 vs 832.9±41.3, $p<0.01$), a reduction percentage of hypometric saccades (61.3±10.3 vs 41.3±16.6, $p<0.01$) and on saccadic latency (301.3±9.9 vs 221.3±15.9, $p<0.01$); during fixation task, we found a reduction of the number of SWI (59.6±31.2 vs 50.4±27.5, $p<0.05$). Smooth pursuits were found improved in CUS (284.1±74.6 vs 300. 1±59.5, $p<0.05$) and in Amp CUS (5.8±7.2 vs 2.4±6.1, $p<0.001$). No differences in terms of MaxAmp were found between T0 and in T1.

Conclusions: We confirmed that eye movements were impaired in PD, as a result of a reduction in dopamine levels in basal ganglia, frontal cortex and superior colliculus. Moreover, L-Dopa was able to improve all saccades and smooth pursuit parameters in PD patients. Eye movement analysis may be useful not only in order to broaden the understanding of the pathogenetic processes of PD, but also to provide sensitive and specific indices of pharmacological effects.

P17

24 months prospective study on advanced Parkinson's disease patients undergoing LCIG treatment

Simona Scalise[1], *R. Cerroni*[1], *P. Imbriani*[1,2], *T. Schirinzi*[1,3], *M. Pierantozzi*[1], *A. Stefani*[1], *N.B. Mercuri*[1,2], *A. Pisani*[1,2]

[1]Centro Parkinson, Clinica Neurologica, Dipartimento di Medicina dei Sistemi, Università di Roma Tor Vergata, Roma, Italy
[2]IRCCS Fondazione S. Lucia, Roma, Italy
[3]Dipartimento di Neuroscienze, IRCCS Ospedale Pediatrico Bambino Gesù, Roma, Italy

Introduction: Parkinson's disease (PD) results from the depletion of striatal dopamine leading to motor, behavioral and cognitive symptoms interfering with daily activities and social interactions impacting upon the individual's quality of life. Chronic oral levodopa is associated with long-term complications such as motor fluctuations. In this context, continuous delivery of levodopa/carbidopa intestinal gel (LCIG) into the jejunum represents one of the best alternatives for advanced PD patients.

Objectives: The primary endpoint was to evaluate the long-lasting safety, including adverse events and suicide rate, and efficacy of LCIG, including how motor symptoms impact upon quality of life.

Methods: We enrolled twenty-five patients, who were examined prior to LCIG initiation and 3-6-12 and 24-month follow-up. Evaluations at each visit included, Houser diary (HD), Unified Parkinson Disease Rating Scale (UPDRS III-IV), Unified Dyskinesia Rating Scale (UDysRS) , Parkinson Disease Questionnaire (PDQ-39), Mini Mental Test Evaluation (MMSE), Beck Depression Inventory (BDI) and Columbia Suicide Severity Rating Scale (C-SSRS).

Results: Out of the twenty-five PD patients, twelve completed the 12-month and four the 24-month follow-up assessments. Data analysis showed the reduction of motor fluctuation, as assessed by HD, UPDRS-III and IV, UDysRS. Moreover, we observed the lack of worsening in term of cognitive impairment (at the MMSE) and the improvement of QoL at the PDQ-39. However, depressive symptoms worsened by comparing the BDI from the 6-month to the 12-month follow-up. Nevertheless, no-changes in C-SSRS were documented.

Conclusions: Our results confirm the efficacy of LCIG in advanced PD patients since this treatment is able to improve motor fluctuation warranting a long-lasting benefit on motor symptoms. Moreover, we observed that no patients revealed suicide ideation, although depressive symptoms may be increased after LCIG. We hypothesized that these last data could be related to the reduction of dopamine agonists in the post- LCIG period.

P18

Continuous subcutaneous apomorphine infusion in parkinson's disease: causes of discontinuation and subsequent treatment strategies

Cinzia Femiano[1], *E. Olivola*[1], *A. Fasano*[3,4], *S. Varanese*[5], *F. Lena*[1], *M. Santilli*[1], *D. Centonze*[1,2], *N. Modugno*[1]

[1]Unit of Neurology and Neurorehabilitation, IRCCS Neuromed, Pozzilli, Italy
[2]Department of Systems Medicine, Tor Vergata University, Rome, Italy
[3]Edmond J. Safra Program in Parkinson's Disease and the Morton and Gloria Shulman Movement Disorders Centre, Toronto Western Hospital, UHN, Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[4]Krembil Brain Institute, Toronto, Ontario, Canada
[5]Department of Neurology, ASL Lanciano-Vasto-Chieti, "S. Pio Hospital", Vasto, Italy

Introduction: Continuous subcutaneous apomorphine infusion (CSAI) is a well-recognized therapeutic option for the management of motor fluctuations in Parkinson's disease (PD), although clinical experience suggests that most patients discontinue CSAI after a variable amount of time due to several causes and circumstances.

Objectives: The objective of the present study was to evaluate the reasons of CSAI discontinuation and to investigate which treatment was adopted afterwards.

Methods: Two independent raters retrospectively reviewed the electronic medical record of 114 patients treated with CSAI for at least 6 months. The records were reviewed regarding efficacy, safety and evolution of CSAI treatment.

Results: Most of PD patients on CSAI had a significant improvement in their clinical condition. Dyskinesia was the most frequent causes of treatment discontinuation. The second reason for CSAI discontinuation was cognitive deterioration. At CSAI discontinuation, younger patients were more likely to undergo deep brain stimulation (DBS), while older patients and patients with cognitive impairment were more likely switched to oral therapy alone.

Conclusions: CSAI is an effective treatment that unfortunately must be discontinued in a great number of patients with advanced PD. As older age is the main limiting factor for accessing second level therapies at CSAI discontinuation, CSAI treatment should not be postponed to older age. CSAI might be considered as a good first-line and fast strategy in patients undergoing a rapid deterioration of their quality of life while waiting for DBS or levodopa/carbidopa intestinal gel therapy.

P19

Biphasic dyskinesias in Parkinson's disease patients treated with levodopa-carbidopa intestinal gel: insights from a multicenter retrospective analysis

Massimo Marano[1], *T. Naranian*[2,3,4], *L. Di Biase*[1,5], *G. Cossu*[6], *A. Di Santo*[1], *R. Arca*[7], *P. Marano*[8], *V. Di Lazzaro*[1], *A. Fasano*[2,3,4]

[1]Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine, Campus Bio-Medico of Rome University, Rome, Italy
[2]Morton and Gloria Shulman Movement Disorders Centre and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital, UHN, Toronto, Ontario, Canada
[3]Division of Neurology, Department of Medicine, University of Toronto, Toronto, Canada
[4]Krembil Brain Institute, Toronto, Ontario, Canada
[5]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK
[6]Neurology Department, AO "Brotzu", Cagliari, Italy
[7]Neurology Department, Brunico Hospital, Brunico, Italy
[8]Neurorehabilitation, Madonna del Rosario Clinic, Catania, Italy

Introduction: The efficacy of levodopa-carbidopa intestinal gel (LCIG) on motor fluctuations has been recognized in randomized trials, while its effect on dyskinesias has been indirectly supported by post-hoc analysis and is currently debated.

Aims: Characterize patients who developed atypical dyskinesias with biphasic features after LCIG.

Methods: This is a retrospective longitudinal case-control study on a large LCIG cohort observed before LCIG, end of titration and last follow-up. Patients with biphasic dyskinesias after LCIG, resistant to titration, were selected and compared to a sample of LCIG patients with conventional motor complications. We collected data on demographic variables, disease duration, Hoehn and Yahr, medications, levodopa equivalence daily doses, dyskinesia phenotype, daily course and management strategies, drop-out causes, BMI, UPDRS IV A/B and LEDD.

Results: Selected patients (30/208, 14.4%) reported the presence of continuous biphasic-like dyskinesias after LCIG with or without prolonged biphasic dyskinesias after pump disconnection at night. A subgroup presented undiscernible peak-dose and biphasic-like dyskinesias (mixed phenotypes; 8, 5.7%). Patients with biphasic-like dyskinesias after LCIG reported history of biphasic dyskinesias on oral levodopa more than patients with conventional motor fluctuations ($p<0.05$). UPDRS IV-A at baseline and UPDRS IV-A/B at follow-up were higher in patients with biphasic-like dyskinesias ($p<0.01$), dyskinesias daily course and clinical management differed respect to patients with conventional motor complications on LCIG ($p<0.01$). Patients with biphasic-like dyskinesias improved increasing the LEDD in half cases while patients with mixed phenotypes had the worst outcome and a high drop-out rate ($p<0.01$).

Conclusions: Biphasic dyskinesias incidence on LCIG is higher than initially thought. They hampered titration and, if mixed phenotypes were present, to a high drop-out rate despite management strategies. A significant number of patients reported history of biphasic dyskinesias on oral therapies. This study suggests caution during advanced therapy selection process, especially when LCIG is aimed to deal with dyskinesias.

P20

Subthalamic nucleus deep brain stimulation for Parkinson's disease: a study on neuropsychiatric symptoms

Elisa Montanaro, C.A. Artusi, M. Lopez, R. Balestrino, M. Fabbri, A. Romagnolo, M.G. Rizzone, M. Zibetti, L. Lopiano

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

Introduction: Deep brain stimulation of the subthalamic nucleus (STN- DBS) is an established treatment for motor complications in advanced Parkinson's disease (PD). However, STN-DBS effects on neuropsychiatric symptoms remain still controversial. Therefore, patients selection and follow-up are still challenging. Some authors, indeed, report the onset or the worsening of pre-existing neuropsychiatric alterations, while other studies refer the improvement of behavioral disorders after STN-DBS.

Objective: Our primary aim was to detect STN-DBS effects on neuropsychiatric symptoms on a large series of PD patients. The secondary aim was to evaluate the influence of medication change on neuropsychiatric symptoms variations.

Methods: 158 advanced PD patients (mean age: 60.2±6.2 years) treated with STN- DBS were submitted to an extensive neurological and neuropsychological assessment before (V0) and approximately one year later neurosurgery (V1). They were also requested to fulfill these questionnaires aimed to investigate neuropsychiatric symptoms: depression (Beck Depression Inventory II – BDI), apathy (Apathy Scale - AS) and anxiety (State-Trait Anxiety Inventory – STAI X Form). Wilcoxon test was used to compare V0 and V1 scores. Binary logistic regression was adopted to explore the influence of medication change on behavioral modifications.

Results: After STN-DBS, AS scores revealed a slight though not statistically significant, increase of apathy (V0=11.8±5.1; V1=12.6±5.1; p=0.300). Anxiety levels showed a slight but not significant decrease (STAI X1: V0=42.9±10.6; V1=41.9±9.8; p=0.169 - STAI X2: V0=44.3±9.7; V1=43.6±9.6; p=0.414). BDI scores, instead, showed a statistically significant difference (V0=12.6±7.6; V1=10.7±6.9; p=0.001), outlining a decrease of depressive symptoms. BDI scores modifications were not influenced by medication change after STN-DBS (% change Total-LEDD: p=0.510; % change Levodopa-LEDD: p=0.886; % change Dopamine agonist-LEDD: p=0.479).

Conclusions: Our findings support the safety of STN-DBS on neuropsychiatric symptoms. The improvement of BDI scores could be related to the reduction of PD motor symptoms and motor complications after neurosurgery.

P21

Long-term effects of intestinal levodopa-carbidopa infusion on axial signs and related prognostic factors in advanced Parkinson's disease

Margherita Fabbri, M. Zibetti, C. Pongmala, C.A. Artusi, A. Romagnolo, L. Lopiano

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

Introduction: Few study have suggested that levodopa (L-dopa) carbidopa intestinal gel (LGIC) infusion may have a benefit on freezing of gait (FOG) and axial signs in general in advanced Parkinson's disease (PD) patients.

Objective: We sought to investigate the long-term effect of LCIG on axial signs and the related prognostic factors.

Methods: We performed a retrospective study on 49 PD patients treated with LCIG. Axial signs as per the Unified Parkinson Disease Rating Scale (UPDRS) axial item score, Hoehn & Yahr (H&Y) scale, Mini Mental State Examination (MMSE), Beck Depression Inventory Scale, and levodopa equivalent daily dose (LEDD) were assessed at baseline (before starting LCIG treatment) and at the last follow-up (FU) under continuous LCIG infusion. Results were stratified for LCIG treatment duration (< 1 year, from 1 to 4 years, and ≥ 4 years).

Results: The disease duration and duration of LCIG therapy were 18±6.9 years and 47.6±30 months, respectively. During this period, total axial score (AS) and single axial items, including freezing of gait (FOG), deteriorated while motor complications were still improved, in spite of a significant LEDD/Kg increment. When adjusted for LCIG treatment duration, a higher AS and FOG severity at last FU were predicted by a lower response to L-dopa and higher HY score ($p<0.01$) at baseline and were associated with a worse performance in activities of daily living at FU (UPDRS-II, $p<0.001$). Single axial items remain stable up to one year and postural instability up to four years of LCIG treatment.

Conclusions: Baseline disease severity and the magnitude of L-dopa response predict the severity of axial signs after four years of LCIG treatment, with consequent implications on the patients' independency in ADLs.

P22

The impact of deep brain stimulation on personality traits in Parkinson's disease patient

Fabiana Ruggiero[1], *F. Mameli*[1], *M. Reitano*[1], *E. Gianoli*[1], *D. Tedino*[1], *L. Borellini*[1], *F. Cogiamanian*[1], *S. Barbieri*[1], *A. Priori*[2,3], *R. Ferrucci*[1,2,3]

[1]IRCCS Ca' Granda Foundation, Neurophysiology Unit, Milan, Italy
[2]"Aldo Ravelli" Center for Neurotechnolgy and Experimental Brain Therapeutics, Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan, Italy
[3]III Neurology Clinic, ASST Santi Paolo e Carlo, Milan, Italy

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) surgery has been an established method in improvement of motor disabilities in Parkinson's disease (PD) patients. It has been also claimed to have an impact on personality trait in PD patients, but little is known about this topic.

Objective: The objective of this study was to assess personality traits before and after STN-DBS in PD patients.

Methods: 21 patients with PD (aged 48–70 years; education 8-17 years; UPDRS part III: 18-54) were assessed with the Eysenck Personality Questionnaire-Revised (EPQ-R) [1] before and after six months (mean±SD: 6.3±0.9) of bilateral STN-DBS surgery. The EPQ-R is a self-report questionnaire evaluates three dimensions of personality measured on a continuum: Extraversion/Introversion (E), Neuroticism/Emotional Stability (N), and sychoticism/ Socialization (P). It is composed by 106 items; each item is responded to using a dichotomous (yes/no) response format. High scores on Extraversion reflect sociability, assertiveness, and the tendency to experience positive emotions. High scores on Neuroticism reflect moodiness, worry, and the tendency to experience negative emotions. High scores on Psychoticism reflect impulsiveness, tough-mindedness, and emotional detachment.

Results: Globally, the comparisons between pre and post-operative EPQ-R scores showed no significant change in the N [(mean±SD) T0: 10.75±4.98 vs T1: 9.55±3.77, p=0.13], P (T0: 7.65±5.20 vs T1: 7±3.29, p=0.58) and E (T 0: 12.30±3.51 vs T1: 11.9±4.21, p=0.46) scores. The individual analysis (Baseline mean ± 1 SD Clinical criterion) evidenced that 5 patients revealed an enhancement of extroversion trait (11%) and 3 patients showed a decrease in N score (46%) that can be related to better mood states. Conversely, 2 patients showed an increase in P score by about 25%.

Conclusions: Our study revealed that, after six months, STN-DBS surgery in PD patients failed to influence the personality traits, even though postoperative behavioral modification can occur in individual patients.

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P23

Lumping or splitting corticobasal degeneration from progressive supranuclear palsy: this is the question

Sofia Cuoco, A. Cappiello, R. Erro, M.T. Pellecchia, P. Barone, M. Picillo

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

Introduction: Pathological studies suggest corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) are different diseases. And yet, those present several overlapping clinical, genetic and therapeutic aspects. The aim of this study was to apply CBD and PSP clinical diagnostic criteria to patients presenting with corticobasal syndrome.

Methods: Between January, 1 2015 and December, 31 2018, twelve patients with corticobasal syndrome were evaluated at our center with an extensive battery of clinical and cognitive assessments. According to clinical diagnostic criteria 7 were classified as having PSP–CBD variant and 5 as having CBD. Differences between groups were computed with Mann-Whitney and Fisher's tests. Groups were compared for the following milestones: mild cognitive impairment and dementia, prominent postural instability, vertical supranuclear gaze palsy, need to use a walking aid or wheelchair, presence of unintelligible speech and dysphagia.

Results: The two groups presented similar demographics as well as disease duration and age at onset ($p>0.05$). PSP–CBD showed more severe clinical features compared to CBD according to the PSP rating scale total and subscores ($p<0.05$). PSP–CBD presented lower scores in cognitive tests evaluating frontal and language cognitive domains ($p<0.05$). The majority of PSP–CBD patients was either affected by dementia (42%) or presented normal cognition (42%). The majority of CBD patients was either affected by MCI–multiple domain (40%) or presented normal cognition (60%). PSP–CBD had higher frequency of prominent postural instability, vertical supranuclear gaze palsy and unintelligible speech ($p<0.05$).

Conclusions: Our study show that both PSP and CBD criteria can be applied to such patients. Indeed, PSP-CBD and CBD present several overlapping clinical features, with PSP-CBD showing a more severe form of disease in term of motor and cognitive impairment. In absence of in vivo diagnostic biomarkers, there's the need to reconsider the utility to apply different sets of clinical criteria to classify PSP and CBD as different disorders.

P24

Validation of the Italian version of the PSP Quality of Life questionnaire

Marina Picillo[1], *S. Cuoco*[1], *M. Amboni*[1], *F.P. Bonifacio*[2], *B. Borroni*[3], *A. Bruno*[4], *F. Bruschi*[5], *I. Carotenuto*[1], *R. Ceravolo*[4], *R. De Micco*[2], *A. De Rosa*[6], *F. Di Blasio*[7], *A. Di Fonzo*[8], *F. Elifani*[9], *R. Erro*[1], *M. Fabbri*[10], *M. Falla*[11], *G. Franco*[8], *D. Frosini*[4], *S. Galantucci*[12], *G. Lazzeri*[8], *L. Magistrelli*[13,14], *M. Malaguti*[15], *N.B. Mercuri*[16], *A.V. Milner*[13], *B. Minafra*[5], *N. Modugno*[9], *A. Nicoletti*[17], *R. Marchese*[7], *E. Olivola*[9], *A. Padovani*[3], *A. Pilotto*[3], *C. Rascunà*[17], *M.C. Rizzetti*[18], *G. Santangelo*[19], *T. Schirinzi*[16], *A. Stefani*[16], *A. Tessitore*[2], *M.A. Volontè*[12], *R. Zangaglia*[5], *M. Zappia*[17], *M. Zibetti*[10], *P. Barone*[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Odontoiatry, University of Salerno, Salerno, Italy
[2]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[3]Centre for Neurodegenerative Disorders, Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[4]Dipartimento di Medicina Clinica e Sperimentale Università di Pisa, Pisa, Italy
[5]Parkinson's Disease and Movement Disorders Unit, C. Mondino National Neurological Institute, Pavia, Italy
[6]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[7]IRCCS Policlinico San Martino, Genova, Italy
[8]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[9]IRCCS Neuromed, Pozzilli, Italy
[10]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[11]Department of Neurology, General Hospital of Bolzano, Bolzano, Italy
[12]Dipartimento Neurologico, IRCCS Ospedale San Raffaele, Milano, Italy
[13]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[14]PhD Programme in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy
[15]UO Neurologia, Ospedale Santa Chiara, Azienda Provinciale per i Servizi Sanitari Provincia Autonoma di Trento, Trento, Italy
[16]UOSD Parkinson, University Hospital of Rome "Tor Vergata", Rome, Italy
[17]Department "G.F. Ingrassia", Section of Neurosciences, University of Catania, Catania, Italy
[18]S. Isidoro Hospital - FERB Onlus, Trescore Balneario, Italy
[19]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Progressive Supranuclear Palsy (PSP) is a rare rapidly progressive, neurodegenerative disease characterized by falls and supranuclear gaze palsy. The use of health-related quality of life (HR-QoL) measures allows assessment of changes in health status induced by therapeutic interventions or disease progression in neurodegenerative diseases. The PSP Quality of Life questionnaire (PSP-QoL) is a 45-item, self-administered questionnaire designed to evaluate HR-QoL in PSP [1]. Here, the PSP-QoL was translated into Italian and validated in 190 PSP (96 women and 94 men; mean age ± standard deviation: 72 ± 6.5; mean disease duration: 4.2 ± 2.3) patients diagnosed according with Movement Disorder Society criteria and recruited in 16 third level movement disorders centers participating in the Neurecanet project.

The mean PSP-QoL total score was 77.8 ± 37 (physical subscore, 46.5 ± 18.7; mental subscore, 33.6 ± 19.2). Ninety-eight percent of data were totally computable. The percentage of missing values was ≤5% for all items. Neither ceiling nor floor effects were observed for the PSP-QoL total score or for the physical or mental subscores. Skewness of total and two subscores of PSP-QoL was within the standard limits. The internal consistency was satisfactory (Cronbach's alpha = 0.954); corrected item-total correlation was > 0.40 for the majority of items. A correlation with other HR-QoL measures (EQ-5D, EQ-visual analogue scale) as well as with motor (PSP rating scale) and disability (Schwab and England) assessments was shown suggesting adequate convergent validity of the scale. Gender and geographic location in Italy (North, Center, South) presented a significant impact on the PSP-QoL in our sample with women and patients from the South of Italy scoring higher than their counterparts. In conclusion, the Italian version of the PSP-QoL is an easy, consistent and valid tool for assessment of HR-QoL in PSP.

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P25

A case of hyperkynetic emergency

Alessio Novelli, I.A. Di Vico, F. Terenzi, S. Sorbi, S. Ramat

NEUROFARBA Department, University of Florence, Florence, Italy

Background: Hyperkinetic emergencies include different clinical syndromes dominated by severe, acute of subacute onset dyskinesias, whose untimely diagnosis and treatment may result in significant morbidity and mortality.

Case presentation: A 62-year-old man, with a 34 years history of Parkinson's Disease (PD) and treated for 19 years with bilateral Deep Brain Stimulation of Subthalamic Nucleus (STN-DBS) came to the Movement Disorder Clinic of Careggi Hospital (Florence) complaining about severe involuntary movements for 3 hours. The patient did not usually present dyskinesias, and had not undergone any recent changes in therapy. He reported only a recent urinary tract infection. On neurological examination, he presented with generalized choreic and ballistic movements and he was in a state of agitation and mental confusion. Patient was febrile, with 40°C body temperature. We immediately lowered the stimulation parameters and referred the patient to the emergency department. The subsequent investigations revealed hyponatremia and elevation of serum creatine-phosphokinases (CPK, up to 4891 U/L). We treated the patient with further gradual reduction of both stimulation parameters and dopaminergic drugs, as well as administering antibiotic therapy and intravenous rehydration. In the following 2 days, dyskinesias decreased and subsequently disappeared; body temperature and CPK values normalized.

Discussion: An acute or subacute onset of severe dyskinesias, with elevation of CPK and hyperpyrexia, in a patient affected by PD, defines a very rare condition known as "dyskinesia-hyperpyrexia syndrome" (DHS). This condition typically occurs in patients with advanced PD undergoing high dopaminergic stimulation, and can be triggered by infections, therapeutic changes, hot weather, dehydration. DHS is a life-threatening condition, for which prompt recognition and therapy are necessary. Management consists of dopaminergic stimulation reduction, support of vital functions, rehydration and treatment of possible triggers. Few cases of DHS are described in literature, and so far none in patients with DBS implant.

P26

Sustained efficacy of Botulinum toxin type A for Holmes tremor secondary to thalamic hemorrhage: follow-up of two patients

Tiziana De Santis, P. Latino, F.E. Pontieri, M. Giovannelli

Dipartimento di Neuroscienze, Salute Mentale e Organi di Senso (NESMOS), Sapienza Università di Roma, UOC di Neurologia Azienda Ospedaliera Sant'Andrea, Roma, Italy

Introduction: Holmes tremor (HT) is a symptomatic, low frequency (<5 Hz), mixed tremor that develops between 1 and 24 months after a lesion in the brainstem in the vicinity of the red nucleus [1] that damage the ascending cerebellothalamic and dentate-rubro-olivary pathways, and nigrostriatal fiber tract [2]. Benzodiazepines, propranolol, anticholinergics, channel-blockers, anticonvulsants, atypical neuroleptics, baclofen, dopamine agonists, and l-dopa are among the drugs used with a variable degree of success. Stereotactic thalamotomy and deep brain stimulation in the ventralis intermedius nucleus have been reported as effective surgical procedures but are invasive and associated with long-term side effects. Botulinum toxin type A (BoNT-A) is a valid option for treatment of focal tremors with long-term safety [3]. Only two case reports in literature reported the use of of BonT-A in HT [4].

Objective: We describe two patients who developed HT of right arm after thalamic hemorrhage successfully treated with BoNT-A that maintained sustained efficacy after two years of follow-up.

Methods: Two patients, 1 M, 45 yo, and 1 F 60 yo, with HT unresponsive to medical therapy have been treated with eight sections (one every three months) of BoNT-A injections. We used Essential Tremor Rating Assessment Scale (TETRAS) to evaluate tremor severity and interference with activity of daily living, and Manual Muscle Testing (MMT) for muscle strength. The first patient was injected with 50 IU of incobotulinum toxin A on biceps brachii and 75 on triceps brachii, the second patient with 100 IU on biceps brachii and 100 IU on brachioradialis. This schedule was maintained along each section of injection.

Results: Patients showed a sustained improvement of tremor severity with no muscle weakness, as measured by MMT score and no other significant side effect during two year of follow-up.

Conclusion: BoNT-A is a long-lasting effective treatment of HT.

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P27

Clinical, genetic and radiological characterization of patients with movement disorders and basal ganglia calcification

Federica Arienti[1], *G. Franco*[1], *E. Monfrini*[1], *A. Seresini*[2], *A. Di Fonzo*[1]

[1]Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy
[2]Medical Genetics Laboratory, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy

Introduction: Fahr's disease or Primary Familial Brain Calcification (PFBC) is a rare neurological disease characterized by idiopathic calcification of basal ganglia. Five genes have been identified to cause the disease, namely SLC20A2, PDGFR, PDGFRB, XPR1 and MYORG. Even if almost all these genes are involved in phosphate-calcium metabolism or in brain blood barrier permeability, the exact pathogenesis of PFBC is still unknown and the treatment is only symptomatic.

Objective: The aim of this study is to present a case series of patients affected by movement disorders and PFBC, analysing clinical presentation, radiological features and genetic profile.

Methods: From our movement disorders database, we selected patients with basal ganglia calcification. Firstly, we analysed the clinical and radiological data; secondly, we performed a genetic panel for 96 genes associated with Parkinson's disease, Fahr's disease, lysosomal and mitochondrial diseases, dystonia, dementia and NBIA.

Results: The case series from our database shows ten patients, five males and five females. The mean (±SD) age at onset of symptoms was 63 (± 8.8) years. Clinically, the most frequent neurological symptoms were rigidity (60%), postural instability (60%) and tremor (50%), while depression and anxiety figured as the main psychiatric disorders. The globus pallidus was the main radiological site affected by calcifications (70%), followed by the cerebellum (40%). Five patients had a positive family history for movement disorders, but in only one patient a causative mutation for Fahr's disease was found. [123]I-ioflupane SPECT was performed in five patients: the acquired brain sections showed significant bilateral lower striatal DaT uptake; however, in all these cases one side resulted more involved than the contralateral.

Conclusions: Although the genetic knowledge of PFBC is increasing, most patients do not show mutations in genes known to cause the disease and exhibit various clinical features, whose neuropathogenesis remains poorly defined. Considering that basal ganglia calcification on CT scans are extremely symmetrical, the finding of lateralization in the [123]I-ioflupane SPECT sequences complicates the understanding of the pathogenetic role of calcifications in relation to the symptoms and to the neurodegenerative process.

P28

Gait assessment of patients hereditary spastic paraplegia after botulinum toxin treatment

Mattia Sansone[1], *M. Costanzo*[2], *B. Corrado*[2], *S. Peluso*[1], *C. Criscuolo*[1], *A. Antenora*[1], *E. Raiano*[1], *F. Iorillo*[1], *F. Manganelli*[1], *M. Esposito*[1]

[1]Department of Neurosciences, Reproductive Sciences and Odontostomatology, Federico II University of Naples, Naples, Italy
[2]Orthopedic Surgery Department, Rehabilitation Unit, Federico II University, Naples, Italy

Background: Hereditary Spastic Paraplegia (HSP), includes different kind of genetic diseases presenting mainly progressive gait disorders and pyramidal impairment. Botulinum toxin (BTX) treatment is helpful to reduce spasticity and can also improve gait in patients with spastic paraplegia. BTS G-WALK® is a new mobile system performing a computerized gait analysis (CGT) that analyses gait motor pattern and balance. Aim of this study is to assess effect of BTX on gait in patients with HSP using BTS G-WALK®system.

Material and Methods: 8 patients (5M, 3F) with HSP (3 with SPG4, 1 with ALS2, 2 with SPG5, in two patients genetic tests are ongoing) were recruited for the study. Patients were treated with BTX-A at lower limbs, all brands commercially available were used (200U of ona/incoBTX-A, 500U of abo-BTX-A). Patients were assessed before (T0) and 4 weeks (T1) after the treatment with BTX. Spasticity was measured with the modified Ashworth scale (MAS). CGT was performed by the BTS G-WALK® system assessing kinetic parameters with a walking motor algorithm and measuring balance by the "timed up and go" test.

Results: At T1 we found a significant reduction of spasticity (p=0.05). CGT showed a significant reduction of CV (coefficient of variation) cycle time at T1 (p=0,017). Remaining kinetic parameters were not changed at T1. The timed up and go analysis showed a change with trend toward statistical significance for the following parameters at T1: "sit to stand" and "stand to sit" phase duration were reduced (p=0.08, P=0.06) whereas stand to sit vertical acceleration was increased (p=0.08).

Conclusions: This is a preliminary study of the BTX effect on walking in patients with HSP using the G-WALK® system. Our results suggest BTX may enhance balance and could also improve walking in HSP patients. More data are needed to confirm those conclusions.

P29

A rare cause of gait ataxia: CLIPPERS syndrome (Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids) complicated by stroke

Francesca Di Biasio, D. Sassos, C. Baglini Rolla, L. Saitta, C. Serrati

IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Introduction: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a central nervous system inflammatory syndrome predominantly affecting the brainstem, cerebellum, and spinal cord, first described in 2010 [1]. This rare condition usually begins with an insidious gait imbalance and early recognition on MRI is crucial.

Aim: We report a rare case of gait ataxia due to CLIPPERS, complicated by stroke.

Methods: We evaluated a 65-year-old male admitted to the hospital for a 20 days' history of gait ataxia and dizziness. The diagnosis of CLIPPERS was made by combining the clinical features with radiological evidences: punctate infiltration of the pons, brainstem and cerebellum [2]. Neurosarcoidosis, infections, central nervous system (CNS) lymphoma and Neuro-Behcet's disease were ruled out by history and investigations, CSF exam included. The patient responded dramatically to steroid therapy recovering completely. Few days after the treatment he developed a hyperintense left ganglionar lesion, in T2/FLAIR, with narrow diffusion in DWI and contrast enhancement, and pneumonia due to Citomegalovirus (CMV) and *Pneumocystis carinii* infection.

Conclusions: To our knowledge this is one of the rare cases reported in literature of gait ataxia due to CLIPPERS, complicated by stroke. The pathophysiology of CLIPPERS is not clear and the reports are quite few. The infections and the good response to steroids raise the hypothesis that CLIPPERS might be an immunomediated disorder, but our case opens a new scenario on the possible risk of acute vascular lesions after the diagnosis. With this report we want to underline: 1. Although rare, neurologists and radiologists should consider CLIPPERS in the differential diagnosis of acute/subacute gait ataxia; 2. Although CLIPPERS seems to be part of the immuno-mediated diseases [3], it is important to study vascular risk factors, since we do not know if itself predisposes to stroke 3. Radiological follow-up is mandatory to optimize the treatment.

