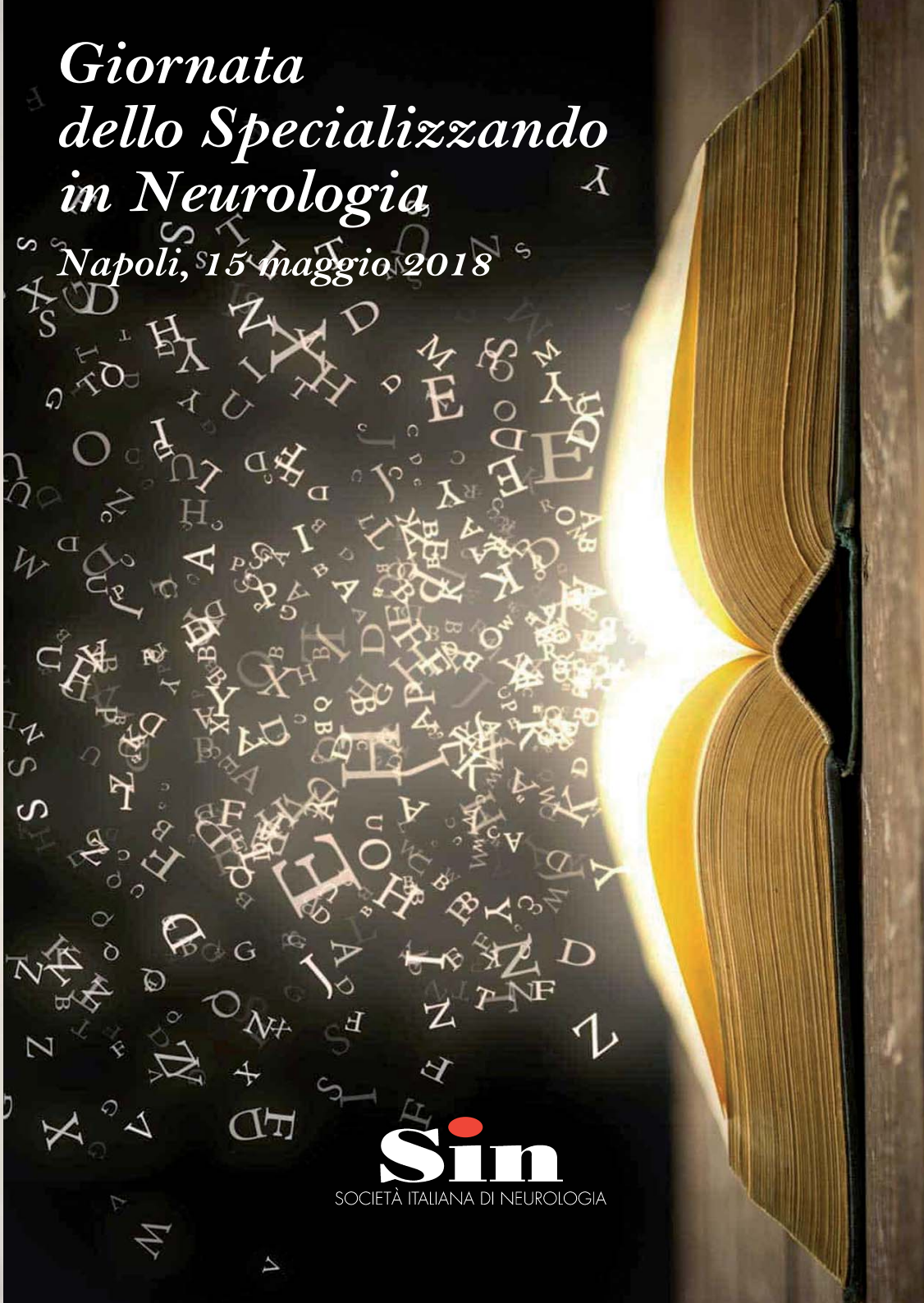
Giornata dello Specializzando in Neurologia

Napoli, 15 maggio 2018



Sin
SOCIETÀ ITALIANA DI NEUROLOGIA

SALUTO DI BENVENUTO

La “Giornata dello specializzando” nasce da una idea del prof. Giovanni Meola, professore ordinario di Neurologia presso il Policlinico San Donato di Milano, che ha organizzato in Lombardia, a partire dal 2012, una intera giornata dedicata alla ricerca svolta dagli specializzandi di neurologia. L’idea è così interessante ed ha avuto un tale successo che la SIN ha voluto generalizzare questa iniziativa, coinvolgendo le scuole di specialità del Nord, che si incontrano il 15 maggio a Milano in un meeting coordinato dal prof. Meola, gli specializzandi del Centro, che si incontrano nella stessa data a Roma presso il Policlinico Gemelli e quelli del Sud, che hanno organizzato il loro Congresso a Napoli presso il Complesso Didattico di Sant’Andrea delle Dame. La ricerca e lo studio sono le attività che rendono così interessante il lavoro del medico, ed in specie quello del neurologo, che è sempre stata una professione con un forte indirizzo di approfondimento e di studio, con l’obiettivo di risolvere i numerosi misteri che avvolgono le malattie del sistema nervoso. Quindi il percorso della ricerca fa parte del percorso formativo dello specializzando ed è una parte non secondaria della scuola di specialità di neurologia. I giovani sono tutti interessati all’approfondimento e alla sperimentazione clinica e di base e nella giornata dello specializzando avranno la opportunità di presentare i loro studi e di discuterli con i senior e i professori della loro Università. In questa giornata gli specializzandi sono i protagonisti e avranno una occasione importante per pensare al loro futuro e agli interessi che dovranno sviluppare alla fine del loro percorso formativo. La SIN ha, fra i suoi obiettivi principali, la formazione dei neurologi e in particolare di coloro che stanno per diventare la neurologia dei prossimi anni e quindi ci adoperiamo tutti in maniera tale che la “Giornata dello specializzando” diventi un appuntamento annuale, importante per lo sviluppo costante della nostra specialità.

Prof. Gianluigi Mancardi
Presidente SIN

9 maggio 2018

INFORMAZIONI GENERALI

Sede del Convegno

Sala degli Affreschi
Complesso Didattico di Sant'Andrea delle Dame
Via Luigi de Crecchio, 7
Napoli

Segreteria Scientifica

Prof. Gioacchino Tedeschi
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Lingua ufficiale

La lingua ufficiale del convegno è l'italiano

Comunicazioni orali e hot topics

Tutte le presentazioni si tengono in lingua italiana. Il tempo a disposizione per ogni comunicazione è di 10 minuti (8 per la presentazione e 2 per la discussione). Si invitano gli autori a consegnare la propria relazione al centro slide almeno 1 ora prima del loro intervento.