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P30

MGLU3 metabotropic glutamate receptors as candidate targets for neuroprotective drugs in the MPTP mouse model of parkinsonism.

Marika Alborghetti[*1], *L. Di Menna*[*2], *A. Traficante*[2], *F.E. Pontieri*[1], *F. Nicoletti*[2,3], *V. Bruno*[2,3], *G. Battaglia*[2,3]

[1]Department of Neuroscience, Mental Health and Sensory Ogans (NESMOS), University Sapienza of Rome, Rome, Italy
[2]I.R.C.C.S. Neuromed, Pozzilli, Italy
[3]Department of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy

*These authors equally contributed to the work.

Introduction: mGlu3 metabotropic glutamate receptors are candidate targets for neuroprotective drugs owing to their ability to stimulate the production of TGF-β and GDNF. We found that systemic treatment with a mixed mGlu2/3 receptor agonist, LY379268, in mice, enhanced GDNF levels in the striatum, and this effect was abrogated in mice lacking mGlu3 receptor. In addition, treatment with LY379268 protected nigro-striatal neurons against neurodegeneration caused by an acute dose of MPTP [1]. The recent availability of subtype-selective agonists of mGlu3 receptors gave us the impetus to further examine the role of the receptor in mechanisms of neurodegeneration.

Objective: To establish whether the genetic deletion of mGlu3 receptors amplifies nigro-striatal damage and whether selective pharmacological activation of mGlu3 receptors is neuroprotective in a chronic MPTP mouse model, recapitulating the progressive degeneration occurring in Parkinson's disease.

Methods: We used mGlu3 or mGlu2 receptor knockout mice and their wild-type counterparts treated with 20 mg/kg of MPTP each other day for 15 or 30 days. In addition, we are planning experiments with a novel, selective, and brain-permeant mGlu3 receptor agonist using the same mouse model. Neurodegeneration is assessed by stereological cell counting in the substantia nigra, and HPLC measurements of dopamine and its metabolites in the striatum.

Results: We found that chronic treatment with MPTP led to a substantial drop in striatal dopamine levels. This effect was amplified in mGlu3 receptor knockout mice, whereas it was attenuated in mGlu2 receptor knockout mice. Studies with the mGlu3 receptor agonist are ongoing.

Conclusions: The use of the chronic MPTP mouse model with genetic deletion supports the hypothesis that mGlu3 receptors exert a neuroprotective activity attenuating the progressive degeneration of nigro-striatal dopaminergic neurons. Whether selective pharmacological activation of mGlu3 receptors causes neuroprotection and by which mechanism (production of GDNF or reduction of neuroinflammation) is currently under investigation.

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P31

Differences in 3D spatio-temporal and kinematic gait parameters between idiopathic normal pressure hydrocephalus associated with parkinsonism and parkinson's disease patients

Giacomo Portaro[1], *G. Mostile*[1], *V. Dibilio*[1], *F. Contrafatto*[1], *P. Cunsolo*[1], *G. Raudino*[2], *F. Certo*[2], *A. Nicoletti*[1], *G.M. Barbagallo*[2], *M. Zappia*[1]

[1]Department "G.F. Ingrassia", University of Catania; Neurology Clinic, Policlinico "G. Rodolico" University Hospital, Catania, Italy
[2]Department "G.F. Ingrassia", University of Catania; Neurosurgery Clinic, Policlinico "G. Rodolico" University Hospital, Catania, Italy

Introduction: Gait dysfunction is a common feature in patients with Parkinson's Disease (PD) as well as in patients with Idiopathic Normal Pressure Hydrocephalus (iNPH) associated with parkinsonism, leading to clinical overlap. There are some evidences of distinctive gait features in iNPH as compared to PD, including reduced gait speed and step length, increased asymmetry in step length as well as alterations in kinematic parameters related to dynamic instability. However, results remain still heterogeneous.

Objectives: To evaluate differences in 3D spatio-temporal and kinematic gait parameters between iNPH associated with parkinsonism and PD patients.

Methods: We used the BTS GaitLab system to evaluate gait kinetic and kinematic parameters in a group of patients with iNPH associated with parkinsonism, who were diagnosed based on clinical characteristics as well as for the radiological evidence of cerebral ventriculomegaly. They were compared to a cohort of patients affected by PD diagnosed according to Gelb et al., who were tested with the same system in their "practical on" motor state if pharmacologically treated.

Results: We enrolled N=7 iNPH patients with parkinsonism (age: 72.3 ±8.1 years; UPDRS-ME score: 29.7±11.2) to be compared with N=39 PD patients (age: 65.8 ±9.7 years; UPDRS-ME score: 31.1±9.7), of whom N=34 (87.2%) L-dopa treated. At univariate analysis, we observed a significant increase in right double support phase while a significant reduction in gait speed, bilateral gait cycle length and dorsi-plantar flexion of left ankle in iNPH patients as compared to PD. Multivariate analysis confirmed reduction in both left gait cycle length and dorsi-plantar flexion of left ankle as independent kinetic-kinematic factors differentiating the two conditions.

Conclusions: Our result confirmed increased gait asymmetry and disturbance of dynamic equilibrium in iNPH as compared to PD. The objective evaluation of specific spatio-temporal and kinematic parameters in patients with parkinsonism may help to differentiate iNPH from PD.

P32

Clinical response to 72-h lumbar csf drainage in idiopathic normal pressure hydrocephalus associated with parkinsonism: timing and correlates

Giovanni Mostile[1], *G. Raudino*[2], *G. Portaro*[1], *F. Certo*[2], *A. Nicoletti*[1], *G.M. Barbagallo*[2], *M. Zappia*[1]

[1]Department "G.F. Ingrassia", University of Catania; Neurology Clinic, Policlinico "G. Rodolico" University Hospital, Catania, Catania, Italy
[2]Department "G.F. Ingrassia", University of Catania; Neurosurgery Clinic, Policlinico "G. Rodolico" University Hospital, Catania, Catania, Italy

Introduction: Clinical response to 72-h lumbar CSF drainage represents a positive prognostic factors for ventriculoperitoneal shunting in patients with idiopathic Normal Pressure Hydrocephalus (iNPH). However, data concerning timing for the assessment of clinical response as well as factors associated with motor response in such patients are still inconsistent, especially for those affected by concomitant parkinsonism.

Objective: To evaluate timing and clinical correlates of motor response after 72-h lumbar CSF drainage in patients with iNPH associated with parkinsonism.

Methods: We analyzed data of iNPH patients who were referred to the Neurosurgery Clinic for a diagnosis of iNPH based on clinical characteristics as well as for the radiological evidence of cerebral ventriculomegaly. All patients were affected by parkinsonism. Before the procedure of ventriculoperitoneal shunting, they underwent long-term 72-h intracranial-pressure controlled CSF external drainage using the LiquoGuard system. A cognitive assessment was performed before the drainage. Clinical motor response pre- and post- the 72-h lumbar CSF drainage was evaluated.

Results: We identified 14 iNPH patients (age: 69.3 ±11.6 years; corrected MMSE score: 24.8±3.9; corrected FAB score: 11.8±3.6). The time between the two clinical evaluations (before and after the drainage) was in average 8±3 days. We observed a significantly motor improvement after the drainage (Pre-UPDRS-ME score: 20.1±6.5; Post-UPDRS-ME score: 18.6±7.9; $p=0.012$). Percent clinical motor response was in average: 10±11%. Overall, 36% of patients presented a motor response greater than 15%. Percent motor response negatively correlated with Pre-UPDRS-ME score ($r=-0.798$; $p<0.001$). A borderline positive correlation was also observed between clinical motor response and FAB score evaluate at baseline ($r=0.54$; $p=0.057$).

Conclusions: A clinically detectable motor response was detected in about one third of iNPH patients with parkinsonism few days after the 72-h lumbar CSF drainage. Patients with more severe cognitive and motor condition at baseline could present a worse acute motor response to the drainage.

P33

Dietary Vitamin E as a protective factor for Parkinson's disease: clinical and experimental evidence

Paola Imbriani[1,2], *T. Schirinzi*[1], *G. Martella*[1,2], *G. Di Lazzaro*[1], *M. Alwardat*[1], *P. Sinibaldi Salimei*[3], *N.B. Mercuri*[1,2], *M. Pierantozzi*[1], *A. Pisani*[1,2]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Santa Lucia Foundation IRCCS, Rome, Italy
[3]Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy

Introduction: Effective disease-modifying treatments are an urgent need for Parkinson's disease (PD). A putative successful strategy is to counteract oxidative stress, not only with synthetic compounds, but also with natural agents or dietary choices. Vitamin E, in particular, is a powerful antioxidant, commonly found in vegetables and other components of the diet.

Objective: The aim of this work is to test if a higher dietary intake of Vitamin E might protect from progressive neurodegeneration in PD.

Methods: We conducted a study including: 1) a retrospective assessment of dietary Vitamin E intake (VEI) in 100 PD patients compared to 100 healthy controls, aimed at determining if a different dietary VEI is associated with diverse clinical conditions; 2) an in vitro protocol in brain slices of a PD mouse model, aimed at evaluating the effects of Vitamin E on synaptic plasticity abnormalities, a peculiar endophenotype observed in distinct PD models. Specifically, we used homozygous PTEN-induced kinase 1 (PINK1) knockout mice (PINK1-/-), an established model of subclinical PD, in which we previously demonstrated the loss of both long-term potentiation (LTP) and long-term depression (LTD) at corticostriatal synapses, in the absence of overt neurodegeneration.

Results: The analysis showed that a higher VEI was inversely associated with PD occurrence independently from age and gender (OR = 1.022; 95% CI = 0.999 – 1.045; $p<0.05$), though unrelated to clinical severity. Moreover, chronic administration of Vitamin E (alpha-tocopherol and the water-soluble analogue trolox) fully restored corticostriatal synaptic plasticity in PINK1-/- mice, which is suggestive of a specific protective action.

Conclusions: Vitamin E might indeed compensate PINK1 haploinsufficiency and mitochondrial impairment, reverting some central steps of the pathogenic process. Altogether, both clinical and experimental findings suggest that Vitamin E could be a potential, useful agent for PD patients. These data, although preliminary, may encourage future confirmatory trials.

P34

Exploring the relationship between motor and non-motor fluctuations in Parkinson's disease: patient's perspective, clinician's assessment and objective measures from a wearable device

Andrea De Angelis[1], *M. Horne*[2], *D. Paviour*[1], *A. Leake*[1], *J. Coebergh*[1], *M. Edwards*[1], *F. Morgante*[1], *L. Ricciardi*[1]

[1]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[2]Centre for Clinical Neurosciences and Neurological Research, St. Vincent's Hospital, Melbourne, Australia
[3]Florey Institute for Neuroscience and Mental Health, University of Melbourne, Parkville, VIC Australia

Introduction: Motor (MF) and non-motor (NMF) fluctuations in Parkinson's disease are difficult to recognize and might have a severe impact on quality of life.

Objectives: To evaluate the relationship between NMF and MF measured with: patient's self-assessment, clinician's evaluation and objective measurement using a wearable device; to explore the relationship between MF, NMF and quality of life.

Methods: Patients' demographic and clinical data were collected. Levodopa equivalent daily dose (LEDD) and LEDD dopamine-agonist (D-Ag LEDD) were calculated. MF and NMF assessment included: Wearing-Off Questionnaire (WOQ-19), Unified PD Rating Scale (UPDRS I-IV), Rusk Dyskinesia Rating Scale (RDRS). The Parkinson's KinetiGraph™ system (PKG®), an accelerometry-based system for automated assessment of dyskinesia and bradykinesia was employed. Non-motor symptoms scale (NMSS) and the 39-item PD Questionnaire (PDQ-39) were administered.

Results: Fifty-six patients were included (37 males, age 60.4±6.5, disease duration 10.5±4.9), 100% self-reported MF, 83% had NMF as per WOQ-19. WOQ-19 motor and non-motor sub-scores were significantly associated (b-coef=0.4, 95% CI(0.2,0.6), $p<0.0001$). Multivariable regression analyses showed that D-Ag LEDD, UPDRS-III-OFF, UPDRS-IV and 'percent time with fluctuation' as per PKG were significantly associated with WOQ-19 motor sub-score. WOQ-19 non-motor sub-score was associated to UPDRS-III-OFF and NMSS. When classifying our patients according to 'percent time with fluctuation' PKG outcome, 50% had no MF, 25% had mild/moderate and 25% had severe MF. Patients without fluctuations had lower D-Ag LEDD, lower score at RDRS and WOQ-motor sub-scale ($p<0.05$). According to 'percent time with dyskinesia' PKG outcome, 55% of patients had no dyskinesia, 23% had mild and 22% had severe dyskinesia. Patients with no dyskinesia had lower D-Ag LEDD and RDRS score ($p<0.05$). Only WOQ-19 psychiatric fluctuation was significantly associated to PDQ- 39.

Discussion: Our findings suggest that MF and NMF are related to each other but independently associated to specific clinical variables. NMF and specifically, psychiatric fluctuations, impact patient's quality of life.

P35

Validation of the DYMUS screening questionnaire to assess dysphagia in Parkinson's disease and atypical parkinsonian disorders

Alessia Putortì[1,2], *M. Avenali*[1,2], *C. Dagna*[1,2], *R. De Icco 1,2, M. Gandolfi*[3], *C. Solaro*[4], *D.A. Restivo*[5], *M. Bartolo*[6], *F. Meneghello*[7], *G. Sandrini*[1,2], *C. Tassorelli*[1,2] *and DYPAK SIRN Group*

[1]Neurorehabilitation Unit, IRCCS Mondino Foundation, Pavia, Italy
[2]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[3]Neuromotor and Cognitive Rehabilitation Research Center (CRRNC), Department of Neurosciences, Biomedicine and Movement, University of Verona, Verona, Italy
[4]Department of Rehabilitation, C.R.R.F. "Mons. L. Novarese", Moncrivello, Italy
[5]Department of Neurology, Garibaldi Hospital, Catania, Italy
[6]Neurorehabilitation, Department of Rehabilitation and Advanced Technologies, Habilita Hospital, Zingonia di Ciserano, Cisternino, Italy
[7]IRCCS Ospedale San Camillo, Venezia, Italy

Introduction: Dysphagia is a common debilitating symptom in people suffering from extrapyramidal disorders. The DYMUS questionnaire, which has already been validated for the early screening of dysphagia in Multiple Sclerosis [1], might also prove useful for screening dysphagia in parkinsonian syndromes.

Aims: Assessing the ability of the DYMUS questionnaire to identify, at an early stage, the presence of dysphagia in patients affected by Parkinson's disease (PD) and atypical parkinsonian disorders (APD).

Materials and methods: This is an observational multi-centric study involving 145 patients affected by PD and ADP. All subjects filled in the DYMUS and the EAT-10 dysphagia scale and underwent a thorough clinical evaluation of dysphagia by the speech therapist. A subgroup of patients also underwent fibroendoscopic evaluation of dysphagia.

Results: the DYMUS questionnaire showed a good level of internal consistency (Cronbach's alfa 0.77). We observed significantly higher DYMUS scores in patients who were mildly (3.9±2.3) or moderately (5.3±2.8) dysphagic at the bed-test evaluation, as compared to non-dysphagic subjects (1.5±1.8), with a $p=0.001$ value for both. ROC curve analysis showed that a DYMUS score > 2 is the cut-off for detecting a potential swallowing impairment.

Conclusions: The DYMUS questionnaire proved to be a reliable screening tool to assess dysphagia in patients suffering from extrapyramidal diseases. It is easy and quick to administer, which makes it adequate for widespread uptake in the clinical practice.

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P36

Fatigue in Parkinson's disease: a systematic review and meta-analysis

Mattia Siciliano[1,2], *L. Trojano*[2,3], *G. Santangelo*[2], *R. De Micco*[1], *G. Tedeschi*[1], *A. Tessitore*[1]

[1]Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, MRI Research Center SUN-FISM, University of Campania "Luigi Vanvitelli", Naples, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[3]ICS Maugeri, Scientific Institute of Telese, Telese, Italy

We conducted a systematic review and meta-analysis aimed at establishing robust prevalence estimates and identifying clinical correlates of fatigue in Parkinson's disease (PD). From 2459 titles and abstracts, we selected 44 relevant studies (n=7427 patients). Overall, the meta-analysis showed a prevalence of fatigue of 50% in PD. This prevalence estimate, however, was significantly moderated by study heterogeneity in measurement scales and cutoff thresholds. In contrast, demographic features, disease severity, cognitive impairment, and depression did not moderate prevalence estimates. Moreover, fatigue prevalence did not differ between *de novo* and treated PD patients. Compared to non-fatigued patients, fatigued patients had sligthly higher age (1.44 years), disease duration (0.93 years), levodopa equivalent daily dose (50.89 units), UPDRS-III (4.99 points), and Hoehn and Yahr (0.33 points), as well as risk of comorbid depression (Risk Ratio=1.89), and had a little lower MMSE score (-0.66 points). Fatigue was moderately associated with apathy (Hedges' g=0.55), anxiety (Hedges' g=0.67), daytime somnolence (Hedges' g= 0.43), sleep disturbances (Hedges' g=0.66), and poorer quality of life (Hedges' g=1.23). Our analyses suggest that fatigue is a frequent, independent non-motor symptom in PD appearing early and persisting throughout the disease course, and that establishing uniform diagnostic criteria for PD-related fatigue is critical. In addition, several non-motor symptoms appear to be associated with fatigue, and negatively impact quality of life. Pharmacological and non-pharmacological interventions targeting fatigue and associated symptoms may improve quality of life in patients with PD.

P37

Alterations of blood pressure circadian rhythm in alpha-synucleinopathies

Alberto Romagnolo[1], *F. Vallelonga*[2], *A. Merola*[3], *C. Di Stefano*[2], *G. Sobrero*[2], *V. Milazzo*[2], *M. Zibetti*[1], *C.A. Artusi*[1], *M. Fabbri*[1], *M.G. Rizzone*[1], *S. Maule*[2], *L. Lopiano*[1]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]Autonomic Unit and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy
[3]Gardner Family Center for Parkinson's Disease and Movement Disorders, Department of Neurology, University of Cincinnati, Cincinnati, OH, USA

Introduction: We sought to analyze the blood pressure (BP) circadian rhythm in Parkinson's disease (PD), multiple system atrophy (MSA), and pure autonomic failure (PAF), evaluating possible differences among the three synucleinopathies.

Methods: BP circadian rhythm of consecutive patients with PD (n=72), MSA (n=18), and PAF (n=17) was assessed by means of 24-h ambulatory BP monitoring (ABPM). ABPM parameters included BP variability, BP load, nocturnal dipping, and awakening hypotension. An unsupervised cluster analysis was also performed to evaluate possible distinct patterns of BP alterations in PD patients.

Results: The average BP was 121±14/72±8 mmHg during daytime and 133 ±20/76±13 mmHg during nighttime ($p<0.01$), with BP load of 24±22/15±16% (daytime) vs. 61±36/52±36% (nighttime) ($p<0.01$). Orthostatic hypotension (OH) was present in 95 patients (89%), and supine hypertension (SH) in 63 (59%). ABPM demonstrated increased BP variability (BPV) in 67 patients (63%), awakening hypotension in 63 (59%), "reverse dipping" in 85 (79.4%), "reduced dipping" in 13 (12.1%). No differences were observed between PD, MSA, and PAF. The use of vasoactive and dopaminergic medications was not associated with significant ABPM differences. Cluster analysis revealed two distinct patterns of BP alterations in PD patients: the first (PD1) was characterized by normal BP loads, low prevalence of SH, and milder ABPM alterations; the second (PD2) by increased nighttime BP, higer BP loads, increased prevalence of SH, higher prevalence of reverse dipping, awakening hypotension and increased BPV. Prevalence of symptomatic OH and severity of cardiovascular autonomic testing were similar between the two clusters. PD2 were older ($p<0.05$) and treated with lower doses of dopamine agonists ($p<0.05$).

Conclusions: Regardless of the neurological diagnosis and pharmacological treatment, patients with alpha-synucleinopathies showed a BP circadian rhythm characterized by increased BP variability, reverse dipping, increased BP load, and awakening hypotension. Two distinctive clusters of circadian BP alterations were detected in PD.

P38

International validation study of the Parkinson's Disease Composite Scale

Fabrizio Stocchi[1], *P. Martinez-Martin*[2], *C. Rodriguez Blazquez*[2], *J. Wetmore*[2], *N. Kovacs*[3], *F. G. Radicati*[1]

[1]Istituto di Ricovero e Cura a Carattere Scientifico San Raffaele Pisana, Rome, Italy
[2]Carlos III Institute of Health, National Center of Epidemiology and CIBERNED, Madrid, Spain
[3]University of Pecs, Department of Neurology Kings College Hospital, Pecs, Hungary

Background: An instrument that can quickly assess the most relevant symptoms experienced by people with Parkinson's disease (PD) in general, and overloaded clinical settings, is needed. The recently validated Parkinson's Disease Composite Scale (PDCS) was designed to fulfill this gap as a quick, comprehensive instrument for PD evaluation.

Objective: Extensive evaluation of the clinimetric properties of the PDCS using a large international sample.

Methods: International, cross-sectional study. In addition to the PDCS, the Movement Disorder Society-Unified Parkinson's Disease Rating Scale and the Clinical Impression of Severity Index for PD were applied. Basic clinimetric attributes of the PDCS were analyzed.

Results: 776 PD patients were included. Missing data percentage was low (3.2%). The PDCS total score showed negligible floor and ceiling effect. Three factors (54.5% of the variance) were identified: Factor 1 including motor impairment, fluctuations, and disability; Factor 2, non-motor symptoms; and Factor 3, tremor and complications of therapy. Cronbach's alpha was 0.66 to 0.79 for the multi-item domains. Inter-rater reliability of 209 cases showed weighted kappa values 0.79-0.98 for items and intraclass correlation coefficient values 0.95 (Disability) to 0.99 (Motor and Total score). The Bland-Altmann method, however, did show irregular concordance. PDCS precision, on standard error of measurement from inter-rater assessments, and convergent validity with equivalent constructs of other measures ($\geq$0.70) was acceptable. PDCS scores were significantly different by HY stage (Kruskal-Wallis test, all $p<0.001$).

Conclusions: Overall, in line with previous findings, the PDCS is a feasible, acceptable, valid, reliable, and precise instrument for quick assessment of PD patients.

P39

Cerebrospinal fluid inflammation correlates with mood and quality of life in early Parkinson's disease patients

Enrica Olivola[1], *M. Stampanoni Bassi*[1], *L. Giglio*[1], *C. Femiano*[1], *G. Ricciardo Rizzo*[1], *R. Furlan*[2], *A. Finardi*[2], *D. Centonze*[1,3], *N. Modugno*[1]

[1]Unit of Neurology and Neurorehabilitation, IRCCS Neuromed, Pozzilli, Italy
[2]Neuroimmunology Unit, Division of Neuroscience, Institute of Experimental Neurology (INSpe), San Raffaele Scientific Institute, Milan, Italy.
[3]Department of Systems Medicine, Tor Vergata University, Rome, Italy

Introduction: Non-motor symptoms, including cognitive deficits and mood disorders, are commonly observed in PD patients at all disease stages and negatively influence quality of life. The pathophysiological mechanisms underlying non-motor symptoms are poorly understood, however previous studies evidenced that neuroinflammation in PD patients could be associated to depression, anxiety and fatigue.

Objectives: The aim of the present study is to explore in a group of early PD patients whether inflammatory cytokines influence disease characteristics.

Methods: Cerebrospinal fluid (CSF) was collected in a group of consecutive PD patients (n=22) at the time of diagnosis. All patients were drug-naïve at the time of CSF withdrawal. The levels of the following pro-inflammatory and anti-inflammatory cytokines were measured in the CSF: interleukin (IL)-4, IL-6, IL-8, IL-10, GM-CSF, tumor necrosis factor (TNF), MIP-1B, IP-10. Motor disability was evaluated using Unified Parkinson's Disease Rating Scale (UPDRS) part-III. The presence of non-motor symptoms was evaluated by UPDRS part-I. Quality of life was assessed by Parkinsons's Disease Questionnaire (PDQ-8). Depression and anxiety were investigated with the Beck Depression Inventory (BDI)-II and the State-Trait Anxiety Inventory (STAI-Y) respectively. Cognitive evaluation was also performed.

Results: A subset of inflammatory molecules showed a positive correlation with both quality of life and mood alterations. In particular, a significant correlation emerged between PDQ-8 score and IL-4, GM-CSF, TNF. Moreover, the severity of depression and anxiety correlated with IL-8 and IL-10 CSF concentrations. In addition, a significant correlation was found between IL-6 CSF levels and BDI-II score. Conversely, no significant correlations emerged between the analyzed CSF molecules and motor symptoms severity.

Conclusions: Our results suggest that neuroinflammation correlates with mood and quality of life in the early stage of disease. Although further investigations are needed, the assessment of CSF cytokines could be proposed as a biomarker of specific non-motor phenotypes in early PD patients.

P40

Visual dysfunction in Parkinson's disease: a standardized protocol for the evaluation of visual condition. Preliminary data

Michele Meglio[1], *E. Olivola*[2], *C. Femiano*[2], *L. Belli*[2], *G. Fioretto*, *D. Centonze*[2,3], *N. Modugno*[2]

[1]Neuro-ophthalmology Unit, IRCCS Neuromed, Pozzilli, Italy
[2]Unit of Neurology and Neurorehabilitation, IRCCS Neuromed, Pozzilli, Italy
[3]Department of Systems Medicine, Tor Vergata University, Rome, Italy

Introduction: Among the non-motor symptoms several visual signs and symptoms have been reported in Parkinson's disease (PD) at different stages of disease, with a significant impact on motor function and quality of life.

Objective: The present study examined visual functions in a group of non-demented PD patients divided into subgroups by stage of disease to establish the evidence of visual dysfunction and to evaluate its impact on patients' motor status and quality of life.

Methods: 22 PD patients and 10 health subjects were included in this study. PD patients were evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS) part I-II-III-IV during their usual treatment. Parkinson's disease questionnaire-39 (PDQ-39) and Visual Function Questionnaire 25 (VFQ-25) were used to assess quality of life. All participants underwent a detailed visual assessment including visual acuity, contrast and color sensitivity, Schirmer tear test and a full orthoptic evaluation including the study of eye movements, vergences, fusional amplitudes.

Results: PD patients significantly differed from controls in VFQ-25 score ($p < 0.01$), Contrast Sensitivity ($p = 0.01$), Convergence ability ($p < 0.01$), Fusional Amplitudes Range ($p < 0.01$), Schirmer Tear Test ($p=0.04$). These results also showed that fusional amplitudes negatively correlate with PDQ-39 score ($R=-0.49$, $p=0.02$). Patients with impaired color sensitivity showed a worse score of UPDRS II and III ($p=0.04$ and $p=0.006$ respectively).

Conclusions: Our standardized protocol was useful to assess visual dysfunction in PD patients. The evaluation of the visual condition, could be considered as a support to identify specific clinical phenotype. The treatment of this dysfunction could be helpful for the improvement of quality of life. However further investigations are needed.

P41

Prevalence of non-motor symptoms in a group of Parkinson's disease patients stratified by stage disease

Michela Sforza, D. Rinaldi, T. De Santis, E. Bianchini, M. Alborghetti, M. Giovannelli, F. Pontieri

Dipartimento di Neuroscienze, Salute Mentale e Organi di Senso NESMOS, Sapienza Università di Roma, Rome, Italy

Introduction: Non-motor symptoms (NMSs) are an highly prevalent subset of manifestations in Parkinson's disease (PD) and could impair significantly the daily-life activities and the quality of life in patients. NMSs can precede the onset of motor symptoms or occur during the disease course, and can be classified as follows: genitourinary, gastrointestinal, cardiovascular, cognitive and psychiatric (behavioural). The prevalence of these symptoms was widely studied in PRIAMO study in 2008.

Objectives: The primary aim of this transversal observational study is the prevalence estimation of NMSs in a group of 200 PD patients recruited consecutively during scheduled follow-up visits in our movement disorders outpatient clinic from January 2018 until January 2019.

Methods: Patients were classified basing on Hoehn & Yahr (H&Y) scale in two groups: H&Y 1- 2 and H&Y 3-4-5. In each group, NMSs have been evaluated using the NMS scale.

Results: The more prevalent NMSs in PD patients at early stage of disease progression (H&Y 1,2) are genitourinary symptoms, in particular urge incontinence, sleep disorders and neuropsychiatric symptoms (depression, apathy and anxiety). In advanced stage (H&Y 3,4,5), the more prevalent NMS is cognitive impairment (attention/memory deficit).

P42

Acute effects of a Golden-Ratio based rhythm on Parkinson disease gait: preliminary data

Antonella Peppe[1], *F. Ferretti*[2], *S. Bottino*[1], *M. Iosa*[1], *G. Vannozzi*[2]

[1]IRCCS Fondazione Santa Lucia, Rome, Italy
[2]Università degli Studi di Roma "Foro Italico", Rome, Italy

Introduction: Intrinsic hidden fractal structures were recently suggested to underlie the repetitive physiological gait cycles [1]. This harmonic structure of walking Golden Ratio "GR", coinciding in healthy subjects with the ratio between stance and swing durations [1]) is impaired in patients with Parkinson Disease (PD) together with their clinical status [2]. While numerous studies investigated the effects of external cueing in PD gait [3], it is still unknown whether this physiological GR could be recovered through an auditory stimulus based on this intrinsic GR rhythm.

Objective: To investigate the acute effects of an external auditory rhythm GR on gait patterns exhibited by a group of PD patients. The rationale of the study relies on the inner intrinsic of self-similarity of GR.

Materials and methods: The study involved 11 patients with PD characterized by bilateral involvement and light balance disorders (UPDRS III >10; H&Y 2), in the absence of dementia (MMSE<26). Gait analysis was performed with a Smart-D BTS optoelectronic system during normal walking and turning. Three experimental walking conditions were studied: A) without-rhythm (before); B) hearing-rhythm; C) without-rhythm (after). The GR auditory stimulus was generated based on the individual comfortable speed. Statistical analyses were performed to find differences among conditions.

Results: Significant differences in gait spatiotemporal parameters were reported for condition B in both stride and stance durations ($p=0.008$). This difference is maintained in C, with a regained limb symmetry and an increased foot clearance and arm swing ($p<0.05$). Gait speed also slightly improved. Spatiotemporal parameters in turning reported significant improvements in lap length and in the jerk parameter ($p<0.05$), but only in the B condition.

Conclusions: In this preliminary study, the acoustic rhythm based on GR resulted effective in improving spatiotemporal parameters in both linear walking and turning, even maintained in linear walking when the stimulus was removed.

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P43

Clinical and fMRI effects of Action Observation and Motor Imagery Training on dual-task performances in Parkinson's disease patients with postural instability and gait disorders

Elisabetta Sarasso[1,3], *F. Agosta*[1], *N. Piramide*[1], *E. Canu*[1], *M. Chiesi*[1], *I. Ravani*[1], *S. Galantucci*[2], *A. Tettamanti*[3], *M.A. Volontè*[2], *Massimo Filippi* [1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan Italy
[3]Laboratory of Movement Analysis, San Raffaele Scientific Institute, Milan, Italy

Introduction: Dual-task is challenging for Parkinson's disease patients with postural instability and gait disorders (PD-PIGD) and impacts on postural stability and gait safety.

Objective: To assess brain functional reorganization and gait changes performing dual-task after 6 weeks of action observation training (AOT) and motor imagery (MI) associated with gait/balance exercises in PD-PIGD patients.

Methods: Twenty PD-PIGD patients were randomized into 2 groups: the AOT-MI-group performed a 6-week (W6) gait/balance training consisting of AOT-MI combined with practicing the observed-imagined exercises; LANDSCAPE-group performed the same exercises combined with watching landscape videos. Exercises were increasingly difficult, up to include dual-task. At baseline and W6, patients underwent: i) functional MRI (fMRI) dual-task (foot anti-phase movements while counting backwards by threes starting from 100) and ii) gait/balance evaluations including Timed-Up-and-Go-test (TUG) and TUG associated with dual-task, Mini-Balance-Evaluation-System-test (MiniBESTest) and Activities Balance Confidence questionnaire (ABC).

Results: At W6 compared to baseline, both groups showed an improvement in TUG execution time, whereas only the AOT-MI group improved in TUG with dual-task, MiniBESTest and ABC. AOT-MI-group also showed improvements in gait speed during the turn phase of TUG and TUG with dual-task, ABC and MiniBESTest relative to LANDSCAPE-group. At W6 relative to baseline, during the fMRI dual-task, the AOT-MI-group showed reduced recruitment of frontal, occipital, insular areas and hippocampus and increased activity of parietal areas. The LANDSCAPE group presented decreased activity of occipital areas and increased recruitment of fronto- temporal areas. AOT-MI relative to LANDSCAPE group showed reduced recruitment of frontal, occipital, and temporal areas and of the right putamen.

Conclusions: Our results suggest that increasingly difficult gait/balance exercises improve gait speed in PD-PIGD patients; however, only when exercises were preceded by a motor-learning facilitation strategy (AOT-MI), patients showed gait/balance improvements and increased brain efficiency during dual-task circumstances, which are among the most challenging for PD-PIGD patients.

P44

Dual-task in Parkinson's disease: a gait analysis and functional MRI study

Elisabetta Sarasso[1,3], *F. Agosta*[1], *A. Gardoni*[1], *S. Galantucci*[2], *A. Tettamanti*[3], *M.A. Volontè*[2], *M. Filippi*[1,2]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy
[2]Department of Neurology, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy
[3]Laboratory of Movement Analysis, San Raffaele Scientific Institute, Milan, Italy

Introduction: Previous studies suggested that PD patients need to hyper-activate brain cognitive networks to control movement. Thus dual-task performance is usually difficult for PD patients, resulting in increased gait difficulties and postural instability.

Objective: To study gait parameters and functional MRI (fMRI) patterns performing dual-task in Parkinson's disease patients with postural instability and gait disorders phenotype (PD-PIGD) and to assess correlations between brain functional activity and gait during dual-task.

Methods: Twenty PD-PIGD patients performed Timed-Up-and-Go (TUG) test, TUG with motor (TUG-MOT) and cognitive (TUG-COG) dual-tasks. TUG-MOT consisted of TUG while holding a glass full of water and TUG-COG consisted of TUG while counting backwards by threes from 100. A six cameras SMART- DX7000 optoelectronic system was used to obtain peak and mean velocity during the turning phase. Patients performed also two fMRI tasks: i) motor-task (foot anti-phase movements); ii) dual-task (foot anti-phase movements while counting backwards by threes starting from 100).

Results: PD-PIGD patients showed increased total time of execution and slower turns during TUG-MOT and TUG-COG relative to simple TUG. During fMRI dual-task relative to motor-task, patients showed increased activation of the fronto-temporo-parietal regions and decreased activity of the sensorimotor areas. Correlation analysis showed that: i) better TUG performance correlated with increased recruitment of the cortical/cerebellar motor areas, the fronto-striatal circuit and the occipital lobe during the motor-task; ii) better TUG-MOT/TUG-COG performance correlated with increased activity of motor areas and decreased recruitment of superior/middle frontal and temporal gyri, superior/inferior parietal gyri, occipital areas and right pallidum during the dual-task.

Conclusions: Dual-task resulted in a slower gait performance particularly during turning, a challenging situation in PD-PIGD patients. This pattern might reflect an increased dynamic postural instability when high cognitive load is requested. FMRI results suggest that an optimized recruitment of motor and cognitive networks is associated with a better dual-task performance.

P45

Four-week trunk-specific exercise program decreases forward trunk flexion in parkinson's disease: a single-blinded, randomized controlled trial

Marialuisa Gandolfi[1,2]*, *M. Tinazzi*[1]*, *F. Magrinelli*[1], *G. Busselli*[1,2], *E. Dimitrova*[1,2], *N. Polo*[1], *P. Manganotti*[3], *A. Fasano*[4,5], *N. Smania*[1,2]*, *C. Geroin*[1]*

* All authors contributed equally to this work

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]UOC Neurorehabilitation, AOUI Verona, Italy
[3]Department of Medical, Surgical, and Health Sciences, University of Trieste, Trieste, Italy
[4]Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital, UHN, Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[5]Krembil Brain Institute, Toronto, Ontario, Canada

Introduction: Pathological forward trunk flexion is a disabling and drug-refractory motor complication of Parkinson's disease (PD) leading to imbalance, pain, and fall-related injuries [1]. Since it might be reversible, the early and multidisciplinary management is emphasised [2,3]. The primary aim was to compare the effects of a four-week trunk-specific rehabilitation program on the severity of the forward trunk flexion. The secondary aim was to compare the training effects on the motor impairments, dynamic and static balance, pain, falls, and quality of life.

Methods: 37 patients with PD (H&Y≤4) and forward trunk flexion were randomised in the experimental (n=19) or control group (n=18). The former consisted of active self-correction exercises with visual and proprioceptive feedback, passive and active trunk stabilisation exercises and functional tasks. The latter consisted of joint mobilization, muscle strengthening and stretching, gait and balance exercises. Protocols lasted 4 weeks (60 min/day, 5 day/week). Before, after, and at 1-month follow-up, a blinded examiner evaluated patients using primary and secondary outcomes. The primary outcome was the forward trunk flexion severity (degree). Secondary outcomes were the UPDRS III, dynamic and static balance, pain, falls, and quality of life assessment.

Results: Significant time per group interaction was measured for the forward trunk flexion severity ($p<0.001$), dynamic ($p=0.03$) and static balance ($p=0.01$) in favour of the experimental training. Comparable effects were reported on the other outcomes. Pre- treatment forward trunk flexion values were highly correlated to post-treatment trunk deviation changes.

Conclusions: The four-week trunk-specific rehabilitation training decreased the forward trunk flexion severity and increased postural control in patients with PD. NCT03741959.

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P46

Postural control and gait in people with Parkinson disease: a pilot study on the promising use of Computer Assisted virtual Reality ENvironment

Vincenzo Cimino, G. Di Lorenzo, C. Sorbera, S. Marino, R.S. Calabrò, A. Buda, G. Paladina, A. Naro, A. Manuli, D. Milardi, P. Bramanti, A. Bramanti

IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by different motor symptoms (rigidity, akinesia, tremor, impairment of balance and gait), cognitive and behavioral impairments. Even though pharmacological treatment has changed the natural course of disease, gait and balance worsen over time, progressively leading to major disability. Several studies have shown that physiotherapy, including cueing techniques, treadmill training and cognitive movement strategies, are useful in improving balance and gait in PD patients. Technology using Virtual Reality (VR) is becoming a promising tool in neurorehabilitation, as it can provide multisensory stimulation to create a realistic environment and improve the motivation and the adhesion of patients in order to carry out an intensive rehabilitation program.

Methods: Fifteen outpatients with PD, who attended the Movement Disorder Laboratory from August 2017 to February 2018, were enrolled in this study. All PD patients underwent 20 Computer Assisted virtual Reality ENvironment (CAREN) sessions. Besides VR, patients were treated with conventional physiotherapy (PT). Outcome measures were retrospectively compared to PD outpatients undergoing only conventional PT. The outcome measures were the Unified Parkinson's Disease Rating Scale section II and III (UPDRS II and III), the Berg Balance Scale (BBS) for balance, the Falls Efficacy Scale International (FES-I), the Timed Up and Go Test (TUG) and ten-metres walking test (10-MtWt).

Results: All patients completed the 4 weeks rehabilitation period. All considered scales improved significantly at the end of the rehabilitation treatment.

Conclusions: We have successfully showed that balance and gait training based on the CAREN system is an effective method in Parkinson disease rehabilitation program. As a complement of standard balance and gait intervention programs, VR training offers a safe and well-accepted intervention with appropriate levels of effectiveness and adherence.

P47

The effect of intensive and multidisciplinary rehabilitative program in Parkinson's disease

Viviana Lo Buono, L. Bonanno, R. Palmeri, M. Berenati, C. Sorbera, V. Cimino, P. Bramanti, G. Di Lorenzo, S. Marino

IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor and non-motor symptoms including cognitive dysfunction and mood alterations [1] that worsen the psychological well-being. Neurorehabilitative training is an important non-pharmaceutical treatment approach that use behavioral adaptations that can assist patients to cope better with their symptoms.

Objective: We investigated the changes in motor, logopedic and cognitive functions, anxiety and depressive symptoms and quality of life perception in PD patients undergoing to intensive and multidisciplinary rehabilitative program.

Methods: This study included 84 PD patients (diagnosis according to UK Brain Bank criteria) who were admitted to hospitalization rehabilitative program for 60 days. The assessments were completed at the date of admission (T0 baseline visit) and 60 days (T1). We used of UPDRS-Part, The Barthel Index rating scales, Addenbrooke's Cognitive Examination-Revised (ACE-R), Beck Depression Inventory (BDI-II) and Hamilton Anxiety Rating Scale (HAM-A), Parkinson's Disease Quality of Life Questionnaire (PDQ-39), the Clinical Bedside Swallowing examinations for dysphagia and Robertson dysarthria profile. Wilcoxon signed rank test and Spearman's coefficient were used for intra-group analysis. Analyses were performed using an open source R3.0 software package. A 95% of confidence level was set with a 5% alpha error. Statistical significance was set at $p<0.05$.

Results: Intra-group analysis showed a significant difference between T0 and T1 in almost all clinical score ($p<0.05$) with an increase of global performance. A correlation between UPDRS and mobility score ($r=0.31$; $p=0.005$), UPDRS and communication score ($r=-0.29$; $p=0.008$), BDI-II and mobility score ($r=0.27$; $p=0.01$), BDI- II and psychological well-being score ($r=-0.23$; $p=0.04$) were found. A significative trend correlation were observed between BDI and psychological well-being score ($r=0.19$; $p=0.08$) and HAM-A and daily activities score ($r=0.20$; $p=0.07$).

Conclusions: Our findings suggest that multidisciplinary rehabilitative program improve motor impairment, cognitive abilities, psychological symptoms, activities of daily living, and quality of life of PD patients.

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P48

Cerebellar transcranial direct current stimulation (tDCS) combined with physical rehabilitation in progressive supranuclear palsy: a double blind randomized sham controlled study

Andrea Pilotto[1,2], *M.C. Rizzetti*[2], *R. Serughetti*[2], *D. Locatelli*[2], *B. Cavaletti*[2], *A. Pedrini*[2], *W. Maetzler*[3], *C. Hansen*[3], *B. Borroni*[1], *A. Padovani*[1]

[1]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]FERB Onlus, Ospedale S. Isidoro, Trescore Balneario, Italy
[3]Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany

Introduction: There are no medical effective treatments for progressive supranuclear palsy (PSP). Physical rehabilitation (PR) has a potential but still limited effect on postural instability and motor function in PSP patients. Several studies showed a positive effect of active transcranial cerebellar anodal Direct Current Stimulation (tDCS) in patients with postural instability.

Methods: Sixteen patients with PSP were assigned to either active cerebellar tDCS plus physical rehabilitation (PR) or sham tDCS plus PR groups. Each patient underwent two weeks of PR and daily application of tDCS for 20 minutes. Each patient was evaluated at baseline and after treatment with an extensive clinical and functional assessment including PSP rating scale (PSP-RS), Berg Balance test (BBS), timed up and go test (TUG) and Six Minutes Walking Test (6MWT).

Results: There was a significant interaction between treatment and time on PSP-RS, BBS and 6MWT. Patients on active tDCS showed significantly higher improvement on total PSP-RS ($p=0.003$), a trend for higher improvement on BBS score ($p=0.06$) and no differences in TUG or 6MWT compared to PSP patients with sham stimulation.

Conclusions: We concluded that physical rehabilitation along with active cerebellar tDCS is a useful combined approach for postural instability and motor symptoms in PSP patients.

P49

Longitudinal cortical changes associated with apathy in parkinson's disease

Francesca Imperiale[1], *F. Agosta*[1], *E. Canu*[1], *T. Stojković*[3], *I. Stankovic*[3], *S. Basaia*[1], *A. Fontana*[4], *V. Markovic*[3], *I. Petrović*[3], *E. Stefanova*[3], *V. Kostic*[3], *M. Filippi*[1,2]

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

Background: Apathy can influence the disease progression in Parkinson's disease (PD).

Objective: To follow clinical/cognitive and cortical thickness (CT) changes in PD patients with stable apathy (PD-sAp), without apathy (PD-noAp), and patients who developed apathy (PD-cAp) during 3 year follow up.

Methods: We selected 96 patients with known apathy outcome at the initial exam or during 3 years of follow-up and 46 age- and sex-matched controls. We identified 37 PD-sAp, 33 PD-noAp, 26 PD-cAp patients. Patients and controls underwent clinical/neuropsychological evaluations and 3D T1-weighted MRI scans at baseline. Patients performed evaluations also once a year for 3 years. CT at baseline and over time was investigated within and between groups adjusting for age, disease severity, global cognition and mood.

Results: At baseline, PD-cAp patients had higher age at disease onset relative to PD-noAp and lower disease severity and shorter disease duration relative to other patient groups. At baseline, the PD-sAp and PD-cAp groups showed worse memory abilities relative to PD-noAp. Over time, apathy worsened significantly every year in the PD-cAp group only. At baseline, PD-sAp patients showed cortical atrophy of bilateral fronto-temporo- parietal areas relative to controls and of left anterior cingulate and superior temporal gyri compared to the other patient groups. PD-sAp did not accumulate further cortical damage overtime. A greater progression of cortical thinning of the right superior temporal, inferior frontal and parietal regions was observed in PD-cAp relative to PD-noAp patients.

Conclusions: This study assessed the longitudinal cortical alteration associated with apathy in PD. We suggested that PD-sAp and PD-cAp are characterized by similar cognitive profile already in the early phase of the disease and by a similar pattern of cortical alterations overtime, involving the right superior temporal, inferior frontal and parietal regions.

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P50

Cortical FDG-PET patterns predict long-term motor progression and disability milestones in Parkinson's disease

Alberto Imarisio[1], *A. Pilotto*[1,2], *E. Premi*[1,3], *S. P. Caminiti*[4], *L. Presotto*[5], *A. Sala*[4], *R. Turrone*[1], *R. Grasso*[1], *A. Alberici*[1], *B. Paghera*[6], *M.C. Rizzetti*[2], *B. Borroni*[1], *D. Perani*[4,5], *A. Padovani*[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Parkinson's Disease Rehabilitation Centre, FERB ONLUS S. Isidoro Hospital, Trescore Balneario, Italy
[3]Neurovascular Unit, Brescia Hospital, Brescia, Italy
[4]Vita-Salute San Raffaele University, Division of Neuroscience San Raffaele Scientific Institute, Milan, Italy
[5]Nuclear Medicine Unit, San Raffaele Hospital, Division of Neuroscience San Raffaele Scientific Institute, Milan, Italy
[6]Nuclear Medicine Unit, University of Brescia, Brescia, Italy

Objective: We recently showed that FDG-PET SPM predict risk of developing dementia in PD patients at 4-year follow-up at single subject level [1]. In the present study, we followed up the same cohort of patients at 6-8 years in order to evaluate single-subject FDG pet pattern as long term predictor of motor progression and disability.

Methods: Forty-nine and 49 out of the initial cohort of 54 patients with FDG-PET underwent follow-up at 6 and eight years, respectively. The correlation between single-subject pattern and the following milestones have been evaluated for each patient: dementia, hallucinations, falls, inability to walk, motor function (assessed by changes in UPDRS-III and levodopa equivalent daily dose).

Results: Patients were classified according to their baseline FDG-PET pattern: normal PD pattern (n=26); DLB-like (n=12), AD-like (n=6), CBS-like (n=3), and FTD- like (n=2). At 8-years follow-up 16 patients progressed to dementia. We confirmed atypical pattern (especially DLB/AD-like) as the best predictor for incident dementia ($p<0.005$). Patients with atypical patterns showed also higher incidence of hallucinations ($p=0.001$), inability to walk ($p=0.018$) and falls ($p=0.033$) at 6 and 8-year follow-up. Motor progression (evaluated by biannual UPDRS-III scores) showed worse motor progression in patients with atypical patterns, (especially in patients with AD-like pattern) independently from dementia ($p=0.04$).

Conclusions: This study suggests FDG-PET as promising progression marker at single-subject level for its ability to predict long term disability in PD. The association between worse motor progression and cortical hypometabolism might indicate that reduced cortical reserve could impact on motor function in PD independently from dementia. This issue need further investigations in PD patients without dementia with extensive biomarkers and longitudinal assessment.

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P51

Age-related changes in dopamine transporter: evidence from a SPECT study in early and late-onset PD patients compared with separated age-matched control groups

Giovanni Palermo[1], *D. Frosini*[1], *S. Giannoni*[1], *M. Giuntini*[1], *D. Volterrani*[2], *U. Bonuccelli*[1], *R. Ceravolo*[1]

[1]Unit of Neurology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[2]Regional Center of Nuclear Medicine, University of Pisa, Pisa, Italy

Introduction: There are convincing data showing differences regarding clinical, genetic, and drug response between Early Onset Parkinson's Disease (EOPD) and Late-Onset PD (LOPD). Younger PD subjects may have more efficient compensatory mechanisms. Down-regulation of presynaptic dopamine reuptake system is reportedly a possible compensatory mechanism in surviving nigral neurons. However, molecular imaging studies comparing Dopamine Transporter (DAT) density between EOPD and LOPD found controversial results since ageing is related to a physiological decline of DAT.

Objective and methods: To test whether the level of denervation in the striatum is different between EOPD (55 years or less) and LOPD (more than 70 years), we compared 76 de novo patients matched for disease duration (within 24 months at scanning time) with 92 healthy controls (HC). We compared LOPD and EOPD pts with their age-matched HC and specific z-scores of putamen and caudate uptake in each PD subgroup was calculated. Our primary null hypothesis was that EOPD have a more pronounced DAT decrement than LOPD with respect to HC age-matched.

Results: The severity of motor impairment (MDS-UPDRSIII) was greater in the LOPD subjects, although not significantly different between the two groups. As expected because of aging, LOPD had a greater dopaminergic dysfunction than EOPD. However by using z-scores, EOPD showed greater ($p < 0.0001$) DAT reduction in the putamen with respect to LOPD.

Conclusions: Our study show lower 123-FP-CIT putaminal binding in EOPD than in LOPD patients when compared to the mean of the age-matched HC suggesting that the compensatory mechanisms in the dopaminergic system might be more effective in EOPD. Interestingly, the failure of such adaptive changes could account, at least in part, for the greater severity of parkinsonian symptoms in LOPD, in contrast with higher DAT density in EOPD patients which in turn could be responsible for a greater risk of motor complications.

P52

Resting state cerebellar connectivity in early-stage drug-naïve patients with Parkinson's disease

Silvia Marino, L. Bonanno, V. Lo Buono, C. Sorbera, V. Cimino, P. Bramanti, G. Di Lorenzo

IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy

Introduction: Cerebellum network is not widely studied in Parkinson's disease (PD), even if it is known that cerebello-thalamo-cortical (CTC) circuit play a critical role in PD.

Objectives: To assess the pattern of RS functional cerebellar connectivity (FC), in de novo drug-naïve PD patients, with tremor-dominant (TD) and healthy controls (HCs).

Methods: We enrolled 30 de novo drug-naïve PD patients (UPDRS median motor subscores was 25, median disease duration was 1.8±1.1 years) and 30 sex-aged normal controls (NC). All subjects were not cognitively impaired. None of the patients took anti-parkinsonian drugs. The study was performed with a 3T MRI scanner.

Results: Compared to HCs, PD patients showed higher FC between cerebellum, paracentral lobule and sensorimotor areas; in addition they showed higher FC between the BG and cerebellum Lobule VI, and among the cerebellum, supplementary motor areas and insula. These data are strictly correlated with UPDRS motor subscore ($P < 0.01$).

Conclusions: Our findings could suggest that cerebellum had hyper-connectivity with the cortical motor cortex, in early and drug-naïve PD patients, even if further studies are needed. Our findings suggest that RS functional connectivity should be closely correlated with early motor impairment, and could be used as predictive rehabilitative marker in de novo PD patients.

P53

Neuroanatomical correlates of long-duration response in *de novo* Parkinson's disease

Giulia Donzuso, G. Sciacca., G. Mostile, A. Nicoletti, M. Zappia

Department "G.F. Ingrassia", Section Neuroscience, University of Catania, Catania, Italy

Parkinson disease (PD) is a neurodegenerative disorder, characterized by asymmetry of motor symptoms and neurological signs and by the response to L-dopa, that still remains the best available symptomatic treatment for PD. The therapeutic response to L-dopa consists of two components: the short-duration response (SDR), an improvement of the clinical condition following the administration of a single dose of L-dopa, and the long-duration response (LDR), a sustained benefit deriving from prolonged administration of L-dopa. Aim of the study is to investigate neuroanatomical correlates of LDR using structural magnetic resonance imaging (MRI) and voxel-based morphometry analysis. Drug-naïve patients with a new diagnosis of PD according to Brain Bank criteria were consecutively enrolled. They underwent an acute challenge with 250/25 mg of L-dopa with the evaluation of SDR. Then, a treatment with 250/25 mg every 24 hours was started and, after two weeks, LDR was evaluated and considered as an improvement of at least the 50% of the maximal improvement observed for the SDR to an acute L-dopa test. Motor severity was assessed using the Unified Parkinson's Disease Rating Scale-Motor Examination (UPDRS-ME). Structural brain MRI data were acquired using a 3D T1-weighted sequence and VBM analysis of MRI data was performed. Twenty-four patients were enrolled (mean age 64.3 ± 11.3 years, mean UPDRS-ME score 26.1 ± 9.4, disease duration 2.1 ± 1.1 years). After two weeks of therapy, 15 patients (62.5%) showed LDR (PD-LDR+), while 9 patients (37.5%) showed no LDR (PD-LDR-). There were no significant clinical differences between the two subgroups. VBM analysis between PD-LDR+ and PD-LDR- showed decreased GM density in left putamen (x-25, y -9, z 10; peak value 5.19) and in superior frontal gyrus (x-22, y 2, z 70; peak value 4.74) in PD-LDR+. This study showed the presence of atrophy in cortical and subcortical areas in PD patients who showed LDR after two weeks of continuative levodopa therapy with 250/25 mg every 24 hours. Functional MRI studies showed the presence of effects induced by L-dopa, enhancing connectivity and reducing signal fluctuations in sensorimotor networks. The presence of basal ganglia atrophy could induce a compensation mechanism, improving connectivity and leading to a sustained response to dopaminergic therapy.

P54

Presynaptic dopamine transporters deficits in idiopathic normal pressure hydrocephalus and *de novo* Parkinson's disease: a [123I]Ioflupane SPECT study

Nicoló Gabriele Pozzi[1,2], *J. Brumberg*[3], *M. Todisco*[1], *B. Minafra*[1], *R. Zangaglia*[1], *G. Trifirò*[4], *R. Ceravolo*[5], *I.U. Isaias*[2], *C. Pacchetti*[1]

[1]Parkinson's Disease and Movement Disorders Unit, Fondazione Istituto Neurologico "C. Mondino", National Neurological Institute, Pavia, Italy
[2]Neurology Department, University Hospital and JMU Würzburg, Würzburg, Germany
[3]Nuclear Medicine Department, University Hospital Würzburg, Würzburg, Germany
[4]Nuclear Medicine Unit, IRCCS Fondazione Salvatore Maugeri, Pavia, Italy
[5]Dipartimento di Neuroscienze, Unità di Neurologia, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy

Objective: The clinical overlap between idiopathic normal pressure hydrocephalus (iNPH) and Parkinson disease (PD) challenges their differential diagnosis and possibly leads to inappropriate treatments [1,2]. Molecular imaging of the striatal dopamine reuptake transporter (DAT) can differentiate PD from other movement disorders, but its application to iNPH is still debated [3,4,5] and it was the aim of this study.

Methods: We enrolled 66 radiologically-confirmed iNPH patients, 36 subjects with *de novo* PD and 67 healthy controls (HC). All subjects performed a detailed clinical investigation and a SPECT with [123I]Ioflupane within 24 months from symptom's onset. Parkinsonian patients were evaluated before starting a dopaminergic treatment. A qualitative analysis of reconstructed images was performed with GE Xeleris Workstation. To correct for anatomical abnormalities, especially in patients with iNPH, SPECT data were coregistered with 3T-MRI, normalized for the striatal volume and corrected for partial volume effect. Images were analysed with PMOD (PMOD Technologies Ltd, Zurich, Switzerland).

Results: Subjects with iNPH and *de novo* PD patients showed a reduced striatal DAT density with respect to HC. Of relevance, in comparison with *de novo* PD patients, subjects with iNPH showed a bilateral striatal DAT loss, prominent in the Caudate nucleus.

Conclusions: Subjects with iNPH show a peculiar pattern of striatal DAT loss, which may help the differential diagnosis with PD and an early and appropriate treatment. The pathophysiology of dopaminergic loss in iNPH remains unclear and deserves further studies.

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P55

Is SPECT with 123I-FP-CIT abnormality in normal pressure hydrocephalus always suggestive of degeneration? Evidences from two case reports

Claudia Del Gamba[1], *A. Bruno*[1], *D. Frosini*[1], *D. Volterrani*[2], *G. Migaleddu*[3], *N. Benedetto*[4], *P. Perrini*[4], *M. Cosottini*[3], *U. Bonuccelli*[1], *R. Ceravolo*[1]

[1]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy
[2]Department of Translational Research and of New Surgical and Medical Technologies, Nuclear Medicine Unit, University of Pisa, Pisa, Italy
[3]Department of Translational Research and of New Surgical and Medical Technologies, Radiodiagnostic Unit, University of Pisa, Pisa, Italy
[4]Department of Neurosurgery, University of Pisa, Pisa, Italy

Introduction: Diagnosis of idiopathic normal pressure hydrocephalus (iNPH) is suspected on the presence of Hakim's triad and ventriculomegaly not due to brain atrophy [1]. Extrapyramidal signs are frequently reported as part of the clinical pictures, sometimes due to the coexistence of a pathologically confirmed underlying idiopathic parkinsonisms, and sometimes not. To distinguish these two setups is of paramount importance, since they carry different response to ventriculoperitoneal shunt (VPS) [2]. SPECT with ^{123}I-FP-CIT was believed to be helpful in this regard, however, its role in predicting the surgical outcome has been recently disputed [3].

Objective: To examine iNPH associated with extrapyramidal signs in order to shed light on their pathogenesis, to understand whether there is an overlap with idiopathic parkinsonisms and its impact on the clinical outcome.

Methods and Results: We selected two patients (Pt-1, 65-year-old lady; Pt-2, 72-year-old lady) with clinical and radiological criteria for iNPH (Evan's index>0.3, DESH criterion, acute callosal angle) and extrapyramidal signs (asymmetric akinetic-rigid parkinsonism). They performed 3T with iron-sensitive sequences (SWAN), with evidence of bilateral preservation of the 3-layered organization of the substantia nigra (SN) in both patients, and a SPECT with ^{123}I-FP-CIT reporting bilateral, although asymmetrical, abnormalities, consistent with clinical asymmetry. They also carried out a chronic trial with levodopa, unsuccessful in either. Furthermore, Pt 1 underwent VPS and two years after she still shows a significant and sustained clinical improvement (MDS-UPDRS III and 10m walking test), as well as an increased striatal tracer uptake.

Conclusions: Our results suggest that an abnormal SPECT with ^{123}I-FP-CIT imaging does not necessarily mean an overlap between iNPH and idiopathic parkinsonisms, since in our cases the preservation of the SN was observed. In addition, the increase in dopamine transporter availability post VPS, suggests a secondary and partly reversible damage to the nigrostriatal dopaminergic pathway consistently with remarkable clinical improvement after VPS.

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P56

Is there evidence of bradykinesia in patients with essential tremor?

Donato Colella[1], *M. Bologna*[1,2], *G. Paparella*[1], *A. Cannavacciuolo*[1], *S. Pietracupa*[2], *A. Guerra*[2], *A. Berardelli*[1,2]

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

Introduction: Essential tremor (ET) is a heterogeneous movement disorder. Recent studies suggest that bradykinesia may be part of the phenotypic spectrum of ET; however none of the previous studies investigated the sequence effect in this condition.

Objective: To evaluate possible abnormalities (bradykinesia) of repetitive finger movements, including the sequence effect, using kinematic techniques in patients with ET.

Methods: Ninety patients with ET and 85 age- and gender- matched healthy controls were evaluated by standardized clinical scales and objective analysis of repetitive finger tapping using an optoelectronic motion analysis system. The kinematic analysis of repetitive finger tapping included total number of movements, movement rhythm, amplitude (hypokinesia) and velocity (bradykinesia) as well as progressive amplitude and velocity reduction during movement repetition (sequence effect).

Results: A between-group analysis revealed lower velocity and impaired movement rhythm in patients with ET in comparison to healthy controls (both Ps < 0.05). A subsequent frequency analysis, showed a significant amplitude decrement (sequence effect) in a subgroup of 13 out of 90 in patients with ET in comparison to 3 out of 85 HC (14.4% vs. 3.52%, X2=0.01). Finally, we found no relationships between the movement parameters and tremor severity in ET.

Conclusions: The present study indicates that slowness of movement is a common feature of patients with ET. In addition a proportion of ET patients has amplitude decrement (sequence effect) during movement repetition, a phenomenon typically present in patients with Parkinson's disease. The data support the notion that ET is a heterogeneous disorder. The results are relevant for a better understanding of ET pathophysiology.

P57

Insight into the hetereogeneity of essential tremor

G. Paparella[1], *M. Bologna*[1-2], *I. Berardelli*[3], *Gina Ferrazzano*[2], *P. Giustini*[1], *D. Alunni-Fegatelli*[4], *A. Berardelli*[1-2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy
[4]Department of Public Health and Infectious Disease, Sapienza University of Rome, Italy

Background: Essential tremor (ET) is a heterogeneous condition. In addition to having postural and kinetic tremor of the upper limbs, some patients with ET may have non-motor symptoms (i.e. cognitive and psychiatric disorders). It is unclear, however, whether motor and non-motor disorders in ET patients, are influenced by their historical features (i.e. family history disease duration and age at onset) or tremor characteristic (i.e. body distribution of tremor).

Methods: We enrolled 70 patients with a diagnosis of ET who were attending the outpatient clinic at the Department of Human Neuroscience, 'Sapienza' University of Rome. Tremor severity was assessed by means of clinical rating scales. A number of neuropsychological tests were also administered. We adopted the structured interviews for DSM-IV, SCID-I and SCID-II to investigate psychiatric and personality disorders. Patients also underwent videotape and kinematic recordings based on an optoelectronic system (SMART motion system, BTS Engineering, Italy); tremor and movement were analysed by means of a dedicated software (SMART Analyzer, BTS Engineering, Italy).

Results: Longer disease duration ($\geq$ 10 years) was associated with more severe tremor, as demonstrated by the clinical rating and altered trajectories during arm movements. ET patients with upper limb tremor plus head tremor exhibited more severe action tremor and a higher occurrence of Axis-I psychiatric disorders than ET patients with upper limb tremor only. Motor, cognitive and psychiatric features did not differ significantly with respect to family history (i.e. familial vs. sporadic ET cases) or age at tremor onset.

Conclusions: These findings support the hypothesis that disease duration and tremor distribution are the main determinants of ET heterogeneity, which is in keeping with the hypothesis of cerebellar neurodegeneration as a cause of this disease.

P58

The effect of intranasal oxytocin in patients with functional motor symptoms: an open label pilot study. The effect of intranasal oxytocin in patients with functional motor symptoms: an open label pilot study

Benedetta Demartini[1,2,3], *D. Goeta*[1,2], *A. Priori*[1,3,4], *O. Gambini*[1,2,3]

[1]Dipartimento di Scienze della Salute, University of Milan, Milano, Italy
[2]Unità di Psichiatria II, A.O. San Paolo, ASST Santi Paolo e Carlo, Milan, Italy
[3]"Aldo Ravelli" Research Center for Neurotechnology and Experimental Brain Therapeutics, University of Milan, Milan, Italy
[4]III Clinica Neurologica, A.O. San Paolo, ASST Santi Paolo e Carlo, Milan, Italy

Introduction: Despite the well-established efficacy of oxytocin in different psychiatric conditions, no studies have examined the effect of intranasal administration of oxytocin in patients with functional motor symptoms (FMS). Aim of this pilot study was to assess the effect of a single dose of intranasal oxytocin in a sample of patients with FMS on the motor symptoms themselves and on some psychological variables.