Badge

I badge dovranno essere ritirati presso il desk di segreteria che sarà aperto 30 minuti prima dell'inizio dell'evento. Si raccomanda ai partecipanti di indossare il proprio badge durante tutta la durata dei lavori.

Attestato di partecipazione

L'attestato di partecipazione sarà rilasciato, al termine dei lavori, presso il desk di segreteria a tutti i partecipanti regolarmente presenti.

Agevolazioni Soci SIN

Esclusivamente per gli associati SIN, in regola con il pagamento della quota associativa annuale, e residenti oltre 250 chilometri dalla sede dell'evento è possibile prevedere (su espressa richiesta da far pervenire alla segreteria sin info@neuro.it) il soggiorno in albergo 3 stelle in camera a due letti (assegnazione a insindacabile giudizio della segreteria) per la notte del 14 maggio, unitamente a un rimborso spese di viaggio fino alla concorrenza di max 150 €. Per coloro che ancora non sono soci Sin, e desiderino diventarlo, le informazioni sono disponibili sul sito www.neuro.it.

Assicurazione

La partecipazione all'evento non implica alcuna responsabilità da parte della segreteria scientifica e organizzativa per qualsivoglia incidente, danni personali o materiali o furti subiti dal partecipante durante la manifestazione.

Avvisi

Si ricorda che è tassativamente vietato fumare nell'area congressuale e che tutti i partecipanti sono caldamente invitati a tenere i cellulari in modalità silenziosa all'interno delle aule dove si svolgono i lavori.

Come raggiungere la sede congressuale

Consulta il sito
https://moovitapp.com/index/it/mezzi_pubblici-Vico_Luigi_de_Crecchio_1-Napoli_e_Campania-site_23471187-882

Cenni storici

Sant'Andrea delle Dame è una delle zone di Napoli, rifatta completamente nel progetto ottocentesco di riorganizzare il piccolo colle a base per le Cliniche Universitarie cuore del Centro Storico diNapoli. La sistemazione di questo comparto urbano partì a fine Ottocento proprio dal restauro del monastero e della chiesa di Sant'Andrea delle Dame, fatto costruire dalle sorelle Parascanodolo e da Marco, l'unico fratello, che s'era fatto teatino assieme all'architetto Valerio Pagano.

La zona fu rivisitata in chiave tipologica nel 1891, onde ricavarne spazio ad uso comunale per i senza tetto ospitati nelle immense sale del monastero, più o meno come capitò per il Real Albergo dei Poveri a Carlo III e alla Santa Casa dell'Annunziata a Forcella; il Genio Civile, entro un piano di contenimento più efficace ne consacrerà l'uso per la ricerca scientifica posseduta dalla Seconda Università di Napoli, facoltà di Medicina Oculustica.

Le azioni di bonifica di questo comparto trasformeranno completamente anche il monastero di San Gaudioso, laddove tutto era partito e, all'indomani del disastroso evento bellico del 4 agosto 1943, il riadattamento d'uso finirà per distruggere completamente il monastero della Sapienza e della Croce di Lucca a piazzetta Miraglia.

PROGRAMMA SCIENTIFICO

9.30 Registrazione dei partecipanti

10.00 Introduzione e presentazione del progetto
Gioacchino Tedeschi, *Napoli*

10.20 **Lettura Magistrale**
La nuova classificazione delle epilessie
Umberto Aguglia, *Catanzaro*

11.00 Pausa Caffè

11.30 **Comunicazioni orali**
Moderatori: Aldo Quattrone, *Catanzaro* - Lucio Santoro, *Napoli*

11.30 **Congenital myasthenic syndromes: clinical and molecular features in a cohort of Italian patients**
Carmen Bonanno, S. Sinicropi, T. Brizzi, A. Lupica, P. Girlanda, G. Vita, A. Toscano, C. Rodolico, *Messina*

11.40 **Gender-specific pattern of sensori-motor network connectivity in de novo Parkinson's disease patients**
Antonio De Mase, R. De Micco, F. Di Nardo, A. Giordano, G. Caiazzo, F. Esposito, A. Tessitore, G. Tedeschi, *Napoli, Baronissi SA*

11.50 **Movement disorders in Angelman syndrome**
Giulia Ferrigno, S. Gasparini, C. Sueri, E. Ferlazzo, V. Cianci, D. Branca, T. D'Agostino, U. Aguglia, *Catanzaro, Reggio Calabria*

12.00 **Lymphocyte count and Body Mass Index as biomarkers of treatment response in a Multiple Sclerosis Dimethyl-Fumarate-treated cohort**
Antonio Iaffaldano, D. Paolicelli, A. Manni, M. D'Onghia, V. Felica, B. Orlando, F. Caputo, P. Iaffaldano, M. Trojano, *Bari*

12.10 **The metabolomic approach in characterizing Parkinson disease patients according to several variables of disease**
Annamaria Landolfi, J. Troisi, C. Vitale, K. Longo, A. Cozzolino, M. Squillante, M. Savanelli, P. Barone, M. Amboni, *Baronissi SA, Montecorvino Pugliano (SA), Napoli, Salerno*

12.20 **Effective Geste Antagoniste in Writer's Cramp**
Valerio Melas, E. Casaglia, G. Defazio, *Cagliari*

12.30 **Clinical Efficacy and Incidence of Motor Complications among Different L-dopa Administration Modalities in Early Parkinson's Disease**
Cristina Rascunà, G. Mostile, V. Dibilio, A. Luca, L. Raciti, E. Cicero, G. Sciacca, A. Nicoletti, M. Zappia, *Catania*

12.40 **Transcranial direct current stimulation in post-stroke aphasia rehabilitation: bilateral vs unilateral online stimulation**
Angelo Torrente, V. Di Stefano, S. Buscarnera, S. Curto, G. Giglia, M. Gangitano, T. Piccoli, V. Costa, G. Cosentino, A. Sack, B. Fierro, F. Brighina, *Palermo, Chieti, Maastricht, Netherlands*

12.50 **The new challenge of the molecular diagnosis in hereditary peripheral neuropathies: next-generation sequencing and whole exome sequencing**
Stefano Tozza, S. Magri, F. Taroni, S. Zuchner, R. Iodice, M. Esposito, R. Dubbioso, L. Ruggiero, A. Topa, E. Spina, A. Iovino, L. Santoro, F. Manganelli, *Napoli, Milano, Miami, United States*

13.00 Pausa pranzo e discussione poster
Moderatori: Alessandra Nicoletti, *Catania* - Giuseppe Salemi, *Palermo*

14.00 **Flashposters**
Moderatori: Paolo Barone, *Salerno* - Giuseppe Di Iorio, *Napoli*

14.00 **An unusual presentation of Syne1 mutation (Arca1 - Beauce ataxia - Scar8): hypogonadism and intellectual disability**
Marta Bellofatto, F. Santorelli, A. Antenora, G. Natale, A. Tessa, T. Fico, S. Barbato, G. De Michele, P. Russo, M. Petruzzo, M. Lieto, A. Roca, D. Galatolo, A. Filla, *Napoli, Pisa*

14.05 **Minimal Clinically Important Change in levodopa-response detecting motor fluctuations in PD patients: usefulness of base-peak evaluation in clinical practice**
Roberta Bonomo, G. Mostile, L. Raciti, V. Dibilio, A. Luca, G. Sciacca, G. Donzuso, A. Nicoletti, M. Zappia, *Catania*

14.10 **Seizures and Migraine-like Attacks after Radiation Therapy (SMART). A new meaning of an old acronym**
Salvatore Maria Cavalli, F. Abate, M. Ascoli, G. Ferrigno, G. Mastroianni, S. Gasparini, V. Cianci, D. Branca, C. Sueri, E. Ferlazzo, U. Aguglia, *Catanzaro, Reggio Calabria*

14.15 **Menstrual cycle and cortical excitability in females with migraine and in healty controls: A study by cross modal sound induced flash illusions**
Salvatore Ferlisi, S. Maccora, N. Bolognini, R. Baschi, G. Cosentino, B. Fierro, G. Vallar, F. Brighina, *Palermo, Milano*

14.20 **Parenthood desire and decision-making in people with Multiple Sclerosis: an explorative web-based study**
Domenico Ippolito, L. Lavorgna, S. Esposito, R. Lanzillo, M. Sparaco, E. Cocco, G. Fenu, G. Borriello, S. De Mercanti, J. Frau, R. Capuano, M. Clerico, A. Laroni, V. Brescia Morra, G. Tedeschi, S. Bonavita, *Napoli, Cagliari, Torino*

14.25 **IVIg vs steroid in CIDP: our experience on immunoglobulin treatment**
Antonino Lupica, A. Mazzeo, C. Barcellona, L. Gentile, P. Girlanda, G. Vita, A. Toscano, *Messina*

14.30 **Patient-centred approach in monitoring Dimethyl-Fumarate: data from a real-life experience**
Alessia Manni, D. Paolicelli, A. Iaffaldano, M. D'Onghia, S. Zoccolella, V. Felica, B. Orlando, F. Caputo, P. Iaffaldano, M. Trojano, *Bari*

14.35 **Longitudinal study of a cohort of MSA-C Patients in south ITALY: survival and clinical features**
Alessandro Roca, *Napoli*

14.40 **Cerebellar and advanced visual network hyperresponsiveness during trigeminal nociception in migraine with aura**
Marcello Silvestro, A. Russo, A. Tessitore, F. Di Nardo, L. Marcuccio, F. Trojsi, R. De Micco, F. Esposito, G. Tedeschi, *Napoli, Salerno*

14.45 Discussione

15.00 **Hot Topic sessione 1**
Moderatori: Antonio Gambardella, *Catanzaro* - Antonio Toscano, *Messina*

L'Imaging dell'amiloide è utile per la diagnosi di malattia di Alzheimer?

15.00 *Pros*
Gianmarco Abbadessa, *Napoli*

15.10 *Cons*
Lorenzo Forino, *Salerno*

15.20 Discussione

Quale terapia per il trattamento di prima linea della CIDP: steroidi o IGEV?

15.25 *Pros*
Emanuele Spina, *Napoli*

15.35 *Cons*
Antonino Lupica, *Napoli*

15.45 Discussione

Biomarcatori con neuroimmagini per la disgnosi di PSP: sono utili?

15.50 *Pros*
Andrea Quattrone, *Catanzaro*

16.00 *Cons*
Giulia Donzuso, *Catania*

16.10 Discussione

16.15 Coffee break

16.30 **Hot Topic sessione 2**
Moderatori: Isabella Laura Simone, *Bari* - Giuseppe Sorrentino, *Napoli*

Forame Ovale Pervio: operare o non operare?

16.30 *Pros*
Chiara Pane, *Napoli*

16.40 *Cons*
Santi Galletta, *Messina*

16.50 Discussione

Peggioramento alle neuroimmagini senza peggioramento clinico: è utile cambiare terapia?

16.55 *Pros*
Antonio Scarafino, *Bari*

17.05 *Cons*
Rocco Capuano, *Napoli*

17.15 Discussione

Antivirali nella paralisi di Bell: sono utili?

17.20 *Pros*
Elisa Casaglia, *Cagliari*

17.30 *Cons*
Luca Cuffaro, *Palermo*

17.40 Discussione

17.45 **Conclusioni and take home message**
Alessandro Filla, *Napoli* - Mario Zappia, *Catania*

POSTERS

Moderatori: Alessandra Nicoletti, *Catania*
Giuseppe Salemi, *Palermo*

1 **Neuro-Behçet's Disease presenting as an isolated progressive cognitive and behavioral syndrome**
Lia Allegorico, D. Saracino, M. Melone, A. Barbarulo, B. Pollio, G. Giaccone, G. Di Iorio, *Napoli, Milano*

2 **New onset refractory status epilepticus (NORSE): a new neuroradiological finding**
Giulia Battaglia, D. Fatuzzo, L. Giuliano, G. Mainieri, G. Sortino, A. Conti, V. Sofia, M. Zappia, *Catania*

3 **Motor, behavioural, and cognitive correlates of fatigue in early, de novo Parkinson's disease patients**
Francesco Paolo Bonifacio, M. Siciliano, L. Trojano, R. De Micco, A. De Mase, F. Garramone, A. Russo, G. Tedeschi, A. Tessitore, *Napoli, Caserta*

4 **Bismuth related acute neurotoxicity as stroke mimic: a case report**
Amelia Brigandi', V. Rizzo, P. Girlanda, *Messina*

5 **Coping strategies associated to increased clinical activity in relapsing remitting MS**
Simone Cepparulo, G. Santangelo, M. Della Corte, M. Sparaco, G. Miele, F. Garramone, M. Cropano, S. Esposito, L. Lavorgna, A. Gallo, G. Tedeschi, S. Bonavita, *Napoli*

6 **An atypical language disorder as variant onset of Alzheimer's disease**
Lorenzo Cipriano, G. Capaldo, D. Saracino, M. Proto, C. Coppola, G. Puoti, S. Pappatà, A. D'Amico, G. Di Iorio, M. Melone, *Napoli*