Materials and methods: Eight patients affected by FMS were recruited. They have been instructed to self-administer the spray. All patients underwent the following assessment prior (T0) and immediately after (T1) the oxytocin administration: video with neurological examination, PMD scale, assessment of depression, anxiety, alexithymia and interoceptive awareness. Self-assessment of outcome was recorded at T1 and T2 (five days after the session).

Results: After the session 87.5% patients rated their general feeling of well-being such as "better" or "much better" on the CGI and 37.5% rated their main symptoms as "better" or "much better" on the IPS. The improvement in the well-being reported by patients remained also at T2. After the oxytocin administration, patients had significantly lower scores at HAM-D, HAM-A and TAS-20. Good outcome was predicted by improvement in the TAS-20.

Conclusions: Our data suggest that a single intranasal administration of oxytocin can provide an improvement in anxiety, depression symptoms and in alexithymic features in the majority of patients with FMS. In addition, the majority of patients rated their general feeling of well-being such as better or much better after the oxytocin administration.

P59

Chorea and life-threatening respiratory disturbances in Anti-IgLON5 disease

Marta Filidei[1], *N. Tambasco*[1], *F. Paolini Paoletti*[1], *S. Simoni*[1], *E. Brahimi*[1], *G. Cappelletti*[1], *P. Nigro*[1], *P. Calabresi*[1,2]

[1]Neurology Clinic, Santa Maria della Misericordia Hospital, University of Perugia, Perugia, Italy
[2]IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Anti-IgLON5 disease is a recently described CNS disorder characterized by non-REM and REM parasomnias and respiratory dysfunction. Other features include bulbar syndrome, gait abnormalities, chorea and cognitive decline. Course is progressive and can lead to life-threatening respiratory disturbances such as central hypoventilation. The disorder is associated with IgLON5 antibodies, HLA DRB1 and HLA DQB1 and tauopathy predominantly involving the hypothalamus and tegmentum of the brainstem, representing a link between autoimmunity and neurodegeneration [1,2].

Objectives: To improve clinical recognition of anti-IgLON5 disease and highlight its life-threatening complications.

Methods: We report a case of anti-IgLON5 disease with chorea and respiratory impairment.

Results: In 2015 a 71-years-old woman was admitted to our Clinic for a one-year-history of progressive insomnia, sleep parasomnias, chorea, behavioral disorders and respiratory disturbances. Her past medical history revealed COPD and diabetes mellitus. She never received antipshycotic therapy. Neurological examination showed choreic movements affecting the limbs, trunk and face. Neuropsychological assessment revealed impaired executive and visuospactial function [3]; brain MRI, molecular analysis of IT-15 gene, acanthocytosis, autoimmune, metabolic and paraneoplastic screening were unremarkable. The patient was discharged with the administration of tetrabenazine, but the drug was withdrawn few weeks later due to gastric disturbances. In 2016, the patient presented psychosis and aggressive behavior; haloperidol was administered; in this context, the patient developed acute respiratory failure and needed intensive care. Moreover, she presented further episodes of respiratory distress and was admitted four times in intensive care. Finally, in 2017, autoimmune, metabolic and paraneoplastic screening were repeated and resulted unremarkable, CSF analysis was normal, positive anti-IgLON5 Ab and HLA DRB1 and HLA DQB1 genes were found. In the 2-years of follow-up, choreic, psychotic and respiratory disorders improved without medication, while sleep disorders still persist.

Conclusions: Anti-IgLON5 is an intriguing CNS disorder; its recognition is crucial to manage serious complications such as acute respiratory failure.

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P60

Spasmodic dysphonia as a presenting symptom of Spinocerebellar ataxia type 12

Francesco Cavallieri[1,2,3], *J. Rossi*[3], *G. Giovannini*[3], *C. Budriesi*[3], *A. Gessani*[3], *M. Carecchio*[4], *D. Di Bella*[5], *E. Sarto*[5], *J. Mandrioli*[3], *S. Contardi*[3], *S. Meletti*[3]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL- IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[3]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[4]Neurological Clinic, Department of Neural Sciences, University of Padova, Padova, Italy
[5]Medical Genetics and Neurogenetics Unit, IRCCS Foundation "Carlo Besta" Neurological Institute, Milan, Italy

Introduction: Autosomal dominant spinocerebellar ataxia type 12 (SCA12) is a rare genetic disorder due to an abnormal CAG repeat expansion (>51 CAG) in the PPP2R2B gene. [1, 2] Two SCA12 patients were previously reported from two families coming from Ferrara area, in North-East of Italy. [1, 3] Action tremor of the upper limbs is the most common sign at onset. [2] Subsequently, mild cerebellar dysfunction, hyperreflexia, parkinsonian features, dystonia and dementia can appear. Spasmodic dysphonia has been observed only in two cases of SCA12 and it has never been reported at disease onset. [4]

Case report: A 61-year-old woman developed at the age of 50 alteration of voice, followed by head dystonic tremor. Few years later she developed gait instability, mild ataxia and cognitive deterioration. Her paternal aunt died from an unspecified neurodegenerative disorder and two first-degree cousins developed a similar condition in their fifties. Neurological examination showed dystonic tremor of the head and the upper limbs, mild left dysmetria, diffuse hyperreflexia and inability to perform tandem gait. Brain-MRI revealed generalized cortical cerebral atrophy particularly evident in the midbrain. Perceptual and acoustic analysis of speech was performed using PRAAT®. The patient could not produce sustained phonemic vowel-like sounds or voluntary change voice fundamental frequency. Perceptual analysis showed frequent voice breaks, strained and dysfluent effortful speech production consistent with spasmodic adductor dysphonia. CAG repeats analysis in the PPP2R2B gene revealed an expanded heterozygous allele with 61 CAG repeats confirming the diagnosis of SCA12. Trihexyphenidyl (4mg/day) partial ameliorated tremor and dysphonia.

Discussion: SCA12 is phenotypically heterogeneous. Rarely, laryngeal dystonia can be the only sign at onset, making a genetic diagnosis challenging. In the present case, the presence of spasmodic dysphonia along with neurological examination and autosomal dominant family history of neurodegenerative disorders led to the suspicion of SCA12, a condition requiring a multidisciplinary team care.

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P61

A prospective evaluation of clinical and instrumental features before and after ventriculo-peritoneal shunt in patients with idiopathic normal pressure hydrocephalus: the Bologna pro-hydro study

Giulia Giannini[1,2], *G. Palandri*[3], *A. Ferrari*[4], *F. Oppi*[2], *D. Milletti*[5], *L. Albini-Riccioli*[6], *P. Mantovani*[3], *S. Magnoni*[1], *L. Chiari*[4], *P. Cortelli*[1,2], *S. Cevoli*[2]

[1]Department of Biomedical and NeuroMotor Sciences (DIBINEM), University of Bologna, Bologna, Italy
[2]Unit of Neurology, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[3]Unit of Neurosurgery, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[4]Department of Electrical, Electronic and Information Engineering-Guglielmo Marconi, University of Bologna, Bologna, Italy
[5]Unit of Rehabilitation Medicine, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
[6]Unit of Neuroradiology, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Introduction: Idiopathic Normal Pressure Hydrocephalus (iNPH) is a complex and often misdiagnosed syndrome, the major challenge is to identify which patients will benefit from surgery. The tap test (TT) is a predictive test with a questionable validity, this heterogeneity could be related to the lack of methodology standardization.

Objective: To describe the clinical/instrumental features, their longitudinal modifications after TT and their progression after surgery in a cohort of iNPH patients.

Methods: Patients compatible with iNPH underwent a 3-Tesla- MRI and an inpatients program with TT including standardized clinical evaluations, neuropsychological assessments and instrumental gait analysis pre- and after- (24-h and 72-h) TT. The multidisciplinary team selected candidates for ventricular-peritoneal (VP) shunt surgery. Patients were evaluated 6- and 12-months after surgery.

Results: 154 consecutive patients were included from 2015 to 2018, 76 with a iNPH diagnosis (43 underwent surgery, 35 were evaluated at 6-months follow-up visit). We observed the following findings: 1) a multidisciplinary team focused on this disease and a standardized protocol help in achieving a correct diagnosis and management of iNPH; 2) surgery improves motor and urinary symptoms and some neuropsychological functions; 3) this iNPH cohort showed a heterogeneous clinical presentation and progression of symptoms; 4) the three iNPH domains showed a different response after TT and the delayed motor assessment is more appropriate than the early one; 5) the instrumental motor measures bring out the motor improvement.

Conclusions: Patients with iNPH improved after surgery, when accurately selected. Our results suggest that delayed motor assessment is more appropriate than the early one, the neuropsychological assessment at 72-h after-TT is not necessary and the instrumental gait parameters enhance the motor improvement. This study could impact the clinical practice and management of iNPH.

P62

Movement disorder in patients with GNAO1 variants: a retrospective analysis

Tommaso Schirinzi[1,2], *G. Garone*[1], *F. Graziola*[1], *G. Vasco*[1], *S. Galosi*[3], *D. Battaglia*[4], *E. Bertini*[1], *A. Capuano*[1], *V. Leuzzi*[3]

[1]Department of Neurosciences, IRCCS Bambino Gesù Children's Hospital, Rome, Italy
[2]Department of System Medicine, University of Roma Tor Vergata, Rome, Italy
[3]Department of Pediatrics and Child Neurology and Psychiatry, Sapienza, University of Rome, Rome, Italy
[4]Department of Child Neurology and Psichiatry, Fondazione Policlinico Universitario Gemelli, Catholic University of Rome, Rome, Italy

Introduction: Hyperkinetic syndromes of childhood include several inherited or acquired conditions, with different clinical course and outcome. Therefore, outlining the clinical profile of every condition is necessary to allow early diagnosis and appropriate clinical management. GNAO1 variants have been recently discovered as causes of epileptic encephalopathies and heterogeneous syndromes presenting with movement disorder (MD); however the phenomenology and natural history of the GNAO1-related MD is undefined yet.

Objective: To describe genetic and clinical features of a large cohort of GNAO1 patients, in order to highlight clues for diagnosis, therapy and prognosis.
Methods: 41 published cases and 5 novel patients were enrolled in the study, collecting data on MD clinical features and course, medical and/or surgical therapies, neuroimaging, follow-up and genetic background. Descriptive statistics and logistic regression analysis were performed.

Results: Mean age of MD onset was 2 years (range 0-8). Phenomenology was complex but dystonia was the most common sign (65.2%), followed by other hyperkinetic features (dyskinesia, choreoathetosis). 45% of patients also presented status dystonicus. Clinical course was severe, fatal in 8% of cases. Surviving patients were further affected by other complications (cognitive and motor disability, speech and feeding problems).
Oral medications controlled up to 21% of patients, being tetrabenazine the most effective. 10 patients, because of severity of MD, underwent surgery (9 GPi-DBS, 1 pallidotomy) with partial improvement. No clear genotype/phenotype correlations emerged, although variants frequently occurred in exons 6 and 7.

Conclusions: GNAO1-related MD is a severe, generalized hyperkinetic condition mainly presenting with dystonia; because of the high risk of status dystonicus, early diagnosis and appropriate medical management are necessary to prevent life-threating emergencies and improve quality of life of such young patients.

P63

Correlation between UPDRS score and accelerometric measurements detected during continuous monitoring of movement disorders

Luigi Battista[1], *A. Romaniello*[2], *E. Ferrante*[2]

[1]Faculty of Medicine and Surgery, Catholic University of the Sacred Heart, Sede di Potenza, Potenza, Italy
[2]Department of Neurosurgery, Neurology Unit, Hospital "San Carlo", Potenza, Italy

Introduction: The clinical assessment of Parkinson's disease (PD) symptoms is typically performed with neurological examinations and simple motor tests; moreover, the current standard for evaluating motor symptom severities is the Unified Parkinson's Disease Rating Scale (UPDRS). However, these examinations may only consider the severity of motor symptoms during the length of the recording and may fail to capture variations in a patient's motor state, which change continuously during the day. Therefore, continuous monitoring of movement disorders in patients with PD may be a viable tool to provide additional information on motor symptoms and on response to treatment. However, some data provided by continuous monitoring systems are not always easy to correlate with the available UPRDS score.

Objectives: The objective is to investigate on a possible relationship between UPRDS scores and the summarizing indexes provided at the end of a continuous and long-term monitoring.

Methods: The UPRDS scoring was performed by a neurologist. Then, continuous monitoring was performed; data were acquired by means of a wrist-worn device (i.e. "Parkinson's disease-watch", PD-Watch) for 24 hours and then processed in order to get concise indexes on the cumulative duration and severity of the various possible hand tremor events detected during the entire duration of monitoring period. Finally, these indexes were correlated to the UPRDS score.

Results: In this study, 22 recording sequences were performed with PD patients. A linear regression model was used in order to correlate UPRDS score and concise indexes of continuous monitoring. As example, a linear correlation coefficient of 0,81 was found.

Conclusions: While results need to be extended with further clinical trials, the considered correlation between UPRDS score and data provided by means of continuous monitoring may be considered as useful information in the context of motor symptoms assessment.

P64

Language disorders in progressive supranuclear palsy: an underestimated condition?

Eleonora Del Prete[1], *L. Tommasini*[2], *D. Frosini*[2], *S. Mazzucchi*[2], *E. Belli*[1], *U. Bonuccelli*[1], *R. Ceravolo*[1]

[1]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy
[2]Department of Medical Specialities, Neurology Unit, AOUP, Pisa, Italy

Introduction: Progressive Supranuclear Palsy (PSP) is characterized by specific neuropsychiatric and cognitive dysfunction. The pattern of early cognitive impairment in PSP is usually a dysexecutive frontal syndrome but language domains could also be affected. New criteria for clinical diagnosis of PSP have recently been published by the Movement Disorders Society. Cognitive dysfunction is now considered one of four core features and speech/language deficit is gaining more relevance. Thus, it is increasingly important to obtain a detailed assessment of the cognitive and languages disorders.

Objectives: We aimed to investigate executive functions and languages abilities in PSP patients and in PSP subgroups [PSP-Richardson's Syndrome (PSP-RS) and PSP-non-RS] according to new Movement Disorders Society criteria. We also evaluated the relationship between cognitive functions and clinical features.

Methods: Twenty-two PSP patients underwent cognitive tests assessing attention, executive function and different domains of language (pictures naming, sentence and single word comprehension, repetition, reading, writing, semantic association and picture description). Cognitive and clinical variables including neuropsychiatric features in all groups and between groups (PSP-RS and non-RS) were analyzed.

Results: PSP patients and PSP subgroups (RS and non-RS) showed an impairment, with respect to normative data, in frontal functions (respectively, FAB 76,2-78,6-71,4%, FAS 59,1-66,7-42,9%, semantic fluency 40,9-53,3-14,3%) and language features (sentences comprehension 27,3-13,3-57,1%, number of verbs/total words 31,8-20,0- 57,1%, number of subordinates/total sentences in pictures description 36,4-40,0-28,6%). Comparing PSP-RS and PSP-non-RS significantly worse performances in PSP-RS in oculomotion as expected (p=0.035), semantic fluency (p=0,044), and FAS (p=0,039) were found. A significant correlation in all PSP patients between clinical and both executive functions and language domains was reported.

Conclusions: The presence of language disorders could be part of PSP-RS phenotype. In our cohort PSP-RS show simplified syntactic structures with paucity of used verbs even if the impairment does not meet criteria for definite agrammatism.

P65

Post stroke cranio-cervical myorhythmia successfully treated with botulinum toxin injection. A case report

Valentina Oppo, M. Melis, G. Cossu

Struttura Semplice Dipartimentale di Neurofisiologia, "A.O. Brotzu", Cagliari, Italy

Background: Myorhythmia is an unusual hyperkinetic involuntary movement disorder consisting of slow, quasi-rhythmic movement typically affecting cranial or limb muscles. It can also involve cervical muscles. It is usually associated with brainstem lesions, particularly with those affecting the components of the Guillain-Mollaret triangle. In this case, palatal myoclonus and ocular convergent-divergent nystagmus may coexist. Myorhythmia is usually poor responsive to medical treatment. We describe an unusual case of myorhythmia involving cervical muscles with excellent response to treatment with botulinum toxin.

Case Report: a 41-years old woman presented with a cervico-cranial, slow, quasi-rhythmic involuntary movement two months after a ponto-mesencephalic hemorrhage due to a ruptured arteriovenous malformation. We labelled this movement disorder as a myorhythmia because: 1) it didn't subside neither change in speed or amplitude during posturing, voluntary movement or with passive head displacement; 2) convergent nystagmus and palatal myoclonus were also present; 3) at head MRI hypertrophy of right inferior olivary nucleus was observed. First line treatment with clonazepam and baclofen was ineffective and was associated with reduced vigilance. We decided then to treat her with incobotulinumtoxinA injection (40 Units into right sternocleidomastoid, 20 Units into right and left trapezius and 20 Units into both scalenus), with subsequent regression of involuntary movement for two months.

Conclusions: Treatment options for myorhythmia involving cranial or cervical muscles should include botulinum toxin injection, due to its safety, feasibility and lack of sedating properties.

P66

Featuring clinical differences in MDS PSP phenotypes

Arianna Cappiello[1], *M. Picillo*[1], *S. Cuoco*[1], *M.F. Tepedino*[1], *G. Volpe*[1], *R. Erro*[1], *G. Santangelo*[2], *M.T. Pellecchia*[1], *P. Barone*[1], the PSP Salerno study group

[1]Center for Neurodegenerative diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience Section, University of Salerno, Salerno, Italy
[2]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy.

Introduction: Movement Disorder Society (MDS) new diagnostic criteria for Progressive Supranuclear Palsy (PSP) identifying different disease phenotypes were recently released.

Objective: The aim of the present study is to report on the cognitive and behavioral features of the different disease phenotypes diagnosed according to the MDS criteria.

Methods: Forty-nine PSP patients underwent an extensive battery of clinical assessments. Differences between PSP subtypes were computed with $\chi 2$ or ANOVA tests. Using the z scores, subjects were classified as having normal cognition, mild cognitive impairment, single or multiple domain, and dementia. A logistic regression model was implemented to investigate the major determinants of the phenotypes.

Results: Half of the cohort presented Richardson's syndrome (46.9%), followed by PSP with parkinsonism and corticobasal syndrome (22.4% and 14.2%, respectively). Few patients displayed the other phenotypes. Richardson's syndrome and PSP with corticobasal syndrome presented a similar burden of disease in terms of motor and cognitive issues. The only cognitive testing differentiating the PSP phenotypes were semantic fluency and ideomotor apraxia. The majority of our cohort was either affected by dementia or presented normal cognition and the highest percentage of dementia was in Richardson's syndrome. The only marker of PSP non-Richardson's syndrome phenotype was better scores in visuo-spatial testing, implying worse visuo-spatial abilities in PSP Richardson's syndrome.

Conclusions: The cognitive testing differentiating the PSP phenotypes were semantic fluency and ideomotor apraxia. In PSP, mild cognitive impairment likely represents an intermediate step from normal cognition to dementia. The only marker of PSP non-Richardson's syndrome phenotype was better scores in visuo-spatial testing.

P67

Paraneoplastic Stiff-Person Syndrome with positivity of amphiphysin anti-glycine receptor antibodies: a case report

Michele Mainardi, M. Carecchio, A. Antonini

Department of Neurology, University of Padova, Italy

Introduction: Stiff-Person Syndrome (SPS) is a rare condition with a prevalence of 1:1,000,000, caused by antiGAD and anti-amphiphysin antibodies either associated with other autoimmune diseases or with a paraneoplastic aetiology. Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM) is due to antiGlyR or anti-NMDA-R antibodies. Clinically, SPS and PERM are partially overlapping conditions.

Objective: To report an atypical case of SPS due to anti-amphiphysin anti-Glycine-R antibodies.

Methods: A 54-year-old woman presented with a generalized seizure. Four months earlier, she had been diagnosed with a left ductal carcinoma and had complained of increasing difficulties in walking, initially attributed to peripheral neuropathy. Neurological examination showed stiffness in the left leg with marked postural instability, absent tendon reflexes throughout, extensor plantars on the left.

Results: EMG/NCS were unremarkable; brain and spinal MRI and an EEG showed no abnormal findings. A whole-body and brain PET-CT scan showed increased uptake in the left breast and in two axillary lymph nodes. CSF analysis showed increased cellularity without neoplastic elements, elevated proteins with hematoencephalic barrier damage without oligoclonal bands. Serum positivity for anti-amphiphysin antibodies was found [1,2]. The patient was started [3] on gabaergic drugs, muscle relaxants, steroids and hormone therapy and later underwent left mastectomy followed by radiotherapy without significant improvement. Given the atypical copresence of seizure and stiffness in a single limb, along with the occurrence of an intense sine materia pruritus in the left side of the lower back, a second-level analysis was carried out. Serum and CSF positivity for anti-Glycine receptor antibodies (anti-GlyR) was found. Plasmapheresis was not beneficial. Given the persistent neurological disability, an immunomodulatory therapy with rituximab has been scheduled.

Conclusions: This case expands the current knowledge about the clinical phenotype associated with anti-amphiphysin antibodies and confirms the non-reversibility of this paraneoplastic condition even after the excision of the underlying neoplasm.

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P68

Therapeutic management of complicated Parkinson's disease: clinical application of the Motor Fluctuation Indices

Roberta Bonomo, G. Mostile, A. Nicoletti, M. Zappia

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

Objectives: To evaluate the usefulness of the Motor Fluctuation Indices to assess clinically relevant change in motor fluctuations in advanced Parkinson's disease (PD) patients after therapeutic interventions on the 12-hour Waking-day Motor Assessment (WDMA).

Methods: Twenty-eight (N=28) patients with complicated PD were selected. All patients underwent a WDMA before and after modulation of dopaminergic therapy. Motorassessment was performed by using the Unified Parkinson's Disease Rating Scale (UPDRS). To quantify the difference in severity of daily motor fluctuations between the first and the second evaluation, the Worsening Index (WI), the Mean Fluctuation Index (MFI) and the Coefficient of Variation (CV) were computed.

Results: At the time of the second assessment, patients presented a slight reduction in the number of levodopa daily intakes with a concomitant increase of the mean dose amount per time-interval. Mean levodopa daily dosage and cumulative LED did not vary significantly. After optimizing the dopaminergic therapy, we observed an improvement in daily motor performance in the second assessment as indicated by the reduction of all three indices score.

Conclusions: Application of the Motor Fluctuation Indices to clinical practice might help physicians to evaluate and quantify the entity of motor fluctuations after therapeutic interventions in PD patients.

P69

Efficacy and safety of the 5-hydroxytryptophan on levodopa-induced motor Complications in Parkinson's disease

Mario Meloni[1], *M. Puligheddu*[2], *A. Cannas*[1], *R. Farris*[1], *M. Figorilli*[2], *G. Defazio*[3], *M. Carta*[4]

[1]Movement Disorders Center, Department of Neurology, AOU Cagliari, University of Cagliari, Cagliari, Italy
[2]Sleep Disorder Centre, Department of Public Health and Clinical and Molecular Medicine, University of Cagliari, Monserrato, Cagliari, Italy
[3]Department of Medical Sciences and Public Health, Neurology Unit, University of Cagliari, Cagliari, Italy
[4]Department of Biomedical Sciences, University of Cagliari, Cittadella Universitaria Monserrato, Monserrato, Italy

Introduction: Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by bradykinesia, tremor, rigidity and postural instability. Several studies have indicated that altered serotonergic neurotransmission may contribute to the motor features commonly associated with PD such as levodopa-induced dyskinesias (LIDs). 5-Hydroxytryptophan (5-HTP) is the immediate precursor of serotonin obtained trough hydroxylation of L-tryptophan. We have recently demonstrated that 5-HTP produces significant antidyskinetic effect in the rat model of PD [1]. To date, there has been inconsistent research on the use of 5-HTP in PD, especially in PD with levodopa-induced motor complications.

Objectives: The purpose of this study was to compare the effects of 5-HTP to placebo on levodopa-induced motor complications in PD patients.

Methods: We performed a single-center, randomized, double-blind placebo- controlled cross-over study; a total of 12 patients were diagnosed with LIDs and motor fluctuactions and subsequently were randomized to intervention. Eleven subjects completed the 16-week protocol. Patients received placebo and 50 mg of 5-HTP daily in a cross-over design over a period of 4 weeks. There was a 4-weeks washout period between treatments. For the assessment of efficacy on the motor functions and levodopa-induced motor complications, the UPDRS (parts III and IV), Unified Dyskinesia Rating Scale (UDyRS), Wearing- Off Questionnaire (WOQ-19) and the self-reported 24-hour home dyskinesia diaries were respectively obtained at screening, baseline and weeks 4, 8, 12 and 16 (T-end).

Results: Repeated measures analysis revealed a significant improvement of LIDs during the 50 mg 5-HTP treatment compared to placebo as assessed by the UDyRS and UPDRS-IV scores.

Conclusions: This study provides preliminary evidence of clinical benefit with 5-HTP for treating LIDs in PD. Larger studies with a longer treatment duration are needed to corroborate these early findings.

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P70

Efficacy and safety of the 5-Hydroxytryptophan on depression and apathy in idiopathic Parkinson's disease

Mario Meloni[1], *M. Pulighedda*[2], *M. Carta*[3], *A. Cannas*[1], *M. Figorilli*[2], *R. Farris*[1], *G. Defazio*[1,4]

[1]Movement Disorders Center, Department of Neurology, AOU Cagliari, University of Cagliari, Cagliari, Italy
[2]Sleep Disorder Centre, Department of Public Health and Clinical and Molecular Medicine, University of Cagliari, Cagliari, Italy
[3]Department of Biomedical Sciences, University of Cagliari, Cittadella Universitaria, Cagliari, Italy
[4]Department of Medical Sciences and Public Health, Neurology Unit, University of Cagliari, Cagliari, Italy

Introduction: Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by the motor symptoms of bradykinesia, tremor, rigidity and postural instability. However, non-motor symptoms such as depression and apathy are also frequent and play a significant role. Several studies have indicated that altered serotonergic neurotransmission may contribute to non- motor features commonly associated with PD such as apathy and depression.The 5-Hydroxytryptophan (5-HTP) is the intermediate metabolite of L-tryptophan in the production of serotonin. Studies in other populations indicate that 5-HTP might be useful in the treatment of depression. To date, there has been inconsistent research on the use of 5-HTP in PD.

Objectives: The purpose of this study was to compare the effects of 5-HTP to placebo on depression and apathy in patients with PD.

Methods: A single-center, randomized, double-blind, placebo-controlled, cross-over trial was employed; 25 subjects were subsequently enrolled into the study, 23 subjects completed the 16-week protocol. Patients received placebo and 50 mg of 5-HTP daily in a cross-over design over a period of 4 weeks. We decided for a washout period of 4 weeks in order to minimize the carry-over effects. For the assessment of efficacy on the depression and apathy the Beck Depression Inventory II (BDI-II), the 21-item version of Hamilton Depression Rating Scale (HDRS21) and Apathy Scale (AS) were respectively obtained at screening, baseline and weeks 4, 8, 12 and 16 (T-end).

Results: Repeated measures analysis revealed a significant improvement of depressive symptoms during the 50 mg 5-HTP treatment compared to placebo as assessed by the HDRS21. There were no significant effects of 5-HTP compared to placebo on apathy symptoms as assessed by the AS.

Conclusions: This study provides preliminary evidence of clinical benefit with 5-HTP for treating depressive symptoms in PD. Larger studies with a longer treatment duration are needed to corroborate these early findings.

P71

Effects of safinamide on cognitive and behavioral symptoms in fluctuating Parkinson's disease patients: a prospective longitudinal study

Sara Satolli[1,2], *R. De Micco*[1,2], *M. Siciliano*[1,3], *F.P. Bonifacio*[1,2], *A. De Mase*[1,2], *A. Giordano*[1,2], *G. Tedeschi*[1,2], *A. Tessitore*[1,2]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]MRI Research Center SUN-FISM, University of Campania "Luigi Vanvitelli", Napoli, Italy
[3]Neuropsychology Laboratory, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Background: Parkinson's disease (PD) patients in chronic levodopa treatment may experience motor and non-motor fluctuations, highly affecting their quality of life (QoL). Safinamide is a new monoamine oxidase-B inhibitor, also exerting a well-documented non-dopaminergic effect, recently approved as add-on therapy in fluctuating PD patients.

Aim: We performed a longitudinal prospective study in a cohort of fluctuating PD patients, aiming to investigate whether safinamide may improve non-motor, cognitive and behavioral symptoms over a 6-months treatment period.

Methods: We enrolled 20 consecutive fluctuating PD patients, who have been prescribed to add safinamide to their dopaminergic treatment. PD patients underwent an extensive clinical and neuropsychological evaluation before safinamide initiation and after 6 months of treatment. At each timepoints, motor and non-motor symptoms were assessed by means of validated scales in PD. Neuropsychological assessment was performed by exploring five cognitive domains.

Results: Statistical analysis showed a significant improvement in Non Motor Symptoms Scale, particularly in the items investigating daytime sleepiness, motivation and interests, and urinary disturbances. Neuropsychiatric assessment showed decreased fatigue and apathy. Motor assessment revealed a significant reduction in the total wake-up time spent in off-state. As expected, decreased motor and non-motor symptoms burden was also associated with a significant improvement of patients' QoL (as reflected by the Parkinson's Disease Questionnaire QOL-39). Follow-up neuropsychological evaluation did not reveal any change compared to baseline.

Conclusions: Our data reveal that, along with motor fluctuations improvement, treatment with safinamide may significantly decrease non-motor symptoms burden in PD patients. Interestingly, non-dopaminergic mechanisms, such as glutamatergic overdrive, have been demonstrated to play a role in many pathways underlying these symptoms. Thus, we hypothesize that the unique neurotransmitter receptor-binding profile of safinamide, which has been shown to eventually modulate also glutamatergic transmission, may explain our findings.

P72

Safety and tolerability of safinamide in elderly Parkinson's disease patients

Domiziana Rinaldi[1], *M. Sforza*[1], *T. De Santis* [1], *S. Tagliente*[1,2], *M. Giovannelli*[1], *M. Alborghetti*[1], *F.E. Pontieri*[1,2]

[1]Dipartimento di Neuroscienze, Salute Mentale e Organi di Senso, Sapienza Università di Roma, Rome, Italy
[2]Dipartimento di Neurologia Clinica e Comportamentale, IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Safinamide (SF) is a reversible MAO-B inhibitor, displaying dopaminergic and non-dopaminergic effects. SF is approved for treatment of levodopa-related motor fluctuation in patients suffering from Parkinson's disease. Under these conditions, SF significantly reduced "off" time. The most frequent side-effect is development or worsening of dyskinesia, that occurs in 25-30% of cases. Despite the large use of SF, data are lacking on the safety and tolerability of the drug in elderly population.

Objective: Here we investigated the efficacy, safety and tolerability of SF (50 or 100 mg/day) in PD patients aged over 70 years, displaying motor fluctuation.

Methods: 30 subjects (18 males, 12 female) were consecutively enrolled in the period between January 2017 - July 2018, during scheduled outpatient visits at our PD service. All patients were aged > 70 years, had a MMSE score > 24/30, were under stable antiparkinsonian therapy for at least 3 months and suffered from motor fluctuations as verified the WOQ-19. In all patients, the effects of add-on therapy with SF were monitored for at least 6 months.

Results: The majority of patients (22/30, 75%) had significant reduction of motor fluctuations at 3-month and 6-month scheduled visit. Three patients (10%) (2 at 50 mg, 1 at 100 mg) displayed either development (n=2) or worsening (n=1) of dyskinesia. In any of these cases, the severity of dyskinesia forced to interruption of treatment. Three (10%) other patients developed hallucinations, in one case forcing interruption of SF. Eventually, one further patient was affected by hip fracture as the consequence of a fall linked to increased postural instability. In all remaining patients (23/30, 77% of cases), SF was well tolerated.