7 **Can the foam cells aid to determinate clots etiology?**
Domenico Cosenza, V. Barresi, S. Galletta, J. De Caro, F. Grillo, R. Musolino, *Messina*

8 **Cognitive impairment: evaluation of Cerebrospinal Fluid Biomarkers in combination with Clinical, Neuroimaging and Neuropsychological assessment: our experience**
Luca Cuffaro, F. Aleo, V. Blandino, F. Lupo, G. Pastorello, R. Monastero, B. Fierro, T. Piccoli, *Palermo*

9 **Metformin and Outcome in Ischemic Stroke Patients Undergoing Reperfusion Therapy**
Carmelo Tiberio Currò, M. Cotroneo, C. Dell'Aera, M. Fazio, R. Musolino, *Messina*

10 **Reversible valproate-induced subacute encephalopathy associated with a MT-ATP8 variant in the mitochondrial genome**
Giovanna De Michele, P. Sorrentino, C. Nesti, A. Rubegni, L. Ruggiero, S. Peluso, A. Antenora, A. Filla, G. De Michele, F. Santorelli, *Napoli, Pisa*

11 **Abnormal pattern of intracortical facilitation in episodic migraine without aura: results of a paired-pulse TMS study**
Salvatore Di Marco, G. Cosentino, W. Capitano, S. Ferlisi, L. Pilati, S. Scardina, A. Torrente, G. La Bianca, B. Fierro, F. Brighina, *Palermo*

12 **Visual cortical excitability in pediatric migraine: a study with sound-induced flash illusions**
Salvatore Di Marco, G. Cosentino, L. Pilati, R. Baschi, S. Maccora, S. Scardina, V. Raieli, G. Santangelo, B. Fierro, F. Brighina, *Palermo*

13 **Apathy is correlated with widespread diffusion tensor imaging (DTI) impairment in amyotrophic lateral sclerosis**
Cinzia Femiano, F. Trojsi, G. Caiazzo, M. Siciliano, C. Passaniti, A. Russo, A. Bisecco, M. Cirillo, M. Monsurrò, F. Esposito, G. Tedeschi, G. Santangelo, *Napoli, Baronissi SA*

14 **Acute stroke treatment in Basilar Artery Occlusion patients. A mothership clinical series**
Isabella Francalanza, P. La Spina, A. Ciacciarelli, D. Cosenza, A. Caragliano, R. Musolino, *Messina*

15 **Isolated Insular Stroke: Clinical Presentation and Management**
Fabrizio Giammello, D. Cosenza, C. Casella, C. Dell'Aera, R. Musolino, *Messina*

16 **Hepatic microabscesses during CMV reactivation in a multiple sclerosis patient after alemtuzumab treatment**
Alessia Giugno, S. Barone, S. Scannapieco, C. Torti, E. Filippelli, V. Pisani, A. Granata, D. Console, G. Demonte, T. Tallarico, S. Polidoro, A. Quattrone, P. Valentino, *Catanzaro*

17 **A case of mild Natalizumab-associated Progressive Multifocal Leukoencephalopathy with a benign course without plasma exchange**
Alfredo Granata, S. Barone, E. Filippelli, S. Polidoro, S. Scannapieco, A. Quattrone, P. Valentino, *Catanzaro*

18 **Clinical effectiveness of perampanel in the treatment of cortical myoclonus**
Antonella Guccione, D. Fatuzzo, L. Giuliano, G. Mainieri, V. Sofia, M. Zappia, *Catania*

19 **Clinical effects of motor cortex tRNS on twenty fibromyalgia patients: results of a randomized sham-controlled trial**
Giuseppe La Bianca, M. Curatolo, G. Cosentino, R. Baschi, G. Salemi, P. Sarzi-Puttini, G. Guggino, M. De Tommaso, B. Fierro, F. Brighina, *Palermo, Milano, Bari*

20 **Neuromyelitis Optica (NMO) and Autoimmune Hepatitis: a rare association**
Ruggiero Leone, E. Cascardi, M. Trojano, I. Simone, *Bari*

21 **Clinical and neuroradiological correlations between Cerebral Microbleeds and different subtypes of Mild Cognitive Impairment**
Mariano Oliva, C. Coppola, D. Saracino, S. Fantasia, R. Conforti, M. Cirillo, L. Fulgione, G. Di Iorio, *Napoli*

22 **Teriflunomide for treatment of multiple sclerosis in comorbidity with chronic immune thrombocytopenia. A case report**
Bianca Orlando, P. Iaffaldano, F. Caputo, A. Manni, A. Iaffaldano, V. Felica, D. Paolicelli, M. Trojano, *Bari*

23 **Age and sex related functional hemispheric asymmetries in healthy subjects as revealed by sound induced flash illusions**
Laura Pilati, S. Di Marco, R. Baschi, S. Maccora, G. Cosentino, S. Scardina, B. Fierro, F. Brighina, *Palermo*

24 **Visual cortex hyperexcitability in cluster headache: a pilot study with sound induced flash illusion paradigm**
Laura Pilati, G. Cosentino, M. Aprile, S. Maccora, R. Baschi, S. Scardina, S. Di Marco, B. Fierro, F. Brighina, *Palermo*

25 **Infarction of the body of the Corpus Callosum: an atypical clinical presentation - Case Report**
Giacomo Portaro, S. Lo Fermo, M. Zappia, *Catania*

26 **Non convulsive status epilepticus presenting as migrainous attack**
Chiara Reale, M. Autunno, G. Di Rosa, A. Magaudda, *Messina*

27 **Microstructural correlates of Edinburgh Cognitive and Behavioural ALS Screen (ECAS) changes in amyotrophic lateral sclerosis**
Dario Ricciardi, F. Trojsi, C. Femiano, G. Caiazzo, M. Siciliano, M. Monsurrò, M. Cirillo, F. Esposito, G. Santangelo, G. Tedeschi, *Napoli*

28 **New diagnostic criteria and the costs for treating Multiple Sclerosis**
Martina Petruzzo, R. Palladino, A. Nardone, A. Nozzolillo, M. De Angelis, R. Lanzillo, M. Triassi, V. Brescia Morra, M. Moccia, *Napoli, Londra*

29 **Cystatin B dodecamer expansion in a mild form of myoclonic epilepsy**
Ilaria Sammarra, F. Fortunato, F. Abate, M. Trimboli, A. Labate, A. Gambardella, *Catanzaro*

30 **The right side of the brain is not merely a silent viewer in terms of language**
Serena Scardina, S. Talamanca, L. Pilati, S. Di Marco, V. Costa, G. Giglia, G. Cosentino, B. Fierro, F. Brighina, *Palermo*

31 **Six-minute walk test as reliable and objective tool to measure improvements in fatigue for cidp patients**
Emanuele Spina, *Napoli*

32 **Adem-like onset of large B-Cell primary central nervous system lymphoma: a case report and neuropathological correlates**
Giulia Straccia, E. Signoriello, M. Fratta, G. Lus, P. Somma, A. D'amico, G. Di Iorio, *Napoli*

33 **Autoimmune Dementia: is that a thing?**
Maria Tappatà, *Bari*

BOOK OF ABSTRACTS

LYMPHOCYTE COUNT AND BODY MASS INDEX AS BIOMARKERS OF TREATMENT RESPONSE IN A MULTIPLE SCLEROSIS DIMETHYL-FUMARATE-TREATED COHORT

Antonio Iaffaldano, D. Paolicelli, A. Manni, M. D'Onghia, V. Felica, B. Orlando, F. Caputo, P. Iaffaldano, M. Trojano

Department of Basic Medical Sciences, Neuroscience and Sense Organs - University of Bari" Aldo Moro" – Bari

Background: In dimethyl-fumarate (DMF)-treated relapsing-remitting MS (RRMS) patients, various extended interval dosing strategies are under evaluation to minimize treatment-associated side effects. Up to now, few and discordant data are available about the role of possible predictive markers of treatment response.
Aims: to assess the predictive value of lymphocyte count (LC) and BMI for treatment response in a real life setting of DMF treated patients. Methods: We collected clinical, demographic and anthropometric data at the beginning (T0). LC were assessed at T0 and after 3 (T3), 6 (T6) month. Relapses within T6 and T12 were considered to evaluate clinical activity; Gadolinium enhancing (Gd+) and new T2 lesions, defined MRI activity at T6 and after 12 months (T12). To correlate LC and BMI with clinical and radiological response, Pearson and Spearman tests were performed. We evaluated using multivariate logistic regression models, whether BMI or LC can predict treatment response.
Results: our cohort of 165 DMF-treated patients was followed up for a mean period of 15±7 months. The mean BMI at baseline was 24,19±4,48. We observed an inverse correlation between BMI and relapses within T6 (r=-0.31, p=0.001) and T12 (r0-0.32, p=0.019). We also found an inverse correlation between BMI and MRI activity at T12 (r=-0.32 p=0.012). At the multivariate models, predictive factors for GD+ lesions at T12 resulted LC at T3 (p=0.037, OR=1.084, CI= 0.997-1) and baseline BMI (p=0.033, OR=0.887, CI= 1.032-2.131). Predictive factors for new T2 lesions at T12 were LC at T3 (p=0.005, OR=1.010 Ci=0.99-1) and baseline BMI (p=0.026, OR=0.997, CI=0.98-1).
Conclusions: As recent studies showed that DMF is a negative regulator of adipogenic differentiation, mediated by STAT3 inhibition, the role of BMI during this treatment must be considered not only to minimize the side effects of the drug, but also to optimize treatment response. Also LC changes must be considered to evaluate treatment response. Further studies on larger cohorts and with longer follow-ups will be necessary to confirm our preliminary results.

References: Gold R, Arnold DL, Bar-Or A, Hutchinson M, Kappos L, Havrdova E, MacManus DG, Yousry TA, Pozzilli C, Selmaj K, Sweetser MT, Zhang R, Yang M, Potts J, Novas M, Miller DH, Kurukulasuriya NC, Fox RJ, Phillips TJ. Long-term effects of delayed-release dimethyl fumarate in multiple sclerosis: Interim analysis of ENDORSE, a randomized extension study. Mult Scler. 2017 Feb;23(2):253-265.
Fox RJ, Chan A, Gold R, Phillips JT, Selmaj K, Chang I, Novas M, Rana J, Marantz JL. Characterizing absolute lymphocyte count profiles in dimethyl fumarate-treated patients with MS: Patient management considerations. Neurol Clin Pract. 2016 Jun;6(3):220-229.
Kang HJ, Seo HA, Go Y, Oh CJ, Jeoung NH, Park KG, Lee IK. Dimethylfumarate suppresses adipogenic differentiation in 3T3-L1 preadipocytes through inhibition of STAT3 activity. PLoS One. 2013 Apr 18;8(4):e 61411.

NEUROMYELITIS OPTICA (NMO) AND AUTOIMMUNE HEPATITIS: A RARE ASSOCIATION

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Introduction: A 76-years old caucasian woman was admitted to our Neurological Unit for visual acuity impairment in OD developed over few months. There was a history of Hashimoto thyroiditis. At the age of 63 the patient had acutely low back pain, paraparesis, gait ataxia and constipation. CSF analysis showed mild blood brain barrier (BBB) damage (77.3 mg/dl), normal cells and absence of oligoclonal bands. Cultures for bacteria, fungi and viral serology were all negative. Despite normal brain MRI, spinal MRI showed diffuse increased signal intensity in the T2-STIR sequence, centrally located, from D4-D5 to D7-D8. Diagnosis was acute myelitis. Partial recovery was obtained with steroids. In the follow-up three recurrent transverse myelitis occurred. MRI brain white matter aspecific gliosis and D5-D8 cord atrophy were found. At the age of 73, unexplained persistent hyperferritinemia (>2000 ng/mL) and hyperaminotransferases (x10-20) occurred. Two years later, the patient had acute amaurosis in OS without remission and after one year a visual impairment in OD occurred, reason for admission at our clinic. The neurological examination revealed paraparesis, sensory gait ataxia, left eye blindness and right eye low visual acuity.
Diagnostics: Blood chemistry analysis confirmed hyperferritinemia and hyperaminotransferases. ANA, anti-SSA, p-ANCA, anti-TPO and anti-TG were positive. Viral hepatitis

markers were negative. PEV were altered in both eyes. Serum anti AQP-4 antibodies (immuno fluorescence) were strong positive. MRI showed previous findings together with swelling of sheaths of the optic nerves. Liver biopsy was performed, that proved histological pattern of an autoimmune hepatitis, grading II (AIH). Anti-phosphoglycerate Mutase 1 (PGAM1) assay is ongoing. Corticosteroids and azatioprine were started. **Discussion:** Association of NMO and systemic organ/non-organ specific autoimmune disorders was already described. Autoimmune thyroiditis is the most association. To our knowledge this is the second report on NMO-AIH association. These findings support the notion that a genetic predisposition to humoral autoimmunity characterizes the NMO.