Conclusions: The results of this observational study indicate the high safety and tolerability of SF in elderly PD patients displaying motor fluctuations.

P73

Overnight switch from rasagiline to safinamide in fluctuating patients with Parkinson's disease: a tolerability and safety study

Laura Vacca, G. Caminiti, M. Casali, C. Coletti, P. Grassini, F.G. Radicati, M. Torti, F. Stocchi

IRCCS San Raffaele Pisana, Roma, Italy

Introduction: Rasagiline label report the indication to wait at least 14 days between discontinuation of rasagiline and initiation of another MAO inhibitor. This results in a major inconvenience for Parkinsonian patients (PD) due to their clinical worsening. Safinamide is a reversible MAO-B inhibitor, characterized by a good safety profile. In clinical practice safinamide is often introduced instead of rasagiline following an overnight switch. The aim of this study is to explore the safety and tolerability of the immediate switch from rasagiline (irreversible MAO-B inhibitor) to safinamide, with the expectation that there will be no adverse events or increased risk of hypertensive crisis for patients with PD or signs of serotonin syndrome.

Objective: The aim of this study is to verify safety and tolerability of the immediate switch from rasagiline to safinamide through monitoring of BP by 24-hour Holter recording. The primary objective of the study will be achieved if the mean BP will not increase by >10 mmHg in the studied population.

Methods: This is an open-label, single-centre study conducted at IRCCS San Raffaele Pisana. Study population included patients with idiopathic PD in the mid-late stage of the disease, suffering from motor fluctuation, on stable treatment with rasagilina and levodopa (alone or in combination with other anti-parkinsonian medication). The protocol contemplates five visits during six weeks, with two 24-hour Holter recording (first in rasagiline and second in first-day of safinamide therapy), monitoring typical symptoms of the serotonin syndrome.

Results and conclusions: 20 patients were enrolled, the results of the study are being analyzed. No adverse events occurred, and no signs of serotoninergic crisis were observed.

P74

Transcranial direct current stimolatin (TDCS) on Parkinson's disease patients with freezing of gait: preliminary findings

Simona Scalise[1], *G. Di Lazzaro*[1], *M. Alwardat*[1], *N.B. Mercuri*[1,2], *M. Patera*[1], *L. Pietrosanto*[3], *G. Saggio*[3], *A. Pisani*[1,2]

[1]Centro Parkinson, Clinica Neurologica, Dipartimento di Medicina dei Sistemi, Università di Roma Tor Vergata, Rome, Italy
[2]IRCCS Fondazione S. Lucia, Rome, Italy
[3]Facoltà di Ingegneria, Università di Roma Tor Vergata, Rome, Italy

Introduction: Freezing of gait (FOG) is one of the most disabling and poorly understood complication of Parkinson's disease (PD). Several lines of evidence suggest that FOG is not only a motor problem, but also arises in part because of deficits in executive function, a cognitive domain mediated by the dorsolateral prefrontal cortex (DLPFC). Overtime, these symptoms may become refractory to both pharmacological and non-pharmacological treatments. Transcranial direct current stimulation (tDCS) is a low-cost, noninvasive neuromodulatory technique, currently considered a valuable option to fill the therapeutic gaps in PD.

Objectives: The primary endpoint of this study was to evaluate the effect of a tDCS protocol with anodal stimulation of the left DLPFC in PD patients presenting FOG.

Methods: This study involved PD patients presenting FOG. They underwent 20 minutes of electric current of 2mA on 10 separate visits (5 in a week) using a pair of large sponges soaked in saline solution. Unified Parkinson's Disease Rating Scale pars 2 and 3 (UPDRSII-III), Hoehn and Yahr (H&Y), New Freezing of Gait Questionnaire (N- FOGQ), Berg Balance Scale (BBS) were performed at baseline (T0), after last stimulation (T1) and at one month follow-up (T2). Moreover, kinematic parameters of gait abnormalities were measured by means of wearable devices (MOVIT G1®) in order to obtaining an objective and reproducible evaluation.

Results: Our preliminary results obtained from a limited cohort of patients demonstrate a significant clinical improvement. Each evaluation scale demonstrate a benefit from our tDCS protocol, both between T0-T1 and additional improvement at T2. Specifically, disturbance of balance and the severity of FOG episodes showed the best outcome.

Conclusions: Coherently with the hypothesis that cognitive executive circuit plays a role in FOG, we may consider anodal tDCS of the DLPFC as a potential adjunctive therapy in PD patients with FOG.

P75

Working memory task related EEG changes in healthy subjects and in Huntington's disease patients

Gaia Bonassi[1], *M. Semprini*[2], *M. Chiappalone*[2], *F. Barban*[2], *E. Pelosin*[3,4], *G. Lagravinese*[4], *R. Marchese*[3], *L. Trevisan*[3], *P. Mandich*[3], *D. Mantini*[5], *L. Avanzino*[1,3]

[1]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy
[2]Italian Institute of Technology (IIT), Genova, Italy
[3]Ospedale Policlinico San Martino-IRCCS, Genoa, Italy
[4]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health Unit, University of Genoa, Genoa, Italy
[5]Research Center for Motor Control and Neuroplasticity, KU Leuven, Leuven, Belgium

Introduction: Huntington's disease (HD) is a fully penetrant neurodegenerative disease characterized by cognitive, motor and psychiatric disturbance. Cognitive disturbance can be seen many years before symptom onset and follows a sub-cortical pattern characterized by impaired emotion recognition, processing speed, visuospatial and executive function. High-density electroencephalography (hdEEG) is now an effective methodology for brain research, because it allows to perform accurate source localization from its signals. hdEEG is especially useful in this context, given its application in a wider variety of experimental framework with respect to traditional brain imaging techniques.

Objective: To use hdEEG analysis for investigating the cortical changes induced by a cognitive task, in healthy people and in pre-symptomatic/early stages HD patients.

Methods: Behavioural task was implemented in Matlab and consisted in n-back working memory (WM) task (n = 2, 3). Neural activity via hdEEG was assessed with a 128 channel EEG recording system (acti128Champ, Brain Products), focusing on changes of activity across the cognitive network. We tested 19 healthy subjects (10 females, 34±10 years) and 5 HD patients (4 females, 51±11 years). We first reconstructed neural oscillations in the cortex and we then applied event related synchronization and desynchronization analysis on the reconstructed signals, and investigated how WM load modulate brain plasticity.

Results: Data on healthy subjects indicated significant ERD in gamma band during the correctly encoded trials, both in the 2-back and 3-back tasks, in cortical areas of default mode network and executive control network (DLPFC, posterior cingulate cortex, inferior parietal lobule). Preliminary analysis on HD group showed a strong gamma band desynchronization in prefrontal areas.

Conclusions: Preliminary results highlighted gamma activity in cognitive areas involved in WM task in healthy subjects. We will acquire further data from HD patients, in order to compare the two populations.

This project was founded by Gossweiler Foundation

P76

Unilateral increase of blink reflex recovery cycle in drug-naïve hemiparkinson syndrome

Giorgia Sciacca[1], *G. Mostile*[1], *I. Disilvestro*[1], *G. Donzuso*[1], *R. Manna*[1], *G. Portaro*[1], *C. Rascunà*[1], *S. Salomone*[2], *F. Drago*[2], *A. Nicoletti*[1], *M. Zappia*[1]

[1]Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, Catania, Italy
[2]Department of Biomedical and Biotechnological Sciences, Section of Pharmacology, University of Catania, Catania, Italy

Background: R2 Blink Reflex Recovery Cycle (R2 BRRC) is a neurophysiological tool, used to measure brainstem excitability and it is known to be enhanced in Parkinson's disease (PD). Previous studies were conducted on Blink Reflex (BR) in early hemiparkinson patients. However, to our knowledge, there are no studies on R2BRRC in drug-naïve patients with hemiparkinson syndrome. We evaluated R2BRRC in drug-naïve PD patients with unilateral tremor and/or rigidity, diagnosed as hemiparkinson syndrome, to evaluate differences in brainstem excitability between affected and unaffected sides.

Methods: We prospectively enrolled 18 drug-naïve PD patients: 7 patients with right hemiparkinson syndrome and 11 patients with left hemiparkinson syndrome. We investigated Blink Reflex and R2BRRC at interstimulus intervals (ISIs) of 100, 150, 200, 300, 400, 500 and 750 ms bilaterally.

Results: All PD patients showed an early recruitment of R2BRRC. Right hemiparkinson patients showed a significant enhanced recruitment in left R2BRRC at ISI of 150 ms ($p<0.05$), whereas left hemiparkinson patients showed a significant early recruitment in right R2BRRC at ISIs of 100, 150 and 200 ms ($p<0.027$; $p<0.006$; $p<0.007$). Our findings showed a contralateral increase of brainstem excitability to the clinically affected side in drug-naïve PD patients.

Conclusions: R2BRRC is a helpful neurophysiological tool to understand pathophysiological mechanisms underneath PD. We hypothesized that an increased state of neurons excitability probably due to a predominant contralateral dysfunction of basal ganglia structures could explain the asymmetric brainstem disinhibition observed in hemiparkinson patients.

P77

Effect of acute L-Dopa administration on eye movement parameters in atypical parkinsonisms

Clara Grazia Chisari, G. Mostile, G. Donzuso, G. Sciacca, G. Portaro, C. Rascunà, F. Patti, A. Nicoletti, M. Zappia

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

Introduction: Various oculomotor disturbances are associated with parkinsonisms, including abnormal saccades and smooth pursuit, and up- and downgaze limitation.

Objective: To evaluate the eye movement parameters in patients with atypical parkinsonisms before and after acute L-Dopa administration.

Methods: We screened patients with parkisonisms syndroms, diagnosed to curretly accepted criteria. Eye movement were recorded at baseline (T0) and 120 min after the administration of carbidopa-levodopa 250+50 mg per os (T1) using an infrared-emitting videobased eye tracker (EyeLink 1000 Plus®). We evaluated: saccades (mean peak-velocity (pvel), mean latency, percentage of hypometric saccades); smooth pursuit (number of catch-up saccades [CUS] during pursuit and the mean of total amplitude of catch-up saccades [Amp CUS]); up- and downgaze limitation (the maximum range of amplitude [MaxAmp]); fixation task (square wave intrusion [SWI]).

Results: We enrolled 9 (mean age 70.8±12.3, 61.3% men) with atypical parkinsonisms (5 progressive sovranuclear palsy [PSP], 3 multiple system atrophy [MSA] and 1 patient was corticobasal degeneration [CBD]). Compared to baseline, we found at T1, for saccadic task, an improvement in pvel (688.6±41,6 vs 742.1±34,6, $p<0.01$), a reduction of percentage of hypometric saccades (88.3±15.5 vs 64,1±11.0, $p<0.01$) and on saccadic latency (341.4±12.4 vs 281.8±21.6, $p<0.01$); during fixation task, a slight but not significant reduction of the mean number of SWI (78.1±29,6 vs 75.8±25.9, $p<0.09$) was observed. No differences were found in smooth pursuit parameters between T0 and T1. MaxAmp for upgaze was found slightly, but not significant, improved between T0 and in T1 (11.5±9.4 vs 12.6±7.9, $p=0.1$); no differences were found in MaxAmp for downgaze.

Discussion: This is the first study evaluating the effect of acute L-Dopa administration on a wide range of eye movement paramters in patients with atypical parkinsonisms. We observed an improvement in saccades, but not in smooth pursuit and fixation parameters and in MaxAmp of up- and downgaze.

P78

Exploratory analysis of electrocortical signal complexity in patients with progressive supranuclear palsy and corticobasal degeneration

Giovanni Mostile, L. Giuliano, R. Terranova, A. Luca, G. Donzuso, G. Portaro, C. Rascunà, V. Sofia, A. Nicoletti, M. Zappia

Department "G.F. Ingrassia", University of Catania; Neurology Clinic, Policlinico "G. Rodolico" University Hospital, Catania, Italy

Introduction: Complexity is a characteristic of self-similar fractal phenomena, which have been described in biological processes. It has been hypothesized that a topographic increased level of neuronal organization can be evaluated by analyzing self-similarity property of site-specific electrocortical activity as expression of brain signal complexity. In untreated Parkinson's disease subjects, an increased level of fronto-temporal neuronal organization has been observed. No data are available for patients clinically affected by suspected tauopathies with dementia and parkinsonism.

Objectives: We evaluated self-similarity of electrocortical activity as expression of brain signal complexity in patients clinically affected by Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) as compared to controls.

Methods: We analyzed data of N=14 PSP, N=7 CBD and N=27 controls subjects group-matched by age who underwent standardized electroencephalography. A Welch's periodogram was applied to site-specific electroencephalographic signal epochs. To investigate self-similarity of electrocortical activity, the power law exponent β was computed for each selected coordinate as minus the slope of power spectrum versus frequency in a Log-Log scale.

Results: PSP subjects presented significant overall lower β values among all sites of recordings as compared to controls. CBD patients presented instead significant lower β values in the posterior temporal-parietal-occipital regions bilaterally with respect to controls, while no significant differences were observed in the frontal regions.

Conclusions: Our findings suggest different patterns of topographic electrocortical organization in patients with PSP and CBD, maybe due to different subcortical-cortical functional networks involved in the two conditions.

P79

First the egg or the chicken? The effects of propofol and curare on muscle rigidity and subthalamic beta activity in Parkinson's disease

Tommaso Bocci[1,2], *F. Cortese*[2], *M. Arlotti*[2], *S. Marceglia*[2,3], *F. Cogiamanian*[2], *G. Ardolino*[2], *M. Locatelli*[4], *P. Rampini*[4], *S. Barbieri*[2], *A. Priori*[1]

[1]Aldo Ravelli" Center for Neurotechnology and Experiental Brain Therapeutics, Department of Health Sciences, University of Milan & ASST Santi Paolo e Carlo, Milan, Italy
[2]Clinical Center for Neurostimulation, Neurotechnology, and Movement Disorders, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[3]Department of Engineering and Architecture, University of Trieste, Trieste, Italy
[4]Laboratory of Experimental Neurosurgery and Cell Therapy, Neurosurgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy

Introduction: Local field potential subthalamic oscillations in the 15-30 Hz range ("beta rhythm") are a biomarker of Parkinson's disease (PD) and strongly correlate with rigidity. However, whether subthalamic beta activity induces rigidity, or viceversa muscle rigidity drives beta ocillations is unknown.

Objective: To assess whether beta activity is a central oscillopathy dependent upon the dopaminergic denervation ultimately leading to rigidity, or, conversely, it arises peripherally from muscle rigidity.

Methods: We assessed changes in local field potential activity combining the use of propofol, a general anesthetic agent which does not interfere with the interpretation of routine EEG and with a peripheral myorelaxating action and curare having a purely neuromuscular blocking effect. We assessed changes in beta power in two PD patients, at baseline and in two different experimental conditions, following propofol alone (25 μg/kg/min) and after the further infusion of curare (propofol and curare). Muscle tone was clinically evaluated by a neurologist and electrophysiological confirmation of neuromuscular block was assessed by acceleromyography ("Train of Four", TOF).

Results: Propofol remarkably decreased rigidity in the four limbs. The following administration of curare did not induce a further reduction of muscle tone. Concerning the STN oscillatory activity, whereas propofol decreased the beta power ($p < 0.01$), curare failed to further change it.

Conclusions: Whereas propofol induces flaccidity and a remarkable reduction of beta power STN oscillatory activity in our patients with PD undergoing anesthesia, the following administration of curare failed to change the power in the beta band. We speculate that, because after propofol curare had no additional myorelaxant effect, the propofol-induced resolution of parkinsonian rigidity arises from peripheral myorelaxation which, in turn, reduced the STN beta activity. Hence, overall our observation suggests that STN beta oscillatory activity in Parkinson's disease might arise from a peripherally driven reafference from rigid skeletal muscles.

P80

Dopaminergic treatment and speech in Parkinson's disease: acoustic analysis and correlation with motor features and dyskinesia

Francesco Cavallieri[1,2,3], *C. Budriesi*[3,4], *A. Gessani*[3,4], *E. Menozzi*[3,4], *S. Contardi*[3,4], *F. Valzania*[1], *F. Antonelli*[3,4]

[1]Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL- IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy
[3]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[4]Azienda Ospedaliero Universitaria di Modena, Modena, Italy

Objectives: Analyse the effects of levodopa on speech and its possible relationship with motor features and dyskinesias in a group of advanced Parkinson's disease (PD) patients.

Methods: We retrospectively evaluated data from 50 PD patients admitted to our department for a preoperative evaluation for Subtalamic Nucleus Deep Brain Stimulation [1]. Disease severity was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) scores and subscores in the ON-state and OFF-state [2]. L-dopa responsiveness was evaluated with a drug-challenge test and ON-state dyskinesias were assessed with the Clinical Dyskinesia Rating Scale (CDRS) [1,3]. Each patient was evaluated ON and OFF-state and performed the following speech tasks: monologue, diadochokinesis, reading of a passage and sustained phonation. A perceptual and acoustic analysis was performed using a standardized protocol and 13 parameters were evaluated, applying PRAAT, a free software for the analysis of speech, for the acoustical part. Statistical analysis was performed using Pearson correlation coefficient and paired t test.

Results: The severity of speech impairment, expressed by the item 18 of the UPDRS Part III (speech subscore) in the OFF-state, correlated negatively with the OFF-state maximum phonation time (p= 0,0296, r-value: -0,3080) and the ON-state mean intensity of sustained phonation (p= 0,0340, r-value: -0,3100). In the ON-state, UPDRS speech subscore correlated positively the Shimmer Local dB (p= 0,0129, r-value: 0,3720). Furthermore, we found a positive correlation between the ON-state UPDRS axial subscore and ON-state speech mean frequency (p= 0.0055, r-value: 0.4114). The total CDRS score and the CDRS subscore related to axial (face, neck and trunk) dyskinesias strongly correlated with the ON-state Shimmer Local dB (p= 0.0141, r-value: 0.3677; p= 0.0030, r-value: 0.4369 respectively).

Conclusions: Our data confirm that the intensity and location of ON-state dyskinesias could negatively influence the ON-state speech quality in PD, with axial dyskinesia that could negatively influence the pneumo-phono-articulatory system.

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P81

Technology-based assessment of bradykinesia, gait and balance in newly diagnosed, drug free Parkinson's disease patients

Giulia Di Lazzaro[1], *M. Ricci*[2], *T. Schirinzi*[1], *M. Alwardat*[1], *A. Pallotti*[2]; *F. Giannini*[2], *N.B. Mercuri*[1,3], *G. Saggio*[2], *A. Pisani*[1,3]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Department of Engineer, University of Rome Tor Vergata, Rome, Italy
[3]IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Nowadays, the diagnosis of Parkinson's disease (PD) is based on clinical evaluation and full diagnostic certainty is impossible during life. Increasing interest have been put on technology-based objective measures (TOMs) of motor functions in PD patients, to monitor response to therapy and to support clinical evaluation, especially in later stages of the disease. Few data are available on the very early phases of the disease.

Objective: To assess motor performances of a population of newly diagnosed, drug free PD patients using wearable inertial sensors and to compare them to healthy controls (HC).

Methods: 30 PD patients and 30 HC were consecutively enrolled and evaluated by UPDRS II-III, H&Y, NMS and MMSE. Then they performed 5 motor tasks (rapid alternating hand movement – RAHM-, foot tapping -FT, heel-to-toe test -HTT-, timed- up-and-go test -TUG-, pull test -PT-) wearing Movit G1-system inertial sensors, to evaluate bradykinesia, gait and balance impairment. Several items from each task were analyzed with parametric and non-parametric test as needed.

Results: PD patients showed significant alterations in all motor tasks. For bradykinesia, the most significant task was RAHM ($p<0.001$), with a good correlation with UPDRS scores ($p=0.002$). In addition, our device was able to detect significant subclinical gait and balance alterations in TUG e PT ($p<0.001$).

Discussion: In our study we found several significant alterations in chosen TOMs to evaluate bradykinesia with respect to HC. In addition, the device proved to be more sensitive than clinical examination in revealing initial gait and postural impairments.

Conclusions: Being able to objectively detect parkinsonian features in an initial phase of the disease, when neurologic signs are milder, is crucial. TOMs could thus provide a reliable tool to support clinicians in diagnosis, identifications of patients with poorer prognosis and quantification of response to therapy. Further studies are needed to standardize these measures.

P82

Technology-based profiling of a population of newly diagnosed, drug free Parkinson's disease patients

Giulia Di Lazzaro[1], *M. Ricci*[2], *T. Schirinzi*[1], *M. Alwardat*[1], *A. Pallotti*[2], *F. Giannini*[2], *N.B. Mercuri*[1,3], *G. Saggio*[2], *A. Pisani*[1,3]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Department of Engineer, University of Rome Tor Vergata, Rome, Italy
[3]IRCCS Fondazione Santa Lucia, Rome, Italy

Introduction: Diagnosis of Parkinson's disease (PD) is still based on clinical evaluation and full diagnostic certainty is impossible during life. Increasing interest have been put on technology-based objective measures (TOMs) in terms of diagnosis and follow-up and to identify PD motor subtypes as early as possible, as they could have different prognosis and be though candidate to different therapeutic approaches.

Objective: To record and analyse motor performances alterations in a population of newly diagnosed, drug free PD patients using inertial sensors in order to detect characterizing motor features for a technology-based distinction between patients and healthy controls (HC) and, among patients, of different motor phenotypes.

Materials: 42 PD patients and 30 HC underwent motor performances evaluation with Movit G1 system. Tremor dominant (TD), Postural instability and gait disorder (PIGD) and mixed (MPD) phenotypes were then clinically identified among PD patients.

Methods: All subjects performed a protocol of motor tasks in order to assess agility, coordination, gait and postural stability, wearing inertial sensors. Several items from each task were analyzed. Data were analyzed with a classification analysis in order to try to discriminate between PD and HC groups. Then, only data from PD group were analyzed to discriminate different PD phenotypes.

Results: We identified two algorithms respectively to distinguish PD from HC and to identify different clinical phenotypes, both with excellent accuracy (95% and 92%).

Discussion: Our algorithm proved to be able to distinguish patients from HC with excellent accuracy, even in early phases of the disease. This could support clinical assessment of patients complaining of a movement disorder. In addition, we were also able to identify different PD phenotypes supporting the early identification of a population of patient with poorer prognosis.

Conclusions: TOMs can provide a reliable tool to support clinicians in diagnosis and identifications of patients with poorer prognosis.

P83

Validation of the Italian version of carers quality-of-life questionnaire for parkinsonism (PQoL Carer) in progressive supranuclear palsy

Marina Picillo[1], *S. Cuoco*[1], *M. Amboni*[1], *F.P. Bonifacio*[2], *B. Borroni*[3], *A. Bruno*[4], *F. Bruschi*[5], *I. Carotenuto*[1], *R. Ceravolo*[4], *R. De Micco*[2], *A. De Rosa*[6], *F. Di Blasio*[7], *A. Di Fonzo*[8], *F. Elifani*[9], *R. Erro*[1], *M. Fabbri*[10], *M. Falla*[11], *G. Franco*[8], *D. Frosini*[4], *S. Galantucci*[12], *G. Lazzeri*[8], *L. Lopiano*[10], *L. Magistrelli*[13,14], *M. Malaguti*[15], *N.B. Mercuri*[16], *A.V. Milner*[13], *B. Minafra*[5], *N. Modugno*[9], *A. Nicoletti*[17], *R. Marchese*[7], *E. Olivola*[9], *A. Padovani*[3], *A. Pilotto*[3], *C. Rascunà*[17], *M.C. Rizzetti*[18], *G. Santangelo*[19], *T. Schirinzi*[16], *A. Stefani*[16], *A. Tessitore*[2], *M.A. Volontè*[12], *R. Zangaglia*[5], *M. Zappia*[17], *P. Barone*[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Odontoiatry, University of Salerno, Salerno, Italy
[2]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[3]Centre for Neurodegenerative Disorders, Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[4]Dipartimento di Medicina Clinica e Sperimentale Università di Pisa, Pisa, Italy
[5]Parkinson's Disease and Movement Disorders Unit, C. Mondino National Neurological Institute, Pavia, Italy
[6]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[7]IRCCS Policlinico San Martino, Genova, Italy
[8]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[9]IRCCS Neuromed, Pozzilli, Italy
[10]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[11]Department of Neurology, General Hospital of Bolzano, Bolzano, Italy
[12]Dipartimento Neurologico, IRCCS Ospedale San Raffaele, Milan, Italy
[13]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[14]PhD Programm in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy
[15]UO Neurologia, Ospedale Santa Chiara, Azienda Provinciale per i Servizi Sanitari Provincia Autonoma di Trento, Trento, Italy
[16]UOSD Parkinson, University Hospital of Rome "Tor Vergata", Rome, Italy
[17]Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Catania, Italy
[18]S. Isidoro Hospital - FERB Onlus, Trescore Balneario, Italy
[19]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

Progressive Supranuclear Palsy (PSP) is a rare, rapidly progressive, neurodegenerative disease characterized by falls and supranuclear gaze palsy. Caring for a partner or relative who suffers from PSP entails a strenuous and demanding task, usually lasting for years, that affects carers' everyday life routines, emotional and social well-being. The 26-item Parkinsonism Carers QoL (PQoL Carer) is a self-administered, concise instrument evaluating quality of life of caregivers of patients with atypical parkinsonism (both PSP and Multiple System Atrophy) [1]. Here, the PQoL Carer was translated into Italian and validated in 162 carers of PSP patients [54.3% women; median age (interquartile range): 68 (22)] diagnosed according with Movement

Disorder Society criteria and recruited in 16 third level movement disorders centers participating in the Neurecanet project.

The mean PQoL total score was 40.66 ± 19.46. Almost one hundred percent of data were totally computable. The percentage of missing values was ≤ 5 % for all items. Neither ceiling nor floor effects were observed for the PQoL Carer. The internal consistency was satisfactory (Cronbach's alpha = 0.941); corrected item-total correlation was > 0.40 for all the items. A correlation with other health-related quality of life measures (EQ-5D, EQ-visual analogue scale) as well as with behavioral assessments (Hospital Anxiety Depression Scale) was shown suggesting adequate convergent validity. PQoL also correlated with patients' severity of disease as assessed with PSP rating scale. The discriminant validity of the scale was evidenced by its capacity to differentiate between carers with varying levels of self-reported health ($p < 0.001$). Analysis showed no significant impact of either gender or geographic location in Italy on PQoL Carer. In conclusion, the Italian version of the PQoL Carer is an easy, consistent and valid tool for assessment of quality of life in carers of PSP patients.

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P84

Re-emergent tremor in Parkinson's disease: the role of the motor cortex

Giorgio Leodori[1], *D. Belvisi*[1], *A. Fabbrini*[2], *M.I. De Bartolo*[2], M. Costanzo[2], *F.A.V. Undurraga*[3], *A. Conte*[1,2], *A. Berardelli*[1,2]

[1]IRCCS Neuromed, Pozzilli, Italy
[2]Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy
[3]Human Motor Control Section, NINDS, NIH, Bethesda, MD, USA

Introduction: Patients with Parkinson's disease (PD) may have tremor present at rest (rest tremor) that appears after a variable latency, while maintaining a posture (re-emergent tremor). Re-emergent tremor (RET) and rest tremor share similar clinical features, but it is unknown whether they also share pathophysiological mechanisms.

Objectives: Concurrent transcranial magnetic stimulation and electroencephalography (TMS–EEG) is a powerful tool to probe brain excitability by recording the TMS-evoked potentials (TEPs). We aimed to investigate pathophysiological mechanisms generating RET by measuring primary motor cortex (M1) excitability, during RET latency, by recording TEPs. We investigated the contribution of M1 to the generation of rest tremor and RET, by measuring the Cortico-muscular coherence (CMC).

Methods: We enrolled 10 PD patients with rest tremor and RET. TEPs generated by TMS delivered below motor threshold on M1 were recorded with a 32-channel EEG during RET latency. CMC between EMG signal recorded on the extensor digitorum communis and cortical activity recorded on C3/C4 was measured during resting tremor and RET.

Results: TMS induced TEPs characterized by the peaks P30, N45, P60 and N100. During posture, and before the reappearance of tremor (i.e. during RET latency), P60 progressively decreased in amplitude. Rest tremor and RET showed significant CMC in the tremor frequency band, with no significant differences between each other.

Conclusions: The observation that in PD patients with RET P60 size progressively decreases while the subjects maintain a posture suggests that RET is accompanied by changes of cortical excitability. In normal subjects, P60 has proved to be a marker of motor cortical excitability that can be modulated by proprioceptive afferent inputs (4-6). CMC results suggest that rest tremor and RET share common pathophysiological mechanisms in which M1 plays a role as a central oscillator. We therefore conclude that cortical mechanisms play a role in the pathophysiology of RET.

P85

Non-motor symptoms of Parkinson's Disease motor subtypes

Tommaso Ercoli, M.M. Mascia, A. Cannas, G. Defazio, P. Solla

Department of Medical Sciences and Public Health Institute of Neurology, University of Cagliari, AOU Cagliari, Cagliari, Italy

Objective: The aim of this observational study is to compare the prevalence of non-motor symptoms across widely recognized different motor subtypes of Parkinson's disease (PD), i.e. tremor-dominant type (TDT), akinetic-rigid type (ART), and a mixed type (MT).

Materials and Methods: Outpatients with PD were enrolled at the Movement Disorder Centre of the University of Cagliari. Age, sex, PD duration, Unified Parkinson's Disease Rating Scale III (UPDRS-III), Hoehn-Yahr (HY) staging and Non-Motor Symptoms Scale (NMSS) were collected from existing clinical records. According to Spiegel J. et al. [1] patients were classified in three different motor groups: TDT, ART, and MT.

Results: The study population included 179 patients meeting the eligibility criteria. There were 102 men and 77 women aged 68.5 years (SD, 9.4), PD duration was 6.1 years (SD, 3.9). Mean HY staging was 2.2 (SD, 0.7), mean UPDRS-III was 27.3 (SD, 15.2), and mean NMSS total score was 61.1 (SD, 47.2). Overall, 65 patients were classified into ART, 89 into MT, and 25 into TDT. On multivariable linear regression analysis, the TDT was characterized by lower motor severity as assessed by HY staging (beta coefficient=-0.27; 95% CI, -0.41 to -0.13; $p<0.0001$) whereas no significant relationship was observed between PD types and NMSS total score (beta coefficient=-0.001; 95% CI, -0.003 to 0.009; $p=0.28$). Nevertheless, including single items of NMSS in multivariable linear regression models yielded greater changes in the interest in sex (beta coefficient=-0.06; 95% CI, -0.013 to -0.11; $p=0.012$) and less olfactory and taste disturbance (beta coefficient=-0.03; 95% CI, -0.06 to -0.01; $p=0.004$) in TDT group.

Conclusions and discussion: Our analyses confirm that TDT patients have lower motor severity and lower frequency and severity of olfactory and taste disturbances [2]. The significant correlation we observe between TDT and a greater burden of altered interest in sex is a novel finding.

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P86

Benign senile Parkinson's disease: a new clinical phenotype?

Andrea Pilotto[1,2], *V. Dell'Era*[1], *A. Lupini*[1], *S. Gipponi*[1], *E. Cottini*[1], *A. Scalvini*[1], *A. Imarisio*[1], *R. Turrone*[1], *B. Borroni*[1], *M.C. Rizzetti*[2], *A. Padovani*[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Parkinson's Disease Rehabilitation Centre, FERB ONLUS – S. Isidoro Hospital, Trescore Balneario, Italy

Introduction: In the aging population the incidence of late-onset Parkinson's disease is expected to increase in the next future. No study evaluated the clinical presentation, response to treatment and clinical course of late onset octogerian PD (PD-L) compared to classical disease with middle-age onset (PD-M).

Methods: We retrospectively analyzed patients with a clinical PD diagnosis with symptoms onset at the age of 80 years or older. All patients underwent CT/MRI, neurological and neuropsychological assessment, with a clinical follow-up for 2-4 years. By using a case-control design, we assigned each PD-L two patients with age at onset between 55 and 69 (PD-M), matched for sex and disease duration at first visit.