References: Kimura A, Sakurai T, Koumura A, Yamada M, Hayashi Y, TanakaY, et al. High prevalence of autoantibodies against phos-phoglycerate mutase 1 in patients with autoimmune centralnervous system diseases. J Neuroimmunol 2010;219(1-2):105-8.
R.G. Romanelli, F. Fassio,F. Cappelli, M.G. Giudizi, I. Cecioni, A. Matucci, F. Castiglione, R. Tarquini,, F. Almerigogna. Autoimmune hepatitis in a patient affected by neuromyelitis optica: A new association. Clinics and Research in Hepatology and Gastroenterology (2014) 38, e33-e35.

PATIENT-CENTRED APPROACH IN MONITORING DIMETHYL-FUMARATE: DATA FROM A REAL-LIFE EXPERIENCE

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Background: The most frequent side effects (SEs) of Dimethyl-Fumarate (DMF) include flushing and gastrointestinal events (GI). AIMS: We investigated about the safety issues in a cohort of 120 Relapsing Multiple Sclerosis (RMS) patients treated with DMF 120 mg BID for 7 days (standard titration) or for 2-4 weeks (slower titration), and then increased to 240 mg BID. Methods: At the time of DMF first prescription, anthropometric measures were assessed. Any SEs were reported immediately upon the occurrence or during the scheduled follow-up.
Results: The mean Body Mass Index (BMI) in our cohort was 23.6±4.38. During an observation period of 10.3±5 months, 120 patients (72.7%) reported at least one SE. The most common was flushing reported by 109 patients (66.1%), usually resolved

spontaneously (except in 10 patients, who were treated for 5 days treatment with acetylsalicylic acid 300 mg /day). Seventy-nine patients (47.9%) reported GI SEs, that in 5 cases lead to drug discontinuation. We found a direct correlation between female sex and SEs ($r = 0.17$; $p = 0.029$): GI ($r = 0.22$, $p = 0.004$), nausea/ vomiting ($r = 0.18$, $p = 0.024$), and flushing ($r = 0.2$; $p = 0.011$). At the multivariate analysis, adjusted for age, sex, concomitant diseases and BMI, the male sex was confirmed as a protective factor against GI ($p = 0.035$; OR = 0.287; 95% CI = 0.9-0.941) and flushing ($p = 0.004$; OR = 0.42; 95% CI = 0.05-0.365). Stratifying patients according to their "weight category", we found that among normal-weight patients (18.5).

References: Mayer L, Fink MK, Sammarco C, Laing L. Management Strategies to Facilitate Optimal Outcomes for Patients Treated with Delayed-release Dimethyl Fumarate. Drug Saf. 2018 Apr;41(4):347-356.
Phillips JT, Selmaj K, Gold R, Fox RJ, Havrdova E, Giovannoni G, Abourjaily H, Pace A, Novas M, Hotermans C, Viglietta V, Meltzer L. Clinical Significance of Gastrointestinal and Flushing Events in Patients with Multiple Sclerosis Treated with Delayed-Release Dimethyl Fumarate. Int J MS Care. 2015 Sep-Oct;17(5):236-43.
Fernández Ó, Giovannoni G, Fox RJ, Gold R, Phillips JT, Potts J, Okwuokenye M, Marantz JL. Efficacy and Safety of Delayed-release Dimethyl Fumarate for Relapsing-remitting Multiple Sclerosis in Prior Interferon Users: An Integrated Analysis of DEFINE and CONFIRM. Clin Ther. 2017 Aug;39(8):1671-1679.

TERIFLUNOMIDE FOR TREATMENT OF MULTIPLE SCLEROSIS IN COMORBIDITY WITH CHRONIC IMMUNE THROMBOCYTOPENIA. A CASE REPORT

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Background: The association between Multiple Sclerosis (MS) and Idiopathic Thrombocytopenic Purpura (ITP) is rare and there are limited reports in the literature, despite some recent studies have demonstrated significant activation of platelets in patients with MS. Disease-modifying therapies (DMTs) approved for relapsing-remitting MS (RRMS) are associated with long-lasting effects on the immune system and/or serious adverse events, for example drug-induced ITP, recently reported with alemtuzumab therapy. In addition, drug-related ITP has been also reported in patients exposed to

interferon beta. Treatment decision in newly diagnosed patients with concomitant RRMS and ITP is challenging.

Case Report: A 22-years-old man was admitted to our Neurology Department in July 2016 with monolateral optic neuritis (ON). According to cerebral spinal fluid (CSF) analysis, magnetic resonance imaging (MRI) and evoked potentials, he had been diagnosed a clinically isolated syndrome (CIS). Blood test showed a platelet count lower than normal, it was $58x10^3$/uL (normal ranges from 150,000 to 450,000 platelets per microliter of blood), with absence of any obvious initiating and/or underlying cause for thrombocytopenia. Physical examination was normal, without splenomegaly or adenopathy. In January 2017 he developed two new brain hyperintense T2 lesions, which were also gadolinium enhancing on T1-weighted images. Thus, according with the 2011 McDonald criteria, a diagnosis of RRMS was made. In February 2017, after haematology consultations and a bone marrow aspirate examination, the diagnosis of chronic immune thrombocytopenia was confirmed. Due to the potential cutaneous side effects of injectable drugs we decided to start treatment with Teriflunomide, a dihydroorotate dehydrogenase (DHODH) inhibitor, with potential immunosuppressive effect. Here we report data of the first year exposure to Teriflunomide on clinical, MRI and laboratory findings. The patient hasn't had new lesions on brain MRI, EDSS score progression or relapse; the platelets count, after one year, is $110x10^3$/uL, almost doubled from last year.

Conclusion: treatment decision in RRMS patients with comorbidities is challenging, also considering the possibility of drug-induced thrombocytopenia with different DMTs. Our case report shows that one year-treatment with Teriflunomide is safe and may be beneficial for both RRSS and ITP.

References: Evidence of platelet activation in multiple sclerosis. Sheremata WA, Jy W, Horstman LL, Ahn YS, Alexander JS, Minagar A.. J Neuroinflammation 2008; 5: 27.Published online 2008 Jun 27.

Profiling of dihydroorotate dehydrogenase, p38 and JAK inhibitors in the rat adjuvant-induced arthritis model: a translational study. C Balagué, M Pont, N Prats, and N Godessart. Br J Pharmacol. 2012 Jun; 166(4): 1320–1332.

Interferon-therapy and risk of thrombocytopenia in multiple sclerosis patients. Koudriavtseva T, Plantone D, Renna R, Mandoj C, Giannarelli D, Mainero C. Neurol Sci. 2015 Dec;36(12):2263-8.

AUTOIMMUNE DEMENTIA: IS THAT A THING?

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Background: At present diagnosis of dementia and cognitive impairment mainly relies on clinical evaluation. In Alzheimer's disease it can be supported by hippocampal atrophy findings on imaging. On the other hand, Autoimmune Encephalitis is characterised by subacute development of short-term memory loss1 and the most frequent form of this pathology is indeed the Limbic Encephalitis, which involves the hippocampus and may lead to hippocampal atrophy as well.
Aims, Matherials and Methods: We provide a scope review of literature and brief analysis of Oxford's approach to patients with cognitive impairment suspicious for underlying autoimmune pathogenesis.
Results: In Oxford's John Radcliffe Hospital patients with cognitive impairment and autoantibodies against the neuronal surface are visited in the Autoimmune Encephalitis Clinic that's held once a month. Cognitive impairment is quantified through the use of the Addenbrooke's Cognitive Examination (ACE-R, 2005 version); anxiety and depression are also measured, through the use of the Hospital Anxiety and Depression Scale (HADS). As the literature shows, most patients are males in their 60s, and the onset of cognitive impairment is tipically acute or subacute. Epileptic seizures are the most common associated symptom, which can help the diagnosis but are not a necessary condition.
Discussion and conclusion: Although Autoimmune Encephalitis is a rare disease, these patients can benefit from immunotherapy. Therefore, when approaching a patient with cognitive impairment, we should always consider autoimmune etiology, especially when the onset is acute/subacute and when the patient present with epileptic seizures or other neurological signs.

References: Graus F et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 2016;15:391–404.

THE METABOLOMIC APPROACH IN CHARACTERIZING PARKINSON DISEASE PATIENTS ACCORDING TO SEVERAL VARIABLES OF DISEASE

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Abstract: Idiopathic Parkinson's Disease (PD) is widely thought to have a multifactorial pathogenesis. Multifactorial diseases can be studied with metabolomics, since the cellular metabolome mirrors the interplay between genes and environment. The aim of our case-control study is to compare entire blood metabolomic profiles obtained from treated PD patients, de novo PD patients and controls, and to study the metabolomic changes correlated with disease duration, disease stage and motor impairment.

Background: Idiopathic Parkinson's Disease is a multifactorial disease, i.e., it is mainly determined by the interplay of a genetic predisposition and environmental factors. Untargeted metabolomics can give new insights about the pathogenesis of PD. Indeed, it can be useful in the characterization of multifactorial diseases because it reflects the interaction between genes and the environment. Untargeted metabolomic studies have already been performed in PD in order to look for biomarkers of disease.

Aims: The aim of our case-control study is to compare entire blood metabolomic profiles obtained from treated PD patients, de novo PD patients and controls, and to study the perturbations correlated with disease duration, disease stage and motor impairment.

Materials and methods: We collected entire blood samples from 16 de novo parkinsonian patients, 84 treated parkinsonian patients, and 42 age matched healthy controls. Metabolomic profiles have been obtained using gas chromatography coupled to mass spectrometry. Multivariate statistical analysis has been performed using the supervised models partial least square discriminant analysis (PLS-DA) for discrete variables and partial least square regression (PLS-R) for continuous variables.

Results: This approach allowed separation between discrete classes (de novo patients from controls, treated patients form controls, de novo from treated patients) and stratification of treated patients according to continuous variables (disease duration, disease stage, motor score). Analysis of single metabolites or entire pathways involved in class separations and patient stratification allowed to discover unexpected possible perturbations or recognize already studied mechanisms correlated with disease onset, stage, duration, motor score and pharmacological treatment.

Discussion and conclusion: The metabolomic fingerprint of PD is influenced by several variables that must be carefully taken into account when characterizing the disease from a metabolomic point of view. In the next future, a comparison with an adequate cohort of control constituted by other neurodegenerative diseases will be essential to distinguish which metabolites and pathways are specific for Parkinson's disease.

References: Dunn WB, Broadhurst DI, Atherton HJ, Goodacre R, Griffin JL. Systems level studies of mammalian metabolomes: the roles of mass spectrometry and nuclear magnetic resonance spectroscopy. Chem Soc Rev. 2011;40:387-426.

Bogdanov M, Matson WR, Wang L, Matson T, Saunders-Pullman R, Bressman SS, et al. Metabolomic profiling to develop blood biomarkers for Parkinson's disease. Brain J Neurol. 2008;131:389-96.

LeWitt PA, Li J, Lu M, Guo L, Auinger P. Metabolomic biomarkers as strong correlates of Parkinson disease progression. Neurology. 2017;88:862-9.

EFFECTIVE GESTE ANTAGONISTE IN WRITER'S CRAMP

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Introduction: Geste Antagoniste (GA) is a highly specific feature of dystonia [1], but its frequency depends upon the affected body district. In cranio-cervical dystonia the prevalence of GA varies from 44% in OMD, 87% in Blepharospasm and 89.6% in cervical dystonia. On the contrary, in arm dystonia the frequency is reported to be around 20% [2]. It has been suggested that variability in the frequency of GA might reflect patophysiological differences among the various forms of focal dystonias.
Aims: To assess the prevalence of effective GA in a cohort of 29 patients with idiopathic adult onset Writer's Cramp (WC).
Materials and methods: Twenty-nine right handed patients, affected by WC participated into the study. Each patient was asked to write a standard sentence twice, before and after GA (The patient was asked to gently grab his right wrist with his left hand). Overall legibility of the two sentences was compared by one blinded observer. Graphologic elements were also measured, including the length of the sentence and the height of the letter d [3].
Results: GA yielded a better comprehension of the written sentence in 13/29 patients (45%). Effective GA was also characterized by sentence shortening and reduction in letter height. There was no correlation between years of disease and the effectiveness of GA.
Discussion and conclusion: Our study shows that an effective GA may be present in about the 45% of patients with arm dystonia, (more than double than what observed in previous studies). GA also affected the assessed writing features (sentence length and letter height), therefore suggesting that the typical disgraphism in WC is probably a macrographia.

References: [1] Ledoux, M. S. (2016). HHS Public Access, 18(Suppl 1), 1–7. http://doi.org/10.1016/S1353-8020(11)70050-5.Dystonia.
[2] Loyola, D. P., Camargos, S., Maia, D., & Cardoso, F. (2013). Sensory tricks in focal dystonia and hemifacial spasm. European Journal of Neurology, 20(4), 704–707. http://doi.org/10.1111/ene.12054.
[3] Bajaj, N. P. S., Wang, L., Gontu, V., Grosset, D. G., & Bain, P. G. (2012). Accuracy of subjective and objective handwriting assessment for differentiating Parkinson's disease from tremulous subjects without evidence of dopaminergic deficits (SWEDDs): An FP-CIT- validated study. Journal of Neurology, 259(11), 2335–2340. http://doi.org/10.1007/s00415-012- 6495-5.