Results: 31 PD-L were identified (mean age at first presentation 85.3 ± 3.4 years) and matched with 62 PD-M (mean age 70.6±5.6). Baseline UPDRS-III was significantly higher ($p=0.01$) in PD-L vs PD-M (20.2±9.5 vs 15.2±7.9). PD-L presented with tremor (85%) and a significantly higher prevalence of early postural instability compared to PD-M ($p=0.02$). PD-M showed higher prevalence of non-motor symptoms namely REM sleep behavioral disorders, constipation and hyposmia compared to PD-L ($p<0.05$). At two years of FU, PD-L showed similar UPDRS-III progression and L-dopa response to classical PD-M. At 4 years, PD-L showed slightly improvement in UPDRS-III compared to PD-M ($p=0.07$) in presence of similar levodopa equivalent dose.

Conclusions and discussion: PD-L is a relative rare condition in movement disorder outpatient clinic and appeared to presents with tremor, postural instability and less non-motor symptoms compared to classical PD. The follow-up suggest a benignant octogerian phenotype potentially underlying a selective isolate nigrostriatal impairment in PD-L compared to classical PD-M.

P87

Retinal thickness and microvascular pattern in early Parkinson's disease

Cristina Rascunà[1], *C. Terravecchia*[1], *A. Russo*[2], *G. Mostile*[1], *C.E. Cicero*[1], *A. Luca*[1], *N. Castellino*[2], *S. Tripodi*[2], *A. Longo*[2], *T. Avitabile*[2], *M. Reibaldi*[2], *M. Zappia*[1], *A. Nicoletti*[1]

[1]Section of Neurosciences, Department "G.F. Ingrassia", University of Catania, Catania, Italy
[2]Department of Ophthalmology, University of Catania, Catania, Italy

Introduction: Physiologically, retinal dopaminergic neurons modulates colour vision and contrast sensitivity. Retinal dopaminergic depletion has been observed in Parkinson's disease (PD), possibly explaining some of the associated visual symptoms. Spectral-domain optical coherence tomography (SD-OCT) studies demonstrated thickness reduction of the inner retinal layer in PD patients, notably in the nerve fiber layer (RNFL)[1]. However, few studies have focused on possible correlation between RNLF thickness and retinal microvascular angiographic pattern [2].

Objective: To detect changes in retinal thickness and their possible correlates with microvascular pattern in early PD patients as compared to controls.

Methods: Patients fulfilling UK-Brain-Bank criteria for PD were recruited. Healthy subjects were also enrolled as controls. Exclusion criteria were glaucoma, concurrent retinal disease, ocular trauma, cataract, high intraocular pression, systemic disease impairing visual system (diabetes, uncontrolled hypertension/hypotension, cardiovascular diseases) and other neurological diseases. Retinal microvascular pattern was analysed using coherence tomography angiography (OCT-A) and segmentation analysis of retinal layers using SD-OCT. Retinal microvasculature was automatically divided into superficial and deep capillary plexus (SCP and DCP) to be analysed.

Results: N=21 eyes from PD patients (63,33±6,78 years) and N=16 eyes from healthy controls (57,25±6.87 years) were evaluated. Considering age difference between-group, statistical inference has been performed using age as covariate. PD patients showed significant lower microvascular density in each macular DCP zones, compared to controls. Thickness of RNFL resulted significantly lower in PD patients as compared to control (p=0.05). In PD patients, there was a positive correlation between RNFL thickness and both superficial and deep foveal microvascular density (respectively, r=0.67, p=0.006; r=0.65, p=0.008).

Conclusions: Retinal microvascular impairment and thinner RNFL were found in PD patients with respect to controls. The correlation we found between foveal microvascular density and intraretinal layers thickness in our PD study patients could partially explained visual symptoms described since the early stage of disease.

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P88

Parkinson's patients at Hoehn and Yahr stage 1 show deficits in reactive but not proactive inhibitory control

V. Di Caprio[1], *Nicola Modugno*[1], *C. Mancini*[2], *E. Olivola*[1], *G. Mirabella*[1,2]

[1]IRCCS Neuromed, Pozzilli, Italy
[2]Department of Anatomy, Histology, Forensic Medicine & Orthopedics, Sapienza University, Rome, Italy

Introduction: It is well known that Parkinson's patients suffer from a deficit in inhibitory control [1,2], however this is not a unitary construct and it is unclear whether Parkinson's patients at early stage of the disease (Hoehn and Yahr stage 1, HY1) exhibit a deficit in outright stopping (reactive inhibition), a deficit in the ability to shape their motor strategy in anticipation of known task demands (proactive inhibition), or both. In addition, as it has been suggested that inhibition relies upon a right-lateralized pathway, we tested whether left-dominant Parkinson's disease (LPD) patients suffered from a more severe deficit in this key executive function than right-dominant PD patients (RPD).

Objective: We wanted to assess whether i) PD patients at HY1 show a global or a selective impairment in inhibitory control; and whether ii) LPD patients have a greater deficit in inhibiting a pending action than RPD.

Methods: Via a reaching stop signal task [1,3,4,5], we assessed both proactive and reactive inhibition in 15 LPD, 15 RPD patients, and in 23 healthy subjects.

Results: We found that reactive inhibition was more impaired in PD patients than in healthy subjects. However, proactive inhibition [4,5] was not affected. Furthermore, we did found no differences between LPD and RPD patients. Importantly, we confirmed these negative findings using not only inferential statistics, but also the Bayesian statistic [6].

Conclusions: For the very first time, we found evidence for a deficit of reactive inhibition in the earliest stages of PD in the absence of evidence for deficits in proactive inhibition. These findings have clinical relevance as they provide key insights on the time-course of the disease. In addition, we confirmed on a different population of PD patients our previous results [4,5] showing that the onset of the disease does not affect inhibition.

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P89

Detection of freezing of gait in people with Parkinson's disease using smartphones

Gabriele Imbalzano[1], *L. Borzì*[2], *C.A. Artusi*[1], *A. Romagnolo*[1], *M. Fabbri*[1], *M.G. Rizzone*[1], *M. Zibetti*[1], *S. Sibile*[2], *M. Varrecchia*[2], *G. Olmo*[2], *L. Lopiano*[1]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Turin, Italy
[2]Department of Control and Computing Engineering, Politecnico di Torino, Turin, Italy

Introduction: Freezing of gait (FOG) is a frequent symptom in Parkinson's disease (PD) patients, associated with increased risk of falls, reduced functional independence and lower quality of life. To date, the FOG assessment is mainly based on poorly reliable self-reports of patients, and clinical examination often fails to objectify and quantify the FOG severity.

Objective: We sought to define a FOG detection algorithm to provide accurate information on presence and duration of FOG episodes by means of a waist-mounted smartphone.

Methods: Data acquisition was carried on 38 unselected PD patients (daily ON) and 21 controls subjects executing a 6-minute walking test. Data collected from inertial sensors embedded in commercial smartphone were analyzed and a combination of two Support Vector Machine classifiers was used for the identification of FOG events, and for distinction from walking, turning, and volitional standing.

Results: More than 3.5 hours of acceleration data were collected. The algorithm yielded a sensitivity of 81.2%, specificity of 98.7%, precision of 88.7% and accuracy of 96.9%. The Receiver Operating Characteristic curve showed an Area Under the Curve of 97.96.

Conclusions: The great accuracy and specificity in detecting FOG, along with the very efficient processing times, make the algorithm a promising tool for reliable FOG assessment during activities of daily living.

P90

Shedding light on the relationship between dyskinesia and impulsive compulsive behaviour disorders in Parkinson's disease

Diana Goeta[1], *A. De Angelis*[2], *C. Siri*[3], *M. Horne*[4,5], *A. Leake*[2], *D. Paviour*[2], *M. Edwards*[2], *F. Morgante*[2], *L. Ricciardi*[2]

[1]Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan, Italy
[2]Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St. George's University of London, London, UK
[3]Parkinson Institute, ASST G. Pini-CTO, ex ICP, Milan, Italy
[4]Centre for Clinical Neurosciences and Neurological Research, St Vincent's Hospital, Melbourne, Australia
[5]Florey Institute for Neuroscience and Mental Health, University of Melbourne, Parkville, VIC Australia

Introduction: Impulsive compulsive behaviour disorders (ICB) and dyskinesia are common and disabling complications occurring during the course of Parkinson's disease (PD). Their pathophysiology is not clear yet, however an association has been suggested.

Objectives: To evaluate the relationship between the presence of dyskinesia objectively detected using a wearable device and the presence of active and past ICB in PD patients.

Methods: Patients' demographic and clinical characteristics were gathered, PD medications were converted in total levodopa equivalent daily dose (LEDD) and LEDD dopamine-agonists. Patients were assessed with: Unified PD Rating Scale (UPDRS) parts I-IV and Rusk Dyskinesia Rating Scale (RDRS). To objectively measure dyskinesia we used a wearable devise, the Parkinson's KinetiGraph™ system (PKG®), an accelerometry-based system for automated assessment of dyskinesia and bradykinesia. Past and active ICB were diagnosed with a semi-structured interview. Questionnaire for Impulsive-Compulsive Disorders in PD-Rating Scale (QUIP-RS) was employed to rate ICB severity. Psychiatric symptoms were evaluated including depression, anxiety, apathy and impulsivity.

Results: Fifty-five PD patients were evaluated (36 males, mean age 60.7±6.7; mean disease duration 10.5±4.9). Twenty-five patients (45%) had dyskinesia as per PKG 'Percent Time in Dyskinesia' score. Nineteen patients had ICB (34%). There was no difference in active/past ICB between patients with and without dyskinesia (p=0.8 and 0.6). Patients with dyskinesia had higher LEDD dopamine-agonists (p=0.005), UPDRS-IV (p=0.02), RDRS (p=0.002). There was no difference between groups in psychiatric symptoms. We categorized patients in 3 groups (none, mild/moderate and severe dyskinesia) and we found no difference among groups in any demographic, clinical, psychiatric and behavioural variable except for LEDD dopamine-agonists (p=0.004), UPDRS-IV (p=0.06), RDRS (p=0.004). Binary regression analysis did not show any association between the presence of dyskinesia and ICB, depression, anxiety, apathy and impulsivity.

Conclusions: Our data suggest that ICB and dyskinesia are common but unrelated disorders in PD.

P91

Parkinson's disease and microbiota in a selected population from center Italy

R. Cerroni[1], *Matteo Conti*[1], *M. Pierantozzi*[1], *N.B. Mercuri*[1], *A. Stefani*[1], *D. Pietrucci*[2], *V. Unida*[2], *S. Biocca*[2], *A. Desideri*[2]

[1]Parkinson Centre, Department of System Medicine, University of Rome "Tor Vergata", Rome, Italy
[2]Department of Biology, University of Rome "Tor Vergata", Rome, Italy

Introduction: In last years, alterations of gut microbiota in Parkinson's Disease (PD) has been corroborated with robust evidence. However, in PD far from established is a specific microbiota fingerprint, to what extent it correlates with clinical features and the role of confounders (such as medication regimen).

Objectives: The aim of our study was to investigate PD dysbiosis of gut microbiome in a well selected population of PD patients from centre Italy, carefully examining the weight of confounders, and to identify potential correlation with clinical features and therapy.

Methods: 150 faecal samples were collected from 79 PD patients, enrolled by tight inclusion criteria, in order to avoid the inclusion of uncertain/mixed diagnosis, and 71 healthy controls, represented almost exclusively by cohabitants. Microbiota compositions was studied through 16rRNA amplicon sequencing and classified to taxonomic rank through a bioinformatic analysis. For identifying differential abundant species between controls and patients, statistical analysis was performed considering the effect of potential confounders.

Results: The analysis on dietary/life habits allowed to recognize as confounding factors weight loss, age, iCOMT. Lactobacillaceae, Enterobacteriaceae, Peprostreptococcaceae and Verrucomicrobiaceae families were significantly higher in faeces of PD patients compared to controls, while Lachnospiraceae and Erysipelotrichaceae were significantly reduced in PD patients. Predictive metagenomics indicated that different genes involved in metabolism and signalling (SCFA and aromatics amino acids) were significantly lower in the PD faecal microbiome, whereas genes involved in lipopolysaccharide biosynthesis and type III bacterial secretion systems were significantly higher.

Conclusions: Our PD population features a specific microbiota picture versus controls. Moreover, functional predictions suggest changes in different metabolic pathways capable to favour a pro-inflammatory environment associated with a reduction in physiological transmitters.

P92

Gut microbiome signatures influenced by clinical phenotypes and drugs in Parkinson's disease

Marta Melis[1], *S. Vascellari*[2], *V. Palmas*[2], *V. Oppo*[1], *M. Sarchioto*[1], *A. Manzin*[2], *G. Cossu*[1]

[1]SC di Neurofisiologia, "A.O.G. Brotzu", Cagliari, Italy
[2]Dipartimento di Scienze Biomediche, Sezione di Microbiologia e Virologia, Università degli Studi di Cagliari, Cagliari, Italy

Background: Previous studies of the dysbiosis of gut microbiota could explain several features of PD. They also suggest a modulating role on microbiome composition of some antiparkinsonian drugs.

Objective: The aim of this work was to study the microbiome of PD patients, looking for any difference between the different phenotypes. We also studied the effect of dopaminergic drugs mainly focusing on the effect of Levodopa (LD) directly injected to the bowel, Levodopa Carbidopa Intrajejunal Gel (LCIG).

Methods: The composition of the microbiota in fecal extracts of 80 PD patients and 51 controls was determined. Patients were divided in tremor-dominant (TD) group and non-TD phenotype and they were also divided in two different treatment groups: Group 1, PD patients on oral LD treatment; Group 2 PD patients under LCIG treatment. Microbiota was studied by 16S rRNA next-generation gene sequencing of DNA extracted from stool.

Results: In our study, the relative abundances of some bacteria showed significant differences: Firmicutes, Proteobacteria, Actinobacteria and Cyanobacteria were less abbundant in PD than in controls. The multivariate analysis considering potential confounders (other medications, diet, gastrointestinal symptoms, constipation and demographics) showed that Brevibacteriaceae, Clostridiaceae and Lachnospiraceae were positively associated with TD phenotype whereas Enterobacteriaceae and Escherichia with non-TD phenotypes. Moreover, Proteobacteria phylum and specific genus from Enterobacteriaceae family (Enterobacter, Escherichia, Serratia and Klebsiella) were specifically more abundant in LCIG Group.

Conclusions: Our study confirms the altered abundance of several bacteria taxa in agreement with previous results, while it suggests for the first time a role for Cyanobacteria in PD. We also identified that the relative abundance of some putative anti-inflammatory bacteria might be influenced by different PD phenotypes. Finally, we suggest a specific independent effect of LCIG in modifying the microbiome composition proposing an association of putative pathobionts bacteria, such as Enterobacteriaceae.

P93

Investigation into the causes of reduced caffeine levels in Parkinson's disease

Maria Ilenia De Bartolo[1], *G. Leodori*[2], *A. Fabbrini*[1], *M. Costanzo*[1], *D. Belvisi*[2], *A. Conte*[1,2], *S. Manetto*[3], *A. Ciogli*[3], *C. Villani*[3], *A. Berardelli*[1,2], *G. Fabbrini*[1,2]

[1]Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed, Pozzilli, Italy
[3]Department of Chemistry and Technologies of Drug, Sapienza University of Rome, Rome, Italy

Introduction: Caffeine has a protective role in Parkinson's disease (PD) [1,2]. One study showed decreased caffeine blood levels in PD patients compared to healthy subjects (HS) [3], even when controlled for caffeine assumption and CYP1A2 genotype, the enzyme responsible for 95% of caffeine metabolism [4]. Beside genetic polimorfisms, CYP1A2 functioning (i.e. phenotype) is influenced by exogenous and endogenous factors [5]. Caffeine levels can be accurately quantified in saliva [6].

Objective: To investigate whether PD patients show decreased salivary caffeine levels. To investigate CYP1A2-phenotype as a possible cause of decreased caffeine levels in PD. To test whether PD patients show decreased caffeine absorption.

Methods: We enrolled 26 early (64.1±8.2) and 16 moderate/advanced (age: 68.9±8.3) PD patients, and 26 HS (age: 59.7±6.3). Daily caffeine intake was recorded. Caffeine and its major metabolite paraxanthine were measured by high-performance liquid chromatography in saliva samples collected before (T0) and 4 hours after (T1) oral intake of 100mg caffeine. CYP1A2-phenotype was calculated as the paraxanthine/caffeine ratio at T1[7]. Caffeine absorption was calculated as the T1 minus T0 difference in caffeine levels.

Results: Although daily caffeine intake was similar in PD patients and HS, moderate/advanced PD patients showed lower caffeine salivary levels at T0. PD patients and HS showed similar CYP1A2-phenotype. PD patients showed lower values of caffeine absorption when compared to HS, but this difference reached statistical significance only for early patients. Participants' age did not correlate with caffeine level, CYP1A2- phenotype or absorption.

Conclusions: Baseline salivary levels of caffeine were decreased in patients with moderate/advanced PD regardless of caffeine intake. Caffeine metabolism was not different between PD patients and HS. PD patients showed decreased caffeine absorption especially in the early stage of the disease. Our results suggest that abnormal caffeine absorption may be a possible mechanism contributing to PD pathogenesis that requires further investigation.

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P94

Psychometric properties of the italian version of Barthel Index in patients with Parkinson's disease: a reliability and validity study

M. Tofani[1], *G. Fabbrini*[2,5], *P. Massai*[3], *A. Berardi*[3], *E. Pelosin*[4,7], *D. Valente*[2], *Giovanni Galeoto*[6]

[1]Neurorehabilitation Unit, Department of Neurosciences and Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy
[2]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[3]Sapienza University of Rome, Italy
[4]Ospedale Policlinico San Martino, IRCCS, Genoa, Italy
[5]IRCCS Neuromed, Pozzili, Italy
[6]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
[7]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health Unit, University of Genoa, Italy

Objective: To validate the Italian version of the Barthel Index (BI) in a Parkinson's Disease (PD) population.

Methods: The BI was administered to a sample of people with PD. Reliability was assessed using Cronbach's alpha for internal consistency and the intraclass correlation coefficient (ICC) for intra and inter-rater reliability. Pearson's correlation coefficient was calculated for validity with the Parkinson's disease Questionnaire (PDQ-39), the Italian version of Geriatric Depression Scale (GDS), the Hospital Anxiety and Depression Scale (HADS) and the Short Form 36-Health Survey Questionnaire (SF- 36).

Results: The BI was administered to 94 individuals. All psychometric properties were significant: Cronbach's alpha was 0.866 and the ICC for intra and inter-rater reliability was 0.998 and 0.993, respectively. Pearson's correlation coefficient showed good correlation with PDQ-39, GDS, HADS and SF-36 ($p<0.01$).

Conclusions: The BI is a valid and reliable tool for measuring disability in PD population. The finding of the study also produce useful information for clinical practice to guide health professionals for rehabilitation recovery of people with PD.

P95

The clinical correlates of suicidal ideation in Parkinson's disease

Matteo Costanzo[1], *D. Belvisi*[2], *I. Berardelli*[3], *G. Ferrazzano*[2], *V. Corigliano*[3], *G. Fabbrini*[1,2], *M. Pompili*[3], *A. Berardelli*[1,2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCSS Neuromed, Pozzilli, Italy
[3]Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy

Introduction: Previous studies showed that suicidal ideation is increased in Parkinson's disease (PD) patients. The possible relationship between parkinsonian motor and non-motor symptoms and suicidal ideation in PD is unknown.

Objective: The aim of the study was to evaluate suicidal ideation in patients with PD in a controlled study specifically designed to identify the clinical correlates of PD suicidal ideation.

Methods: We consecutively enrolled 100 patients with PD and 80 healthy subjects. Motor symptoms and complications were evaluated by using the Movement Disorder Society- Unified Parkinson's Disease Rating Scale. PD patients were classified in tremor-dominant-PD and non-tremor-PD. Non-motor symptoms were evaluated by means of the Non-Motor Symptoms assessment scale for PD. All patients also underwent a psychiatric evaluation that included the administration of the Columbia Suicide Severity Rating Scale.

Results: Suicidal ideation was present in 31% of PD patients and 2% of healthy controls. PD patients showing suicidal ideation have more frequent motor complications, more severe non-motor symptoms and a higher perceived disability than patients without suicidal ideation. Fifty-two of PD patients with suicidal ideation were tremor-dominant while 48% were non-tremor patients. Suicidal ideation correlated with the presence of motor complications as well as with non-motor symptom severity, perceived disability severity and the presence of psychiatric disorders.

Conclusions: Our findings showed that suicidal ideation is increased in PD patients compared with healthy controls and that several clinical PD features, including motor complications and non-motor symptoms, are associated with suicidal ideation in PD. The results suggest a multi-factorial origin of PD suicidal ideation.

P96

Modified berg balance scale: Italian validation in a population with Parkinson disease

Marco Tofani[1], *G. Galeoto*[2], *A. Berardi*[3], *G. Fabbrini*[4,5]

[1]Neurorehabilitation Unit, Department of Neurosciences and Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy
[2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
[3]Sapienza University of Rome, Rome, Italy
[4]Department of Human Neurosciences Sapienza University of Rome, Rome, Italy
[5]IRCCS Neuromed Pozzilli, Italy

Introduction: The BBS is an objective measure of balance abilities. In 2012 a Rasch Analysis Study was carried out with the aim of verifying validity and reliability of the BBS in a sample of patients with different etiologies in neurorehabilitation, re-defining the questionnaire in the Italian population from 14 to 12 items. The study supported properties of the 12-items BBS (BBS-12) as a measurement tool independent of the etiology of the neurologic disease causing the balance impairment.

Objective: Considering that in the sample of the BBS12 validation there were no people with extrapyramidal diseases, but the use of the BBS-12 is propagating in clinical practice also for people with PD, the primary objective of this study is to evaluate validity and reliability of the BBS-12 in a PD population.

Methods: Reliability was investigated using intraclass correlation coefficient (ICC). Pearson correlation coefficient was used to explore its validity with the PASE and Tinetti Scales.

Results: The BBS-12 was administered to 50 people. The internal consistency showed an α coefficient of 0.886. Item-total correlation analysis reveled statistically significant values (0.872-0.889). The reliability study showed an ICC 0.986 and 0.987 for intra and inter-rater reliability, respectively. The Pearson's correlation coefficient analysis showed good linear correlation with the Tinetti and with the Sport and Home subscales of the PASE-I ($p<0.01$).

Conclusions: The BBS-12 is a valid and reliable tool for measuring balance in PD population. In any case, it would be useful to check differences between the scales and determine their actual usefulness inclinical practice.

P97

Pain in Parkinson's disease with motor fluctuations: an observational, prospective, clinical and neurophysiological study in patients under L-dopa add on therapies

Christian Geroin, S. Ottaviani, G.M. Squintani, A. Segatti, T. Bovi, M. Tinazzi

Dipartimento di Neuroscienze, Biomedicina e Movimento, Università di Verona, Verona, Italy

Background: Pain is a frequent non-motor symptom of Parkinson's disease (PD) especially in the intermediate phase of disease and has a significant negative impact on the patient's quality of life.

Objective: To investigate possible changes of pain and laser evoked potentials (LEPs) in PD patients with pain treated with anti PD drugs as add-on therapy to L-dopa.

Patients and Methods: We recruited PD patients with chronic pain symptoms and motor fluctuations while receiving L-dopa alone or with other dopaminergic treatments who underwent add-on drugs therapy (safinamide metansolfonato 100 mg/day, or rasagilina mesilato, 1mg/day) based on their clinical needs in terms of motor fluctuations. Clinical (UPDRS total, III and IV, King's Pain Scale, Brief Pain Inventory: BPI, NRS, PDQ-39, Clinical global impression: CGI score) and LEPs data were collected at baseline and at 12 weeks and only comparisons within each group over time were performed.

Results: A total of 20 PD patients have been enrolled for the study: 11 were treated with Safinamide metansolfonato 100 mg/day (Group 1) and 9 with rasagilina mesilato (Group 2).

Group I PD patients showed a statistically significant improvement of total UPDRS, UPDRS III and IV scores after 12 weeks as well as a statistically significant reduction of pain as shown by a reduction of King's pain scale, NRS, and BPI score. CGI and PDQ-39 scores also significantly improved. Likewise, Group II PD patients showed an improvement of motor impairment (total UPDRS, UPDRS III and IV), pain (King's pain scale, BPI, NRS) and quality of life (PDQ-39 and CGI), although this improvement was less marked that in Group 1. No correlation was found between reduction of pain and improvement of motor symptoms. In both groups, LEPs recorded after 12 weeks were not significant different in terms of amplitude from those recorded at baseline.

Conclusions: These preliminary results suggest that safinamide is effective in reducing pain in PD and this effect appears not related to the concomitant motor improvement.

P98

Subjective disperception of speech disorders in different stages of Parkinson's disease

Donato Melchionda[1], *D. Perfetto*[2], *R. Goffredo*[1], *C. Avolio*[1]

[1]S.C. Neurologia Universitaria, Azienda Ospedaliero-Universitaria di Foggia, Foggia, Italy
[2]Azienda Sanitaria Regionale Molise (ASReM), Campobasso, Italy

Introduction: Parkinson's Disease (PD) is a common neurodegenerative disease. Speech disorders are specific motor symptoms in PD. For the clinical evaluation of speech disorders objective and self- assessment tests are required.

Objectives: To study the subjective alterations of speech disorders in patients with PD in order to detect early deficits and to evaluate their impact on the quality of life.

Methods: We studied 5 men and 5 women, age from 52 to 78 years, affected by Idiopathic Parkinson's Disease with duration of illness between 4 and 10 years. For the clinical evaluations we used the UPDRS-III scale. For subjective evaluation of speech disturbances we used a self-assessment survey, according to Therapy Outcomes Measures Scale.

Results: We found deficits in self-evaluation test, indicative of an alteration in the perception of linguistic deficits. The alteration of sensory feedback was 20% in language, 25% in the verbal fluency and 32.5% in vocal quality. The correlation between duration of the disease and alteration of sensory feedback in the three areas explored was about 20-25%.

Conclusions: We found the presence of speech alterations in PD patients after subjective evaluations. Self assessment tests can give us informations about the quality of life of PD patients with speech disorders. An early logopedic assessment is recommended to start an intensive logopedic treatment.

P99

Cardiovascular autonomic function and MCI in Parkinson's disease

Calogero Edoardo Cicero[1], *L. Raciti*[1], *R. Monastero*[2], *G. Mostile*[1], *G. Sciacca*[1], *A. Luca*[1], *C. Terravecchia*[1], *L. Giuliano*[1], *R. Baschi*[2], *M. Davì*[2], *M. Zappia*[1], *A. Nicoletti*[1]

[1]Department "G.F. Ingrassia", Neuroscience Section, University of Catania, Catania, Italy
[2]Department of Biomedicine, Neuroscience and Advanced Diagnostic, University of Palermo, Palermo, Italy

Background: Orthostatic hypotension could have a role in cognitive impairment associated with Parkinson's Disease (PD).

Objective: To evaluate the association between cardiovascular dysautonomia and Mild Cognitive Impairment (MCI) in PD patients.

Methods: Non-demented PD patients belonging to the PaCoS cohort, a large multicenter study on PD and cognition. All subjects underwent a comprehensive instrumental neurovegetative assessment including the study of both parasympathetic and sympathetic function (30:15 ratio, Expiratory-Inspiratory ratio [E-I] and presence of Orthostatic Hypotension [OH]).

Results: We enrolled 185 PD patients aged 64.6 ± 9.7 years; 102 (55.1%) were men. MCI was diagnosed in 79 (42.7%) patients. Presence of MCI was associated with an altered 30:15 ratio (adjOR 2.83; 95%CI 1.25-6.40; p=0.01) but not with an altered E-I ratio or the presence of OH.

Conclusions: An alteration of the parasympathetic function may represent an intermediate step in patients with PD-MCI before the development of OH and dementia.

P100

Influence of peripheral immune system on cognitive profile in Parkinson's disease

Luca Magistrelli[1,2], *E. Storelli*[3], *A.V. Milner*[1], *E. Rasini*[3], *F. Marino*[3], *M. Cosentino*[3], *C. Comi*[1]

[1]Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[2]PhD Programme in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy
[3]Centre of Research in Medical Pharmacology, University of Insubria, Varese, Italy

Background: Dementia is frequent in advanced Parkinson's disease (PD), while mild cognitive deficits may be present even in early to intermediate disease stages. Peripheral immunity plays a role in neurodegeneration but its influence on the development of cognitive decline in PD is still unknown.

Objective: To investigate the influence of the peripheral immune profile in the development of cognitive impairment in PD.

Methods: Fifty PD patients (30 males; mean age at onset 68.9±8.3; mean disease duration 4.6±3.5.) were recruited. All patients underwent a cognitive evaluation with MMSE and Addenbrooke's cognitive examination (ACE-R). Mean MMSE score was 26.7±2.0; mean ACE-R was 85.6±8.7. The complete peripheral immune phenotype (CD4+lymphocytes sub-populations Th1 and Th2) was examined with flow cytometry and data were retrospectively taken from a previously created database.

Results: Patients were divided in 3 groups depending on the ACE-R score (group 1: ≥90; group 2:89-80; group 3:<80). We found that age at onset was significantly higher in patients with higher compared to lower ACE-R scores. Conversely, disease duration was similar among the 3 groups. Total number (x106/L) of Th1 lymphocytes increased (group 1:96.8±79.2; group 2:101.9±52.2; group 3:107.9±59.1) and Th2 decreased (group 1:65±53.5; group 2:62.78±63; group 3:49.6±20.9) progressively from group 1 to group 3.

Conclusions: Higher age at onset is the main risk factor for dementia in PD. Patients with a worse ACE-R score showed a predominantly pro-inflammatory peripheral immune phenotype. Immune system may indeed represent a contributing factor in the development of dementia in PD.

P101

Neural bases of Impulse Control Disorders in Parkinson's disease: a systematic review and an ALE meta-analysis

S. Raimo[1,2,3], *M. Cropano*[1], *C. Vitale*[4], *P. Barone*[5], *L. Trojano*[1,6], *Gabriella Santangelo*[1]

[1]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Department of Medical and Surgical Sciences, University of "Magna Graecia", Catanzaro, Italy
[3]Neuropsychology Unit, I.R.C.C.S. Fondazione Santa Lucia of Rome, Rome, Italy
[4]Department of Motor Sciences and Wellness, University "Parthenope", Naples, Italy
[5]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[6]Salvatore Maugeri Foundation, Scientific Institute of Telese, Telese Terme, Italy

Introduction: Impulse control disorders (ICDs) occur in some patients affected by Parkinson's disease (PD). Previous studies revealed an involvement of basal ganglia in ICD but recent morphological, molecular and functional imaging studies have shown that alterations of some extrastriatal regions contribute to development of ICD in PD, with mixed results.

Methods: To integrate findings from the literature and identify brain regions underlying ICDs in PD, an ALE meta-analysis and a systematic label-based review of morphometric and functional studies were performed.

Results: ALE meta-analysis on 14 whole brain activity studies revealed a cluster of hypoactivation associated with ICD in Anterior Cingulate Cortex (ACC) and a cluster of hyperactivation in ventral striatum. The label-based review of functional studies divided according to neuroimaging techniques (i.e., PET, SPECT-fMRI) confirmed significant functional changes in PD patients with ICDs: in particular, an increased functional activity in the Ventral Striatum and OrbitoFrontal Cortex and a decreased functional activity in ACC was found. The label-based review on 12 structural studies revealed no significant changes in any cortical and subcortical region in patients with ICDs.

Conclusions: The present results confirm that ICD in PD is related to a dysfunctioning of limbic divisions of the striatum and of prefrontal cortex and provide a neurofunctional basis for devising potential therapeutic interventions.

P102

Mild cognitive impairment in Parkinson's disease: a systematic review and meta-analysis

Chiara Baiano[1], *P. Barone*[2], *G. Santangelo*[1]

[1]Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Center for Neurodegenerative Disease-CEMAND, University of Salerno, Salerno, Italy

Introduction: Mild cognitive impairment (MCI) is characterized by a subjective or objective cognitive decline with a minimal impairment in daily functioning. MCI in Parkinson's disease (PD-MCI) has been suggested to be a predictor for the development of PD dementia. Despite the importance of early identification of PD-MCI, its prevalence and association with demographic, clinical and behavioral features are still debated.

Objectives: This meta-analysis aims to: i. provide a robust estimate of prevalence rate of PD-MCI; ii. explore the differences between patients with and without PD-MCI in demographic, clinical and behavioral features.

Methods: The meta-analysis included 55 primary studies, which met the following criteria: (1) peer-reviewed journals in English; (2) publication dates from 2004 up to January 2019; (3) presence of statistical results about comparison on demographic, clinical, cognitive and behavioural measures between patients with and without PD-MCI; (4) assessment of MCI through specific diagnostic criteria. The effect sizes from data reported in the primary studies were computed using Hedges'g unbiased approach. Heterogeneity among the studies was assessed using Q and I2 statistics index. We conducted meta-regressions to explore the possible influence of demographic and clinical variables on each outcome.

Results: The meta-analysis showed a prevalence of MCI of 41% (n= 9515; 95% CI 37- 46%) in PD. The type of diagnostic criteria (before versus after Litvan et al.'s criteria), demographic features, disease severity and presence of major depression did not influence prevalence estimates. PD-MCI patients had higher levels of apathy (Hedges' g= 0.37), depression (Hedges' g= 0.29), poorer quality of life (Hedges' g= -0.33) and functional autonomy (Hedges' g= -0.26) compared to patients without PD-MCI.

Conclusions: The present meta-analysis provided a solid estimate of PD-MCI prevalence in PD of 41%; moreover the results of a significant association between PD-MCI and higher levels of neuropsychiatric symptoms, more reduced quality of life and functional autonomy highlighted the importance of assessing PD-MCI.

P103

Cortical atrophy and electrocortical networks of electroencephalographic signal in parkinson's disease patients with mild cognitive impairment. The PaCoS study

Giulia Donzuso[1], *L. Giuliano*[1], *R. Monastero*[2], *R. Baschi*[2], *G. Mostile*[1], *A. Luca*[1], *C.E. Cicero*[1], *M. Zappia*[1], *A. Nicoletti*[1]

[1]Department "G.F. Ingrassia", Section Neuroscience, University of Catania, Catania, Italy
[2]Department of Experimental Biomedicine and Clinical Neurosciences, University of Palermo, Palermo, Italy

Mild cognitive impairment (MCI) is common in Parkinson's disease (PD), but the potential underlying pathological mechanism has not been fully understood. Structural neuroimaging and electrocortical studies showed the presence of atrophy and abnormal electrocortical activity in PD with cognitive decline, respectively. VBM and quantitative EEG (qEEG) analysis of electrocortical activity could be used to identify in vivo neuropathological and electrocortical markers linked to the development of MCI in PD patients. From the PaCoS (Parkinson's disease Cognitive impairment Study) cohort, a sample of PD patients with and without MCI were recruited, including those patients with one EEG recording and a T1-3D MRI data, acquired at the same time. VBM analysis was performed and EEG signal epochs were analysed using Independent Component Analysis LORETA. Fifty-eight PD patients were enrolled (mean age 65.8 ± 8.2 years, mean UPDRS-ME 28.0 ± 11.3, disease duration 2.2 ± 2.4 years), including 35 patients with normal cognition (PD-NC) and 23 PD with MCI. PD-MCI showed reduction in grey matter density in a para hippocampal areas, left temporal lobe, left cerebellum, precuneus, cingulate gyrus and right inferior parietal lobule. LORETA analysis revealed decreased network involving alpha activity over the occipital lobe, associated with an increase over the frontal lobe and an increased network involving theta activity over the occipital lobe associated with reduction over the frontal lobe. The parietal lobe showed a decreased network involving beta, delta and theta activity. Finally, a reduction of networks involving alfa and beta activity in the superior parietal lobule and inferior temporal gyrus respectively, was also found. Our study showed, with a multimodal approach, the presence of widespread anatomical and electrocortical abnormalities with a common pattern in PD with MCI, involving mainly the parietal and temporal lobe. These results could be used as potential biomarkers of cognitive impairment in PD.

P104

Intrinsic functional connectivity changes in drug-naïve Parkinson's disease patients with mild cognitive impairment

Francesco Paolo Bonifacio[1,2], *R. De Micco*[1,2], *M. Siciliano*[1,3], *F. Di Nardo*[1,2], *S. Satolli*[1,2], *G. Caiazzo*[1,2], *F. Esposito*[4], *G. Tedeschi*[1,2], *A. Tessitore*[1,2]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Napoli, Italy
[2]MRI Research Center SUN-FISM, University of Campania "Luigi Vanvitelli", Napoli, Italy
[3]Neuropsychology Laboratory, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[4]Department of Medicine, Surgery and Dentistry, Scuola Medica Salernitana, University of Salerno, Salerno, Italy

Background: Mild cognitive impairment (MCI) is a common nonmotor symptom in Parkinson's disease (PD), which may arise both at the disease onset and over the disease course. MCI in PD is also considered a risk factor for developing dementia.

Aims: Using resting-state functional MRI, we aimed to investigate intrinsic brain networks connectivity correlates of MCI in a cohort of drug-naïve patients with PD. Moreover, we correlated functional connectivity changes with cognitive outcomes.

Methods: 3T MRI images of 40 drug-naïve non-depressed PD patients (PD-MCI and PD-noMCI), and 20 matched healthy controls (HCs) were analyzed. MDS Task Force Level II diagnostic criteria were applied to determine the presence of MCI. Single-subject and group-level independent component analysis was used to investigate intra and inter-network functional connectivity differences within the major neurocognitive networks (i.e. frontoparietal network, FPN, default-mode network, DMN, ventral and dorsal attention network, VAN and DAN, and salience network, SN) between patients sub-groups and HCs. Finally, linear regression analysis was used to investigate correlations between imaging and clinical data.

Results: Compared to PD-noMCI patients, PD-MCI patients showed decreased connectivity within the right FPN, the DMN and the VAN. Inter-network connectivity between DMN/DAN and DMN/VAN was significantly positive in PD-MCI patients compared to PD-noMCI, suggesting the presence of a specific functional coupling between these networks. Finally, functional connectivity measures among these neurocognitive networks were found to be correlated with neuropsychological outcomes.

Conclusions: Our findings demonstrate the presence of a specific intrinsic functional connectivity pattern involving the most important neurocognitive networks in early PD patients with MCI. This connectivity pattern is not biased from dopaminergic medication. We hypothesize that this functional architecture may reflect the presence of diffuse neuropathological changes, which may be present at the diagnosis and represent a potential early biomarker for developing clinically significant cognitive impairment overtime.

P105

Prevalence and risk factors for impulsive compulsive behaviors in a cohort of Parkinson's disease patients

Simone Simoni[1], *N. Tambasco*[1], *P. Eusebi*[1], *P. Nigro*[1], *E. Brahimi*[1], *F. Paolini Paoletti*[1], *M. Filidei*[1], *G. Cappelletti*[1], *P. Calabresi*[1,2]

[1]Clinica Neurologica, Azienda Ospedaliera e Universitaria di Perugia, Perugia, Italy
[2]IRCCS Fondazione "S. Lucia", Roma, Italy

Introduction: Impulsive compulsive behaviors (ICBs) are a frequent complication in Parkinson's disease (PD), occurring in up to 20% of PD patients [1]. These disorders have a significant impact on quality of life, straining relationships, and worsening caregiver burden. Objective of the study was to analyze the risk factors for the development of these behaviors.

Methods: 251 PD patients receiving outpatient care at our Centre were consecutively enrolled. After clinical data were collected, each patient underwent a quick interview to determine whether or not they were suitable for ICBs diagnosis. Then QUIP, BIS, MoCA, AES and Olfactory Identification Test (IOIT) were administered to all the patients. Reliability of the Italian version of the Questionnaire for Impulsive and Compulsive Behaviors (QUIP) was also tested.

Results: The prevalence of ICBs was 31.1%. Age of disease onset ($p < 0.001$), longer PD duration ($p< 0.001$) and Hoehn & Yahr stage ($p=0.020$) were related to QUIP positivity. No significant correlation with non-motor symptoms were found, including apathy (AES), cognitive deficits (MoCA) or olfactory dysfunction. Regarding dopamine replacement therapy, total daily dosage of levodopa ($p = 0.017$), dopamine agonists (OR=1.8 95% CI=1.0-3.2) as well as entacapone use (OR=2.8 95% CI=1.1-7.4) were associated with higher risk of developing ICBs. I- QUIP test-retest reliability was demonstrated.

Conclusions: Dopamine replacement therapy is associated with increased odds of having ICBs. Other significant risk factors included younger age, longer disease duration and a more severe disease presentation. No correlation with the non-motor features analyzed was found.

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P106

The atrophy of the medulla oblongata is the single best MRI predictor of non-motor signs in patients with multiple system atrophy

Massimiliano Todisco[1], *I.U. Isaias*[2], *P. Vitali*[3], *E. Alfonsi*[4], *R. Zangaglia*[1], *B. Minafra*[1], *M. Terzaghi*[5], *R. Manni*[5], *C. Pacchetti*[1]

[1]Parkinson's Disease and Movement Disorders Unit, IRCCS "Casimiro Mondino" National Neurological Institute, Pavia, Italy
[2]Department of Neurology, University Hospital Würzburg and Julius-Maximilians-University, Würzburg, Germany
[3]Brain MRI 3T Research Center, IRCCS "Casimiro Mondino" National Neurological Institute, Pavia, Italy
[4]Department of Neurophysiopathology, IRCCS "Casimiro Mondino" National Neurological Institute, Pavia, Italy
[5]Sleep Medicine and Epilepsy Unit, IRCCS "Casimiro Mondino" National Neurological Institute, Pavia, Italy

Introduction: Multiple system atrophy (MSA) is a rare neurodegenerative disorder characterized by prevailing parkinsonian (MSA-P) or cerebellar (MSA-C) motor signs and several non-motor signs such as dysautonomia, REM sleep behavior disorder (RBD), stridor, and dysphagia. Predicting the appearance of non-motor signs would be of particular relevance for a prompt intervention to ameliorate the quality of life of these patients.

Objective: To define MRI predictors of the appearance and severity of motor and non-motor signs in MSA subjects.

Methods: We consecutively recruited 60 patients with the diagnosis of "probable" MSA (45 with MSA-P and 15 with MSA-C; male/female: 26/34; age at onset: 61.75 ± 7.59 years; disease duration at diagnosis: 4.80 ± 2.21 years). The motor severity was assessed through UMSARS part II score (27.72 ± 9.63). All the subjects performed cardiovascular autonomic tests, video-polysomnography to detect the presence of RBD and stridor, and fiberoptic endoscopic evaluation of swallowing (FEES) to define the "Dysphagia Outcome and Severity Scale" (DOSS) scores. For all patients we acquired indexes of ponto-bulbar atrophy and parameters of microstructural brainstem damage with a 3 Tesla brain MRI.

Results: Cardiovascular dysautonomia and dysphagia levels were more severe in MSA-C patients, whereas the presence of RBD, stridor, and dysphagia did not differ between the two MSA phenotypes. MSA-C patients had greater atrophy and increased microstructural damage at the level of pons, medulla oblongata, middle and inferior cerebellar peduncles. Among all MRI measures, the normalized medulla oblongata volume was the single best predictor of the presence of non-motor signs, regardless of MSA phenotype, age at onset, disease duration at diagnosis, and gender. MRI parameters did not predict UMSARS part II score.

Conclusions: The assessment of the normalized medulla oblongata volume is a useful measurement to define the risk profile of appearance of non-motor signs in MSA patients.

P107

Unapproved indications for dopamine transporter scan in clinical practice

Annamaria Landolfi[1], S. Scannapieco[1], *M. Picillo*[1], *M.T. Pellecchia*[1], *L. Pace*[2], *P. Barone*[1], *R. Erro*[1]

[1]Department of Medicine and Surgery, Scuola Medica Salernitana, Neuroscience Section, University of Salerno, Italy
[2]Department of Medicine and Surgery, Scuola Medica Salernitana, University of Salerno, Italy

Introduction: Single photon emission computed tomography (SPECT) with Ioflupane I-123 for dopamine transporter visualization ([123]I-ioflupane SPECT) is currently approved for: 1) differentiating between tremor due to neurodegenerative parkinsonism and other non-neurodegenerative types of tremor; and 2) differentiating between Alzheimer disease and Lewy body dementia. Any other uses should be considered as off-label.

Objectives: The aim of our study was to review all [123]I-ioflupane SPECT referrals in our institution in the last year, in order to verify their appropriateness.

Methods: All [123]I-ioflupane SPECT exams performed in our institution in the year 2018 were evaluated in terms of their reason for referral.

Results: Forty-six [123]I-ioflupane SPECT exams were analysed. Twenty-one of them (45.7%) were performed within the approved indications, whereas the remaining (25/46; 54.3%) were not. Among the off-label indications, the most frequent was the confirmation of a clinical diagnosis of Parkinson disease (13/25; 52%), followed by the differential diagnosis between neurodegenerative and drug-induced parkinsonism (10/25; 40%).

Conclusions: Our data show that the reasons for requesting a [123]I-ioflupane SPECT exam go far beyond the approved indications, with the confirmation of a clinical diagnosis of PD being the most common. However, it has been demonstrated that using this exam contributes no additional impact on clinical management when added to the diagnostic work-up. On the other hand, we found 4/13 scans being negative, which leaves arguments to both sides as to whether or not [123]I-ioflupane SPECT might be useful to confirm a diagnosis of degenerative parkinsonism. Finally, we found a surprisingly high rate of positive scans in cases with suspected drug-induced parkinsonism, which also questions the utility of this technique in this context. Approved [123]I-ioflupane SPECT indications do not reflect use of dopamine transporter scanning in current practice. Due to the limited diagnostic value of this technique beyond the approved indications, practical guidelines should be implemented to avoid unnecessary scans.

P108

Asymmetric isolated rest and action tremors: an evaluation of nigrostriatal degeneration by means of dopamine transporter spect evaluation

Michelangelo Turazzini[1], *G. Salomone*[1], *P. Tocco*[1], *L. Ferigo*[1], *R. Del Colle*[1], *S. Rossetto*[2], *A. Polo*[1]

[1]Neurology Unit, Mater Salutis Hospital, Legnago, ULSS 9, Verona, Italy
[2]Radiotherapy and Nuclear Medicine Unit, Mater Salutis Hospital, Legnago, ULSS 9, Verona, Italy

Aim: Parkinson's disease (PD) and essential tremor (ET) are both conditions in which tremor is one of the most frequent (PD) or the distinctive (ET) clinical symptom. Usually, it is easy to identify the semeiological features that differentiate those conditions, but there are some circumstances in which is not, and patients may remain labeled as 'atypical' tremor, waiting for the occurrence of other signs that steer the right diagnosis. This is commonly the case of deeply asymmetric limb tremor, with prominent action and rest component, without other clinical signs that could fulfill diagnostic criteria for PD. If those cases could represent the very initial phase of a degenerative process is not known, and instrumental examination are rarely discriminative. In this study, we examined a group of these patients, and evaluated their nigrostriatal dysfunction by means of [123]I-ioflupane SPECT.

Matherials and methods: We selected 12 consecutive patients with asymmetric isolated resting and action tremor not fitting PD and ET clinical criteria (5 right-predominant and 7 left-predominant), and normal [123]I-ioflupane SPECT. As control group, we used 14 patients diagnosed with ET according to current clinical criteria, who underwent [123]I-ioflupane SPECT.

Results: The case group, despite [123]I-ioflupane SPECT was labeled as normal when evaluated singularly, had a significant decrease in dopamine transporter ligand reuptake in the basal ganglia compared to control group, confined to the deep nuclei contralateral to the side involved in the worst tremor symptomatology (right-predominant tremor: left-striatum p=0.02; left-putamen p=0.01; left-anterior putamen p=0.02; left-posterior putamen p=0.00 – left-predominant tremor: right-striatum p=0.04; right-caudate p=0.05; right-putamen p=0.04; right-anterior putamen p=0.04; right-posterior putamen p=0.05).

Conclusions and discussion: Our study suggests that mixed (rest and action) tremor may be anatomically subtended by a mild impairment of nigrostriatal dopaminergic transmission, revealed as a group-effect, but missed in single exam evaluation. As a whole, even though [123]I-ioflupane SPECT assists in distinguishing parkinsonian syndrome from essential tremor, it is not possible to rely on a single normal exam to exclude a concomitant nigro-striatal degeneration. Patients who do not fit clinical criteria for a disease entity need to be followed up and evaluated for response to treatments. Moreover, it is not possible to exclude that a mildly evolving Parkinsonian phenotype, with isolated tremor and mild presynaptic dopaminergic deficiency, exists.

P109

MRI brainstem morphometric assessments in MDS PSP subtypes

Filomena Abate[1], *M. Picillo*[1], *S. Ponticorvo*[1], *M.F. Tepedino*[1], *R. Erro*[1], *M.T. Pellecchia*[1], *D. Frosini*[2], *P. Cecchi*[3], *M. Cosottini*[3], *R. Ceravolo*[2], *R. Manara*[1], *P. Barone*[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Dentistry, Neuroscience Section, University of Salerno, Salerno, Italy
[2]Dipartimento di Medicina Clinica e Sperimentale Università di Pisa, Pisa, Italy
[3]Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa, Italy

Introduction: A major challenge faced during the MDS revision of Progressive Supranuclear Palsy (PSP) criteria was to determine whether to support a role for neuroimaging in the diagnosis of PSP subtypes.

Objective: Aim of the present study is to explore the role of different MRI brainstem morphometric assessments in a large group of PSP patients diagnosed according to MDS subtypes.

Methods: Only assessment with receiver operating characteristic curve (AUC) >0.6 according to ROC analysis were noted and corresponding sensitivity and specificity were computed. Seventy-nine patients with PSP [38 with Richardson's syndrome (PSP-RS); 21 with predominant parkinsonism (PSP-P); 10 with predominant corticobasal syndrome, 6 with progressive gait freezing, 4 with predominant frontal dysfunction (PSP non-P-non-RS)], thirty-five Parkinson's disease (PD) and thirty-eight healthy controls (HC) were included in this study. PSP-P and PSP non-P-non-RS were also grouped as PSP non-RS.

Results: As for PSP-RS versus PSP non-RS, ROC analysis demonstrated that Midbrain-Pons area ratio (AUC=0.744, 0.633–856, p<0.001) and MRPI (AUC=0.667, 0.544–0.789, p=0.014) had AUC>0.6. As for PSP-RS versus PSP-P, ROC analysis demonstrated that Midbrain-Pons area ratio (AUC=0.779, 0.643–0.914, p<0.001) and MRPI (AUC=0.670, 0.513–0.827, p=0.037) had AUC >0.6 As for PSP-RS versus PSP non-P-non-RS, ROC analysis demonstrated that Midbrain-Pons area ratio (AUC=0.708, 0.559–0.857, p=0.012) and MRPI (AUC=0.663, 0.507–0.830, p=0.059) had AUC>0.6. As for PSP-P versus PSP non-P-non-RS, ROC analysis demonstrated that only Midbrain midsagittal area (AUC=0.607, 0.427–0.788, p=0.255) had AUC>0.6, although non significant.

Conclusions: Midbrain-Pons area ratio, MRPI and Midbrain midsagittal area presented variable discriminant power in differentiating different MDS PSP subtypes.

P110

Atrophy and perfusion patterns in synucleinopathies

Sara Scannapieco[1,2], *R. Erro*[1], *M. Picillo*[1], *S. Ponticorvo*[1], *F. Esposito*[1], *R. Manara*[1], *P. Barone*[1], *M.T. Pellecchia*[1]

[1]Center for Neurodegenerative Disease (CEMAND), Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Universty Magna Graecia, Catanzaro, Italy

Introduction: The objective of this study is to explore the value of magnetic resonance imaging (MRI) in detecting basal ganglia and cerebellar atrophy - using voxel-based morphometry (VBM) - and perfusion - using the arterial spin labelling (ASL) technique - for differentiating MSA from PD.

Objective: The objective of this study is to explore the value of magnetic resonance imaging (MRI) in detecting basal ganglia and cerebellar atrophy - using voxel-based morphometry (VBM) - and perfusion - using the arterial spin labelling (ASL) technique - for differentiating MSA from PD.

Methods: Clinical and MRI data were analyzed for 94 subjects: 29 PD, 29 MSA and 33 healthy controls (HC) with a similar age (62.4±8.04, 59.86±8.31, 59.41±6.68, respectively) and sex distribution (7M/12F, 13M/16F, 16M/17F, respectively). Patients with PD and MSA had a similar disease duration (5.16±3.55 and 5.33±2.9, respectively). VBM and ASL were calculated for 5 basal ganglia region of interest (ROI) and 10 cerebellar ROIs.

Results: MSA showed the highest degree of atrophy in almost all basal ganglia and cerebellar ROIs, when compared to both PD patients and HC. PD patients and HC did not differ in terms of atrophy. On the other hand, MSA did not show perfusion reduction in any cerebellar ROIs when compared to PD, whereas PD patients showed decreased perfusion in both thalami and right caudate compared to both MSA patients and HC. Discriminative analyses using both VBM and ALS showed poor accuracy in allocating individual subjects in each group.

Conclusions: Our results indicate a low discriminative value of VMB and ALS in the differential diagnostis between MSA and PD. However, the evidence in PD of reduced perfusion in some cerebellar and basal ganglia areas, where no atrophy could be detected, might suggest a functional involvement of these subcortical structures, which likely depends on the underlying pathophysiology of the disease.

P111

Probabilistic tractography study of the nigrostriatal pathway in Parkinson's disease

Stefania Tagliente, H. Wilson, Z. Chappell, T. Yousaf, E. De Natale, G. Pagano, M. Politis

Neurodegeneration Imaging Group, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

Background: Loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), which projects to the dorsal striatum, is the main pathological feature of Parkinson's disease (PD). Probabilistic tractography, that analyses in vivo white matter trajectories can be employed to study the connectivity between brain regions.

Objectives: To investigate changes in connectivity of the nigrostriatal and striatonigral pathways in PD and association with clinical symptoms.

Methods: Probabilistic tractography was performed in 24 PD patients and 16 healthy controls (HCs) to measure the nigrostriatal connectivity using as a seed the SNpc manually delineated on neuromelanin sensitive MRI and the striatonigral connectivity using as a seed the dorsal striatum manually delineated on T1 MRI. Neuromelanin-sensitive MRI allows the identification of dopaminergic neurons within the SNpc to differentiate the SNpc from SN reticulata.

Results: Mean nigrostriatal ($P<0.001$; -79%) and striatonigral ($P<0.01$; -52%) streamline number was lower in PD compared to HCs. Moreover, in PD the number of streamlines of the nigrostriatal tract correlated positively with the neuromelanin area ($r=0.435$; $P<0.05$) and negatively with UPDRS-III scores ($r=-0.431$; $P=<0.05$).

Conclusions: Abnormal tractography characteristics in both the nigrostriatal and striatonigral pathways suggest loss of integrity of the motor control circuitry in PD. Degradation of the nigrostriatal tract in PD is associated with the severity of motor symptoms. The loss of pigmented neurons inside the SNpc is correlated with the loss of microstructural integrity inside the motor circuitry. Our results suggest that probabilistic tractography and neuromelanin-sensitive MRI are a potential diagnostic marker of the disease.

P112

Susceptibility weighted imaging in essential tremor

Sara Pietracupa[1], *M. Bologna*[1,2], *S. Tommasin*[2], *F. Elifani*[1], *F. Vasselli*[2], *G. Paparella*[2], *N. Petsas*[1], *A. Berardelli*[1,2], *P. Pantano*[1,2]

[1]IRCCS Neuromed, Pozzilli, Italy
[2]Dipartimento di Neuroscienze Umane, Università di Roma "Sapienza", Rome, Italy

Introduction: Essential tremor (ET) is a heterogeneous condition that is clinically characterized by postural and action tremor of the upper limbs as well as the possible involvement of other body segments (e.g. head, voice, lower limbs). A number of issues such as uncertainties exist regarding the relationship between ET and neurodegenerative phenomena have yet to be clarified. Evaluation of neuroimaging biomarkers such as iron deposition and the presence of the 'swallow tail sign', which indicates the integrity of nigrosome-1 can help to differentiate ET from other neurodegenerative movement disorders.

Objective: To evaluate the role of neuroimaging biomarkers of neurodegeneration in patients with essential tremor (ET).

Methods: We studied 19 ET patients and 15 healthy subjects (HS). Tremor was assessed by means of Fahn-Tolosa-Marin Tremor Rating Scale (FTM-TRS). We ruled out cognitive impairment using by Montreal Cognitive Assessemnt (MoCA). Participants underwent a standardized 3T-MRI protocol. We assessed iron deposition obtained from Susceptibility Weighted Angiography (SWAN) images in seven specific Regions of Interest (ROIs): thalamus, putamen, globus pallidus, caudate, substantia nigra, red nucleus and dentate nucleus. We also assessed the presence of the 'swallow tail sign', on SWAN images. We then investigated possible correlations between clinical scores and neuroimaging data.

Results: No differences in iron deposition in the 7 ROIs were found. The 'swallow tail sign' was present in all the 19 ET patients and 15 HS.

Conclusions: Our results, indicate that neurodegeneration biomarkers are not present in ET patients. Thus, certain MRI findings can help to differentiate ET patients from patients who can evolve in PD. MRI is not expensive, does not expect radiation exposure and it can represent the first diagnostic approach to a patient with movement disorders. To confirm the usefulness of imaging biomarkers further prospective studies, including larger samples of patients, are needed in the future.

P113

The obsessive-compulsive personality disorder as risk factor for executive dysfunctions in Parkinson's disease

Antonina Luca, A. Nicoletti, G. Mostile, C. Rascunà, C. Terravecchia, C. D'Agate, G. Donzuso, C.E. Cicero, G. Portaro, G. Sciacca, M. Zappia

Dipartimento di Specialità Medico Chirurgiche e Tecnologie Avanzate "G.F. Ingrassia", Università degli Studi di Catania, Catania, Italy

Introduction: Aim of the study was to evaluate the possible relationship between Obsessive-Compulsive Personality Disorder (OCPeD) and executive dysfunction in patients with Parkinson's disease (PD).

Methods: Patients affected by PD diagnosed according to the UK Parkinson's disease Society Brain Bank criteria, with a Mini Mental State Examination (MMSE) >24, were enrolled in the study. At baseline, patients have been interviewed with the Structured Clinical Interview for Personality Disorders-II (SCID-II) to evaluate the presence of OCPeD. The executive functions have been assessed with the Frontal Assessment Battery (FAB) at baseline and in a follow-up time during a period of maximum 48 months (between 12 and 48).

Results: Thirty-one PD patients (17 men and 14 women; mean age 59.9 ± 10.6 years) were enrolled. Fourteen (45.2%) patients presented an OCPeD. At baseline, no significant differences in MMSE and FAB score were recorded between patients OCPeD+ and those OCPeD-. At follow-up (mean follow-up time 29.7±11.5), patients with OCPeD obtained significantly lower FAB score than patients without OCPeD, respectively 12.6±2.8 versus 15.2±1.8, p-value 0.004.

Conclusions: Our study seems to confirm an association between executive disturbances and OCPeD in PD patients, possibly related to a common impairment of the frontostriatal circuits. Larger studies are needed to confirm our results.

P114

Mild behavioral impairment in Parkinson's disease: data from the Parkinson disease Cognitive impairment Study

Roberta Baschi[1], *V. Restivo*[3], *A. Nicoletti*[2], *C.E. Cicero*[2], *A. Luca*[2], *D. Recca*[1], *M. Zappia*[2], *R. Monastero*[1]

[1]Department of Biomedicine, Neuroscience and advanced Diagnostic, University of Palermo, Parlemo, Italy
[2]Department G.F. Ingrassia, Section of Neuroscience, University of Catania, Catania, Italy
[3]PROSAMI Department, University of Palermo, Palermo, Italy

Introduction: Neuropsychiatric symptoms (NPS) have been frequently described in Parkinson's disease (PD), even in the earliest stages of the disease. Recently the construct of Mild Behavioral Impairment (MBI) has been proposed as an at-risk state for incident cognitive decline and dementia.

Objectives: The aim of the present study is to evaluate the prevalence and associated factors of MBI in PD.

Methods: Cross-sectional data from 429 consecutive PD patients enrolled in the Parkinson's disease Cognitive impairment Study (PaCoS) were included in the study. All subjects underwent neuropsychological assessment, according to the MDS Level II criteria. NPS were evaluated with the Neuropsychiatric Inventory (NPI). Multivariate logistic regression models were used to evaluate clinical and behavioral characteristics, which are associated with PD-MBI.

Results: PD-MBI was ascertained in 361 (84.1%) subjects of whom 155 (36.1%) were newly diagnosed patients (disease duration ≤1 year) and 206 (48.0%) had a disease duration >1 year. Furthermore, 68 (15.9%) out of 429 subjects were PDw (without MBI). Across the MBI domains, Impulse Dyscontrol was significantly more prevalent among PD-MBI with disease duration >1 year than newly diagnosed patients. The frequency of Social Inapropriateness and Abnormal Perception significantly increased throughout the entire PD-MBI sample with increasing Hoehn and Yahr (H&Y) stages. PD-MBI in newly diagnosed PD was significantly associated with H & Y stage (OR 2.35, 95% CI 1.05-5.24) and antidepressant drug use (OR 2.94, 95% CI 0.91-9.47), while in patients with a disease duration >1 year was associated with UPDRS-ME (OR 3.37, 95% CI 1.41-8.00).

Conclusions: The overall MBI frequency in the PaCoS sample was 84% and 36% amongst newly diagnosed patients. The presence of MBI mainly related to motor impairment and disability.

P115

The role of the motor subtypes on the relationship between anxiety and cognitive dysfunctions in Parkinson's disease

Gianpaolo Maggi[1], *A. D'Iorio*[1], *M. Amboni*[2], *D. Di Meglio*[1], *P. Barone*[2], *C. Vitale*[3], *G. Santangelo*[1]

[1]Neuropsychology and Memory Clinic, Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy
[2]Department of Medicine, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Salerno, Italy
[3]Department of Motor Sciences and Wellness, University ''Parthenope'', Naples, Italy

Introduction: Anxiety is a common neuropsychiatric symptom in Parkinson's disease (PD), with a prevalence of 31%. Despite these high rates it has historically been overshadowed by the motor symptoms and by some neuropsychiatric disorders as depression, so it remains frequently underdiagnosed and undertreated. Several studies revealed a relationship between anxiety and motor symptoms in PD as confirmed by a recent meta-analysis of Van der Velden et al. [1] but no study has yet explored the association between motor subtypes (TD, tremor dominant and PIGD, rigidity/bradykinesia dominant) and anxiety disorder.

Objectives: The aims of the present study are: 1. to investigate the relationship between anxiety and motor subtype of PD; 2. to explore the relationship with anxiety and cognitive dysfunctions within each motor subtype of PD.

Methods: Consecutive PD outpatients were screened and divided in two groups subtype of disease according to Jankovic et al. [2] criteria. All participants underwent a neuropsychological battery to evaluate anxiety, apathy, the global cognitive functioning, memory abilities, executive and visuo-constructional functions.

Results: We identify 36 patients with TD-PD subtype and 36 patients with PIGD-PD subtype. The two groups did not differ on demographical, clinical, cognitive and behavioral aspects. Regression analysis revealed that anxiety contributed to reduced verbal memory ability in both TD-PD and PIGD-PD, whereas anxiety and Levodopa Equivalent Daily Dose (LEDD) contributed to reduced visuo-constructional abilities in PIGD-PD group.

Conclusions: Our findings suggest that there are no differences on anxiety levels between the two subtype. Moreover, the results support the fact that anxiety might affect memory abilities in PD patients indipendently of motor subtype [3], whereas it might affect visuo-constructional abilities only in PIGD-PD subtype. Since deficit of visuospatial functions are predictors of faster cognitive decline in PD, anxiety and visuospatial dysfunctions might be predictor of cognitive decline in PIGD-PD.

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P116

Qualitative scores of Rey-Osterrieth complex figure: comparison between progressive supranuclear palsy and behavioral variant of frontotemporal dementia

Luca Tommasini[1], *C. Pagni*[2], *E. Del Prete*[4], *J. Bonaccorsi*[2], *C. Radicchi*[3], *S. Cintoli*[2], *G. Tognoni*[4], *U. Bonuccelli*[4], *R. Ceravolo*[4]

[1]Department of Medical Specialities, Neurology Unit, AOUP, Pisa, Italy
[2]NEUROFARBA Department (Department of Neurosciences, Psychology, Drug Research and Child Health), University of Florence, Florence, Italy
[3]Institute of Neuroscience, National Research Council, Pisa, Italy
[4]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy

Introduction: The Boston Qualitative Scoring System (BQSS) consist of multiple qualitative scores for the Rey–Osterrieth Complex Figure (ROCF), capturing the executive aspects of figure reproduction. Previous studies have shown that patients with executive dysfunction are used to adopt a disorganized approach when copying the ROCF [1,2]. However, no studies has investigated qualitative indices of ROCF among dysexecutive syndromes.

Objectives: The present study aimed to assess whether BQSS executive scores of ROCF copy differ between patients with Progressive Supranuclear Palsy (PSP), behavioral variant Frontotemporal Dementia (bvFTD) and healthy control subjects.

Materials and Methods: 21 patients with PSP, 12 patients with bvFTD and 25 matched healthy controls were enrolled. All participants underwent cognitive evaluation including measures of global functioning, ROCF and executive tests. The copy of ROCF drawings was scored using Osterrieth and BQSS methods.

Results: Both PSP and bvFTD groups performed significantly worse than HC in ROCF scored according to Osterrieth method ($p<.05$). As for BQSS scores, bvFTD patients showed more Perseveration with respect to HC ($p<.01$), while PSP showed poorer scores in Planning ($p<.001$), Neatness ($p<.001$) and Organization ($p<.01$) and elevation on Rotation ($p<.05$) and Perseveration ($p<.01$) compared to HC. As for clinical groups, PSP patients performed significantly worse in Organization ($p<.05$), Planning ($p<.05$) and Neatness ($p<.005$) with respect to bvFTD. Performance on ROCF did not correlate with PSP-Rating scale Ocular motor exam subscore. No differences emerged between the two groups in ROCF scored with Osterrieth method, global cognitive status and executive tasks.

Conclusions: Our results showed that the Organization, Planning and Neatness of BQSS were the more suitable scores to discriminate different pattern of ROCF copying impairment in PSP and bvFTD patients.

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P117

Olfaction and taste in Parkinson's disease: the association with mild cognitive impairment and the single cognitive domain dysfunction

M.P. Cecchini[1], *A. Federico*[2], *A. Zanini*[1], *E. Mantovani*[2], *C. Masala*[3], *M. Tinazzi*[2], *Stefano Tamburin*[2]

[1]Section of Anatomy and Histology, University of Verona, Verona, Italy
[2]Section of Neurology, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[3]Department of Biomedical Sciences, Section of Physiology, University of Cagliari, Cagliari, Italy

Introduction: Mild cognitive impairment (MCI) and chemosensory dysfunction are non-motor symptoms of Parkinson's disease (PD), but their association is unclear.

Objective: The aim was to explore if MCI and the involvement of single cognitive domains influence olfaction and taste in PD.

Methods: We recruited 50 PD patients without dementia, no other reasons for cognitive impairment, no condition that could influence evaluation of cognition, olfaction and taste. They underwent a full neuropsychological and chemosensory (i.e., olfaction and taste) test with the Sniffin' Sticks Extended test (SSET), Whole Mouth test (WMT) and Taste Strips test (TST). Fifty age- and sex-matched healthy subjects served as controls.

Results: Olfactory function and sweet identification were worse in PD than controls. MCI negatively influenced odor identification. Age, overall cognition, apathy and visuospatial dysfunction negatively influenced SSET score. Sour identification was affected by MCI and executive dysfunction, and salty identification by executive dysfunction. MCI, age and executive dysfunction worsened TST score. Awareness of olfactory dysfunction was impaired in PD with MCI. Education positively influenced SSET and TST scores.

Conclusions: Our data confirmed that olfaction is abnormal in PD, while taste was only slightly impaired. MCI and the dysfunction of some cognitive domains (i.e., executive, visuospatial) was associated with worse chemosensory function, suggesting shared pathology between these non-motor symptoms.

P118

Action observation with dual task for improving cognitive abilities in Parkinson's disease: a pilot study

Edoardo Bianchini, A. Fineschi, T. De Santis, M. Sforza, D. Rinaldi, M. Giovannelli, F.E. Pontieri

Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Università "Sapienza" di Roma, Rome, Italy

Introduction: Action Observation Therapy (AOT) has been recently proposed as a new rehabilitation approach for treatment of motor deficits in Parkinson's Disease (PD). Besides motor symptoms, cognitive deficits are increasingly recognized as a challenging subset of non-motor complications in the spectrum of PD. Patients affected by these impairments have difficulty filtering out irrelevant information and tend to lose track of the task goal. To date, AOT has never been used to deal with cognitive impairment in PD patients.

Objective: In the present pilot study, we investigate, for the first time, the efficacy of a rehabilitation program of AOT within a dual task framework for treating cognitive deficits in patients with PD.

Methods: Ten PD patients underwent a 45-minute treatment that consisted in watching a video of an actor performing a daily-life activity and then executing it while performing distractive tasks (AOT with dual task). The treatment was repeated three times per week for a total of four weeks. Patients' cognitive/motor features were evaluated through standard tests one month before treatment, the first and the last day of treatment and one month after treatment.

Results: The results showed a significant improvement in cognitive aspects related to working memory (verbal and visuospatial memory) and attention in PD patients who underwent this approach.

Conclusions: We propose that using AOT together with a dual task may train the brain systems supporting executive functions through two mechanisms: (i) stimulation of goal setting within the mirror neuron system through action observation; (ii) working memory and persistent goal maintenance through dual task stimuli. This approach may be effective in the treatment of cognitive deficits in PD patients.

P119

Short term response to bilateral GPi DBS in a patient with PLA2G6-associated neurodegeneration

Nico Golfrè Andreasi[1], *M.C. Malaguti*[2], *L.M. Romito*[1], *A.E. Elia*[1], *G. Devigili*[1], *P. Soliveri*[1], *A. Novelli*[1], *S. Rinaldo*[1], *A. Di Fonzo*[3], *R. Eleopra*[1]

[1]Neurology Unit 1 - Parkinson and Movement Disorders Unit, Fondazione I.R.C.C.S. Istituto Neurologico "Carlo Besta", Milano, Italy
[2]Neurology Unit, S. Chiara Hospital, APSS Trento, Trento, Italy
[3]Neurology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Introduction: Phospholipase A2-associated neurodegeneration (PLAN) comprise a group of rare neurodegenerative disorders with a broad phenotype and frequent association with movement disorders [1].

Objective: Describe the outcome of bilateral Deep Brain Stimulation (DBS) of the Globus Pallidus interna (GPi) in a patient with homozygous mutation in PLA2G6 gene with adult onset dystonia-parkinsonism (AODP).

Methods: A 34 years old female patient was admitted to our clinic because of rapid worsening of parkinsonism and generalized dystonia associated with cognitive decline and loss of independence in all activities of daily living. The patient had already received diagnosis of AODP and the case has been recently described [2].

Results: After bilateral GPi implantation we observed an early and fast improvement of the dystonic features and after one month the patient was able, with only supervision, to safely travel short distances. After three months she started again to feed, drink and wash by herself. Parkinsonism had a good response to levodopa, but we had to keep very low doses (25 mg BID) because of agitation.

Conclusions: Bilateral GPi DBS could be useful to treat patients with AODP in order to improve motor skills and activities of daily living. Unfortunately, the fast rate of cognitive decline in these patients could prevent a reduction in overall disability. Nonetheless we believe that the young age, the reduced burden for caregivers and the potential recovery of skills like feeding and walking could justify the use of DBS in these patients.

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P120

Identification of Parkinson's disease biomarkers through RNA sequencing of peripheral blood leukocytes

Valentina Tommasini[1], *M. Catalan*[1], *M. Romano*[2], *G. Mazzon*[1], *T. Cattaruzza*[1], *L. Antonutti*[1], *P. Polverino*[1], *C. Bertolotti*[1], *E. Buratti*[3], *P. Manganotti*[1]

[1]Neurology Unit, Department of Medical, Surgical and Health Sciences, University of Trieste, Triste, Italy
[2]Department of Life Sciences, University of Trieste, Trieste, Italy
[3]Molecular Pathology Group, International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy

Background: There is a compelling need for biomarkers for the diagnosis, staging and treatment of Parkinson's disease (PD). Especially, identifying reliable biomarkers for early diagnosis and prediction of at-risk patients is a priority and a challenge in the field. Transcriptomics is becoming an important tool to investigate the potential of cells to adapt gene expression and protein synthesis in different physiological and pathological states. However, only few studies have focused so far on transcriptomic profiling as PD biomarker, and research of such biomarkers in peripheral blood is particularly lacking.

Objective: The aim of this study is to investigate gene expression changes occurring in peripheral blood leukocytes (PBL) as potential biomarkers of PD.

Methods: Blood leukocyte samples were collected from four different groups of patients: early PD (EPD), advanced PD with dementia (PDD), Alzheimer's disease (AD) and healthy volunteers as controls (CTR). RNAseq - MACE (Massive Analysis of cDNA ends) has been performed on available samples to obtain an unbiased landscape of transcript expression changes between patients and controls.

Results: Our high throughput analysis has enabled us to identify a number of genes that are most upregulated/downregulated in the patients' PBL and which, most importantly, are specific for any disease condition (Early Parkinson, Parkinson with Dementia, or Alzheimer Disease). Particularly, we detected several gene expression changes that could represent potential biomarkers for Parkinson with Dementia (1055), early Parkinson (328) and Alzheimer's Disease (400).

Conclusions: Validation studies of the top-ranking candidate genes are currently ongoing by recruiting new independent cohorts of patients. The results of the present study seem to be promising in the short/mid-term challenge to improve PD diagnosis, assess disease severity, and prognosticate course of disease.

P121

GBA recombinant alleles identification increases diagnostic yield in Parkinson's Disease (PD) and Lewy Body Dementia (LBD)

Edoardo Monfrini[1], *G. Franco*[1], *L. Straniero*[2], *A. Pilotto*[3,4], *A. Padovani*[3], *S. Duga*[2], *A. Di Fonzo*[1]

[1]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Humanitas Clinical and Research Center, Rozzano, Italy
[3]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[4]Parkinson's Disease Rehabilitation Centre, FERB ONLUS – S. Isidoro Hospital, Trescore Balneario, Italy

Introduction: The peculiar chromosomal localization of GBA gene and pseudogene makes the formation of GBA recombinant alleles very frequent. The identification of GBA recombinant alleles in PD and DLB patients can be difficult - or impossible - with standard GBA genetic analysis (Sanger sequencing). Furthermore, quantitative RT-PCR analysis of GBA gene and pseudogene, which is the gold standard for identifying GBA recombinant alleles, is not routinely done because it is very costly and time-consuming.

Objective: Our objective is to find a feasible approach to screen all the PD and DLB patients for GBA recombinant alleles.

Methods: A standard PCR amplifying both gene and pseudogene was performed in PD and DLB patients. The intensity ratio of the two electrophoretic bands (gene and pseudogene) was used to identify carriers of recombinant GBA alleles.

Results: We found up to 5% of patients carrying a GBA recombinant allele. Those patients resulted negative for GBA mutations previously analyzed by Sanger sequencing.

Conclusions: We propose a time- and cost-effective PCR-based method to increase the diagnostic yield of GBA mutational screening in PD and DLB patients.

P122

ITM2B-related cerebral amyloid angiopathy mimicking atypical parkinsonism

Pierluigi Tocco[1], *F. Rossi*[1], *L. Ferigo*[1], *A. Lupato*[1], *G. Salomone*[1], *G.M. Fabrizi*[2], *A. Polo*[1]

[1]Department of Neurology, Hospital of Legnago, Verona, Italy
[2]Department of Neurology, University Hospital of Verona, Italy

Introduction: ITM2B-related cerebral amyloid angiopathy (CAA), also known as familial danish dementia (FDD), is an extremely rare early-onset disorder characterised by progressive cognitive impairment, spasticity and cerebellar ataxia. Since its first report in 1970 [1] only few cases have been described, and its phenotype is still unclear. Here we report a case of ITM2B-related CAA presenting with cerebellar ataxia and parkinsonian features, resembling atypical parkinsonism such as cerebellar variant multiple system atrophy (MSA-C).

Case: A 61-year old caucasian woman presented with subacute onset uncertain gait and unilateral tremor, associated with slowness and mild speech impairment in the last year. She was under treatment for rheumatoid arthritis and hypertension. The neurological examination disclosed hypomimia, bradykinesia, dysarthria, unsteady gait with mild dystonia of the right leg, right postural and kinetic tremor, deep tendon hyperreflexia and asymmetric plantar reflex. She underwent to brain MRI showing diffuse cortical atrophy. The neuropsychological examination was normal, and the neurophysiology disclosed an abnormal cortical excitability. Cerebrospinal fluid analysis was normal. 123I-FP-CIT was normal, and the brain 18F-FDG PET showed hypometabolism of fronto-temporo-parietal cortex and cerebellar lobes bilaterally. Genetics for the spino-cerebellar ataxias (SCA) was negative. She started levodopa up to 450 mg tid, without any strikyng improvement. First a diagnosis of possible atypical parkinsonism such as MSA-C was made. At follow-up she presented a mild cognitive impairment, and after three years a pronounced cognitive dysfunction with aphasia. Then, we performed genetics for early-onset dementias and a mutation of the ITM2B gene was found.

Discussion: Our patient presented with clinical features suggestive of MSA-C. But, atypical progression with impairment of cognitive more than motor functions represented a red flag to rethink the diagnosis. Although this condition is extremely rare, we suggest to keep in mind ITM2B-related CAA in case of atypical atypical parkinsonism.

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P123

A new X-linked recessive Parkinson-plus syndrome? A young-onset case associated with mutations in RLIM gene

Daniela Frosini[1], *B. Toschi*[2], *C. Congregati*[2], *A. Provenzano*[3], *A. La Barbera*[3], *S. Giglio*[3], *V. Nicoletti*[1], *R. Ceravolo*[1]

[1]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa
[2]Department of Clinical and Experimental Medicine, Internal Medicine Unit, University of Pisa
[3]Department of Biomedical Experimental and Clinical Sciences "Mario Serio" Medical Genetics Unit, Meyer Children's University Hospital, Florence, Italy

Introduction: Mutations of the X-linked RLIM gene are associated with a rare pediatric syndrome (Tonne-Kalscheuer syndrome) presenting with psychomotor retardation, language problems, autism, and other behavioural disorders. The genetic transmission is X-linked recessive. Generalized seizures, intention/rest tremor, gait disturbances are rare neurological manifestations described.

Methods: The patient, male, (now 34 yrs-old) had in infancy a disharmonious personality with disorders in language and learning. At 28-yrs-old age he had generalized seizures, one year later motor slowness, bilateral asymmetric (left worse) rigidity and resting tremor appeared. Brain MRI was normal, SPECT with FP-CIT was suggestive of clear-cut degeneration of bilateral nigro-putaminal pathway (worse at right side). The response to levodopa was excellent but very soon motor fluctuations and dyskinesias appeared. His older brother, had since infancy intellectual problems, behavioural disorders (autism, obsessive-compulsive disturbance, social retirement with self-harming behaviours).

Results: The analysis of clinical exome by NGS detected in both the presence of the mutation c.533A>C (p.Asn178Thr) in the exon 5 of RLIM gene. The same mutation was detected in their mother, asymptomatic. Such mutation c.533A>C has not been reported so far. However its frequency in general population is very low (0,21%), thus it could be considered as pathogenic. Other causes of monogenic parkinsonism were excluded in the patient.

Discussion: RLIM gene encodes for a widely expressed zing-finger protein that acts as an E3 ubiquitin ligase having a crucial role along with other proteins in ubiquitin-proteasome complex, essential for protein turnover by modulating the development and maintenance of neuronal structures and transmission. An ubiquitin ligase E3 is also the product of parkin gene whose defect is responsible for the most common recessive juvenile parkinsonism. The previous description in some patients of resting tremor and slowness confirms the possibility that mutations in RLIM gene could determine a new X-linked recessive parkinson-plus syndrome.

P124

A novel PEO1 mutation in autosomal dominant Parkinson's disease with ptosis but no ophthalmoplegia

G. Franco, Edoardo Monfrini, F. Arienti, M. Percetti, A. Di Fonzo

IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

A 64-year-old woman presented to our clinic with a 3year history of left hand rest tremor. Neurological examination revealed mild bradykinesia and rest tremor in her left hand, with good response to levodopa treatment. Idiopathic Parkinson's disease was diagnosed. In her past medical history she reported the presence of ptosis in both eyes treated with blepharoplasty. Her family history was remarkable for the presence of PD and ptosis in her mother and grandfather. Gene panel identified a C.1618g>a heterozygous variant in the PEO1 gene, which would lead to a p.G540R substitution. PEO1 encodes for twinkle, a DNA helicase that plays a key role in mitochondrial DNA replication. Mutation in this gene are known to cause progressive external ophtalmoplegia (PEO) and mitochondrial multiple deletions or depletion syndromes. In our patient ocular movements were unremarkable. This finding broadens the clinical spectrum of PEO1 gene mutations and further implicates loss of mitochondrial DNA integrity in the pathogenesis of Parkinson disease.

P125

Genetic screening revealed TARDBP and CHMB2P mutations in familial atypical parkinsonism

Giacomo Bitetto[1], *F. Morgante*[2,3], *C. Sorbera*[3], *C. Fenoglio*[4], *R. Del Bo*[1], *A. Di Fonzo*[1]

[1]IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Dino Ferrari Center, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[2]Institute of Molecular and Clinical Sciences St. George's University of London, London, UK
[3]Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy
[4]University of Milan, Centro Dino Ferrari, Milan, Italy

Objective: To investigate the genetic causes of familial cases of atypical parkinsonism.

Methods: Eight patients with autosomal dominant atypical parkinsonism were selected for genetic analysis, including the C9ORF72 expansion, TARDBP Sanger sequencing and a Next Generation Sequencing panel for genes involved in familial dementia.

Results: Two patients reported known pathogenic variants: Case 3 presented at the age of 62 with progressive supranuclear palsy and rigidity suggestive of Richardson syndrome. The mother and grandmother were affected by parkinsonism. MRI of the brain showed midbrain and superior cerebellar peduncle atrophy. Genetic analyses revealed the presence of a c.800A>g in exons 6 of TARDBP, leading to a p.N267S on the encoded TDP-43 protein. The mutation was identified in FTD, ALS and CBS, but not in a PSP phenotype. Case 6 presented at 54 with progressive parkinsonism and supranuclear palsy. The mother was affected by PD with onset at 40 years. MRI of the brain shows a severe frontotemporal atrophy. NGS panel revealed the c.85A>G, p.I29V mutation in CHMP2B. This variant was described in frontotemporal dementia, motorneuron disease and primary muscular atrophy.

Conclusions: This study broadens the spectrum of phenotypes associated to TARDBP and CHMP2B and highlights the genetic heterogeneity of familial atypical parkinsonism.

P126

Extracorporeal shock wave therapy (ESWT) in freezing of gait (FoG): a pilot study

Paola Polverino, C. Bertolotti, M. Catalan, G. Mazzon, P. Manganotti

Clinical Unit of Neurology, Department of Medical Sciences, University Hospital and Health Services of Trieste, University of Trieste, Trieste, Italy

Introduction: Freezing of gait (FoG) is one of the most disabling symptom of Parkinson's disease (PD). Its pathogenesis is not completely understood even if proprioceptive integration impairment could be a potential underlying mechanism. Many pharmacological and rehabilitative strategies have been proposed with contrasting results. Extracorporeal shock wave therapy (ESWT) is a safe, non-invasive treatment that has been successfully used to manage different conditions, mainly concerning muscoloskeletal system. The aim of this study was to test the efficacy of ESWT in improving FoG by enhancing proprioceptive feedback and manipulating muscoloskeletal structures.

Materials and Methods: 10 PD patients with FoG were enrolled in this study. All patients underwent a neurological examination (UPDRS III, H&Y staging), the administration of FoG-Questionnaire (FoGQ and a video evaluation (Standing-Start-180°Turning-Test, Timed- Up-and-Go and a 15m-walking trajectory with FoG-inducing tasks) to assess FoG severity. All patients were evaluated in ON-condition before and immediately after ESWT and 1-month later. ESWT protocol consisted of 1500 shocks to both feet soles at an intensity ranging from 0.25 to 0.45 mJ/mm2, according to patients' tolerance.

Results: No significant differences in FoGQ-scores were found comparing baseline to 1-month evaluation; only one patient reported a subjective improvement in FoG severity. Video analyses showed no significant differences both in tasks execution time and in number/duration of FoG episodes.

Conclusions: In this pilot study ESWT showed no significant efficacy in improving FoG. This result may be due to different causes such as small sample size or inadequacy of the stimulation protocol (stimulation intensity, sites and number of sessions), even if a lack of efficacy of this approach should be considered. Further investigations are needed to better understand the underpinning mechanisms of FoG and to experiment novel therapeutic strategies for this disabling symptom. Different ESWT protocols are ongoing to better assess the potential effect of this non-invasive treatment.

P127

Efficacy of physiotherapy interventions in patients with cervical dystonia: systematic review and meta-analysis

Giovanni Galeoto[1], *M. Tofani*[2], *A. Berardi*[1], *J. Sansoni*[1], *G. Fabbrini*[3]

[1] Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
[2]Neurorehabilitation Unit, Department of Neurosciences and Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy
[4]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

Objective: The objective of this systematic review of randomized controlled trials is to evaluate the efficacy of physiotherapy treatment in patients with cervical dystonia.

Method: Databases (PubMed, Pedro, Otseeker, Scopus, Cinhal and Web of Science) were searched to identify randomized controlled trials (RCTs) of physiotherapy interventions for people with Cervical Dystonia, for the period ending 22 January 2019 and with no restriction on language. The primary outcome of the meta-analysis is an evaluation of lateral flection and rotation of head.

Results: We identified 6 [1,6] RCTs that met the inclusion criteria. These 6 studies, four [3-6] deal with torticollis and two [1,2] with cervical dystonia. The meta-analysis was only possible on two studies concerning torticollis.

Conclusions: Physiotherapy, combined with other rehabilitative interventions, may be effective in improving the quality of life, lateral flection and rotation of head in patients with Cervical Dystonia, when compared to conventional treatment. The strength of the evidence due to the limited number of studies available should be considered as moderate.

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P128

Three-year retrospective observational study of a group of Parkinson's patients treated with physiotherapy combined or not with focal mechanical-vibration. Follow up for at least one year

F. Serio[1], *C. Minosa*[1] *M., De Luca*[1], *P.G. Conte*[1], *G. Albani*[2], *Antonella Peppe*[2]

[1]Department of Rehabilitation ASL Taranto, Taranto, Italy
[2]Department of Neurology and Neurorehabilitation Italian Auxological Institute, IRCCS Piancavallo, Verbania, Italy
[3]Fondation S. Lucia IRCSS, Rome, Italy

Introduction: Falls are a critical point in people with Parkinson's disease (PD), not only for the clinical relevance, but even for the social-economic impact. Postural performances are strictly correlated with falls events [1] and the proprioceptive stimulation with focal Mechanical Stimulations (FV) by focal vibration device Equistasi®, seems to be able to improve this problem [2].

Objectives: Retrospectively evaluating whether FV with rehabilitation improves the rate of falls in patients with PD.

Methods: Fifty-five PD patients were consecutively recruited for a focal vibration training trial (T0). After 8 weeks (T1) the sample was divided in two groups: the FV training responders (PE group, 25 pts) who went on to use the device (2 hours in the morning and 2 hours in the afternoon for 5 days a week) combined with a rehabilitative program (3 sessions per week), and a second group, the FV training not-responders (NPE group, 30 pts) who went on to follow only the rehabilitative program (3 sessions per week). We used T.U.G., Tinetti, UPDRS Part. III, BBS and Falls Rate. Since July 2018 we have extrapolated the data of the last patients visits (T2) to observe any differences in the falls rate.

Results: After at least 1 year of the program (PE or NPE) all patients were evaluated (T2). The PE Group shows a decrement of falls rate from 2.1 to 1.25 (p .036) and a stability of the levodopa daily dosage (from 505.2 to 465.7 mg/die, p .163). The NPE group shows an increment of daily dosage from 1.9 to 1.94 (p .420) and of the levodopa daily dosage (from 531.2 to 582.7 mg/die, p .040) and not static difference (p .420) of falls rate (from 1,9 to 1,94).

Conclusions: In selected PD patients, long term focal vibration training with Equistasi® device, may significantly ameliorate postural performances and reduce falls rate.

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P129

Rehabilitation strategies for gait disorders in people with Parkinson's disease

S. Mazzoleni[1], *E. Battini*[1], *E. Ancona*[2], *M. Simonini*[2], *A. Quarenghi*[2], *Giovanni Pietro Salvi*[2]

[1]The BioRobotics Institute, Scuola Superiore Sant' Anna, Polo Sant' Anna Valdera, Pontedera, Italy
[2]Istituto Clinico Quarenghi, Riabilitazione Neuromotoria, San Pellegrino Terme, Italy

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder that affects dopaminergic neurons of the substantia nigra. Symptoms include muscle rigidity, tremors, and changes in speech and gait. Usually rehabilitation treatments are focused in order both to increase mobility and to reduce the risk of falls through balance work, gait re-education and strengthening.

Aim: The aim of our study is to evaluate the effects of an integrate rehabilitation program in Parkinson's disease. We focused our attention on improvements in stiffness, gait and balance analysis.

Methods: In Neurorehabilitaion Ward of Istituto Clinico Quarenghi we evaluated 40 inpatients affected by Parkinson's disease. Exclusion criteria were severe bedsores, major osteoarticular problems, heart failure and recently diagnosis of PD (less than 12 months). Each rehabilitation session lasts 30 minutes for five times a week for one month and includes exercises in order to improve balance, dynamic load and gait phases (both the swing and the stance one). We used also a balance board and a treadmill for gait training both for 15 minutes per session. We tested each patients with FIM scale and with UPDRS scale. We analyzed collected data with Wilcoxon test ($p<0.05$).

Results: Patients well accepted this rehabilitation program and we noticed improvements both in FIM and UPDRS scores. We also recorded improvements both in Stability Index and in Balance Index collected by the balance board.

Conclusions: The study suggest this rehabilitation program for people with Parkinson's disease improves gait pattern and balance index.

P130

Efficacy of physiotherapy on freezing of gait in Parkinson's disease: a systematic review and meta-analyses of randomized controlled trials

Carola Cosentino[1], *M. Putzolu*[1], *G. Lagravinese*[1], *R. Marchese*[2], *M. Baccini*[3], *L. Avanzino*[2,4], *E. Pelosin*[1,2]

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[2]IRCCS San Martino Teaching Hospital, Genoa, Italy
[3]Functional Rehabilitation Unit and Motor Analysis Laboratory, Piero Palagi Hospital, Local Health Unit "Toscana Centro," Florence, Italy
[4]Department of Experimental Medicine, Section of Human Physiology, University of Genoa, Genoa, Italy

Introduction: Freezing of Gait (FOG) is a very disabling symptom in Parkinson's disease (PD) whose pathophysiology is still largely unknown. Due to its paroxysmal and unpredictable nature and the lack of responsiveness to pharmacotherapy, many types of rehabilitative interventions have been proposed to control this phenomenon.

Objective: The aim of this systematic review with meta-analyses is to analyze current scientific evidence concerning the efficacy of physiotherapy on FOG in PD.

Methods: An extensive research, from inception to January 2019 was conducted on PubMed, Cochrane, Scopus and PEDro databases to identify randomized controlled trials (RCT) that studied the efficacy on FOG of any rehabilitative intervention compared to other treatments, no treatment or a placebo. RCTs were assessed with the Cochrane risk-ofbias tool. Whenever possible, findings were summarized as effect size (ES) with 95% CI in random effects models.

Results: Altogether, 654 potentially relevant articles were identified and 20 RCTs met our inclusion criteria. Detection bias and selective reporting were the most frequent risks of bias. Due to the heterogeneity of interventions, we summarized data just about 3 comparisons: Action Observation Therapy (AOT) vs AOT sham (3 RCTs), exercise program plus cueing vs usual care (2 RCTs) and cueing versus no intervention (4RCTs). Meta-analysis showed a significant effect of AOT on Freezing of Gait Questionnaire (FOG-Q) scores measured at 4-6 weeks follow up (ES=-0.50; 95% CI [0.88,-0.11]; p=0,01) and of exercise program plus cueing on FOG-Q (ES=-0.35; 95% CI [-0.69,-0.01]; p=0.04) and Fall Efficacy Scale (FES-I) (ES=-0.35; 95% CI [-0.59,-0.11]; p=0.004) postintervention.

Conclusions: These findings showed a lack of strong evidence regarding possible efficacy of physiotherapy on FOG. AOT and cueing plus exercise programs seem to attenuate FOG but results should be interpreted with caution due to the small sample sizes and the high risk of bias observed in some studies. Further research is needed.

P131

Is there any room for rehab in oromandibular dystonia? A case-series on a rare disorder

Massimo Marano[1], *V. Deidda*[2], *F. Motolese*[1], *J. Lanzone*[1], *L. Di Biase*[1], *V. Luccarelli*[2], *V. Di Lazzaro*[1]

[1]Unit of Neurology, Neurophysiology and Neurobiology, Department of Medicine, Campus Bio-Medico of Rome University, Rome, Italy
[2]Unit of Otorhinolaryngology, Department of Medicine, Campus Bio-Medico of Rome University, Rome, Italy

Introduction: Oromandibular dystonia (OMD) is a rare movement disorder, leading to hyperkinetic dysarthria. The gold standard therapy is Botulinum neurotoxin (BoNT) while Speech-Language therapy (SLT) can be used as complementary treatment in speech/swallowing disturbances. In this regard, orofacial myofunctional therapy (a SLT-technique) acts through enhancing proprioception.

Aims: To investigate the feasibility and efficacy of orofacial myofunctional therapy in three oromandibular dystonia patients.

Methods: We performed a retrospective analysis of 3 OMD and hyperkinetic dysarthria treated with SLT coupled with BoNT. All subjects received a period of isolated EMG-guided BoNT, followed by a period of combined approach (BoNT + SLT). SLT consisted of 6 steps with therapist and home-based exercises. All subjects were treated by the same injector (MM) and speech therapist (VD). Outcomes were evaluated by seriated video recordings, oromandibular dystonia questionnaire 25 (OMDQ-25) and clinical global impression scale at three time points (baseline, 2- weeks on BoNT, 2 weeks on BoNT+SLT).

Results: 3 patients were followed-up (2 focal-OMD, 1 OMD-Meige). BoNT injections alone were effective (OMDQ-25 reduction: -26%, -43%, -26%) with mild side effects in 2/3. Patients with focal OMD presented a further improvement with SLT (-28%, -20%); although a subjective benefit was reported, the patient with Meige OMD improved only by 4% at OMDQ-25. All patients reported fatigue with home-based exercises, none accomplished prescribed exercises completely.

Conclusions: OMD is a rare and heterogeneous movement disorder causing severe impairment of everyday life. SLT is a feasible and cost-effective complementary treatment for OMD (especially primary focal form), in association with BoNT injections. A major limitation is the frequent lack of compliance to SLT due to fatigability. Moreover, a specific scale exploring motor functioning in OMD is missing, so limiting the reproducibility of the clinical assessment. Further collaborative studies are required on a larger sample with the use of standardized assessment tools.

INDICE AUTORI

Per visualizzare i contributi
cliccare sui codici alfa-numerici

B

C

D

E

F

G

H

I

K

L

M

N

O

P

Q

R

S

T

U

V

W

Y

Z