NEW ONSET REFRACTORY STATUS EPILEPTICUS (NORSE): A NEW NEURO-RADIOLOGICAL FINDING

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Introduction: New Onset Refractory Status Epilepticus (NORSE) is a recently described syndrome characterized by a super-refractory status epilecticus occurred in young adults without a history of epilepsy after mild fever or illness. Up to date, even if a viral and an autoimmune origin was hypothesized, the ethiology of the syndrome is unknown.
Case report: Here we present a case of a 29 year-old man without a history of remarkable neurological disease who presented a tonic-clonic seizure one week after a febrile episode, followed by repetitive motor seizure and psychomotor agitation. He was referred to the Intensive Care Unit (ICU) where he was treated with deep sedation with propofol (4 mg/kg/h) and a combination of high doses of antiepileptic drugs; because of a lack of clinical response a cycle of immunoglobulin (0.4 g/kg/day for 5 days) was then administered. CFS examinations and extensive researches for infectious agents and auto-antibodies on both serum and CSF were performed and all were negatives. Serial brain MRI showed atypical findings with a peculiar temporal course. The first MRI performed 24 hours after the onset showed a small, oval-shaped high-intense signal on T2-weighted series, restricted on diffusion weighted imaging (DWI) and hypointense on apparent diffusion coefficient (ADC) series in the splenium of the corpus callosum. This alteration disappeared four days later on second MRI which showed a slight hyperintense signal in T2-weighted and FLAIR sequences over both hippocampi.
Discussion: Reversible splenial lesion was found in mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) and in patients undergoing withdrawal of antiepileptic drugs, two hypothesis excluded because of the persistence of refractory status epilecticus and the absence of AEDs use. Recently communication fibers between the two medial temporal lobes have been found in the splenium of the corpus callosum, through advanced tractography methods. This finding may explain the involvement of this region during persistent temporal ictal activity as found in our case.

MINIMAL CLINICALLY IMPORTANT CHANGE IN LEVODOPA-RESPONSE DETECTING MOTOR FLUCTUATIONS IN PD PATIENTS: USEFULNESS OF BASE-PEAK EVALUATION IN CLINICAL PRACTICE

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

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

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

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

CLINICAL EFFECTIVENESS OF PERAMPANEL IN THE TREATMENT OF CORTICAL MYOCLONICA

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Background: Perampanel (PER) is a novel non-competitive selective antagonist alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor, approved for add-on therapy of focal and primary generalized tonic-clonic seizures (1). In addition some case reports (2,3) showed a good therapeutic effect in drug-resistant myoclonic seizures.

Clinical Case: We reported the clinical case of a 52-year-old male patient affected by focal seizures since infancy, characterized by loss of contact, stiffness of the right limbs and sporadic secondary generalizations with frequent traumatic falls. The seizures occurred daily and mostly in wakefulness. Various antiepileptic drugs have been used over the years (valproate, phenytoin, topiramate, levetiracetam, tiagabine, zonisamide), without positive effects. Since 2010 he began to report hand tremor, postural instability and walking anomalies with increase of traumatic falls. On February 2018 the patient was on polytherapy with: carbamazepine 600 mg daily, lacosamide 250 mg daily, phenobarbital 100 mg daily, clobazam 20 mg daily, rufinamide 2200 mg daily. His brain MRI showed a left frontal cortico-subcortical lesion with microcystic and gliotic components, compatible with dysembrioblastic neuroendocrine tumor (DNET). At the neurological examination he presented a constant, rapid and irregular myoclonic movements of the distal segments of the four limbs, with right prevalence and evocated by the action that impaired the daily activities. He underwent electrophysiological study with EEG-EMG polygraphy, Jerk-locked back averaging, somatosensory evoked potentials, reflexology studies (C reflex) and a cortical myoclonus was diagnosed. For this reason, PER was introduced (2 mg daily) and then carbamazepine was gradually reduced until complete withdrawal with a drastic reduction of both the seizures and the myoclonus, in term of amplitude and frequency.

Conclusion: we reported this case to highlight the beneficial effect of perampanel on cortical myoclonus, even at low dosage, with a important subsequent improvement of autonomy and quality of life.

References: Greenwood J, Valdes J. Perampanel (Fycompa): A Review of Clinical Efficacy and Safety in Epilepsy. P T. 2016 Nov;41(11):683-698.
H. Argente-Escrig, A. Gómez-Ibáñez, and V. Villanueva. Efficacy of perampanel in a patient with epilepsia partialis continua. Epilepsy Behav Case Rep. 2017; 8: 105–107.
Maya Dirani, Wassim Nasreddine, Fatima Abdulla, Ahmad Beydoun. Seizure control and improvement of neurological dysfunction in Lafora disease with perampanel. Epilepsy Behav Case Rep v.2; 2014.

INFARCTION OF THE BODY OF THE CORPUS CALLOSUM: AN ATYPICAL CLINICAL PRESENTATION - CASE REPORT

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Abstract: infarcts of the corpus callosum are rare and show common clinical and radiological features with neoplastic processes. A 64-year old man with an history of parkinsonism presented an acute worsening of motor symptoms. An MRI showed an hyperintensity within the body of corpus callosum, decreased on a subsequent evaluation. Spectroscopy study revealed reduction of Cho, Cr and NAA peaks and a Lac peak, confirming the infarction.

Background: Infarcts of the corpus callosum are considered a rare entity due to a rich blood supply from the secondary branches of three main arteries: the anterior cerebral artery, the anterior communicating artery and the posterior cerebral artery (1). Acute infarction of the corpus callosum arises without distinctive symptoms and signs because it often occurs together with other cerebral ischemic lesions. It can involve more often the splenium than the body and the genu (2). The lack of specific clinical features and the radiological appearance show common features with neoplastic processes, making the differential diagnosis difficult. For this reasons, in few cases, biopsy of the lesion has been prompted (3).

Case report: A 64-year-old man with a past medical history of hypertension, mechanical mitral valve replacement and atypical parkinsonism presented an acute worsening of motor symptoms associated with dysarthria, dysphagia and right hand tremor. A non-contrast CT showed diffuse hypodensity of periventricular white matter, insula and deep white matter. A contrast-enhanced MR imaging, performed few days later, showed on

long-TR images, in addition to multiple white matter hyperintensities, a 14 mm high signal intensity within left posterior part of the body of the corpus callosum with a mass effect on the medial cell of the left lateral ventricle, with diffusion restriction and a subtle enhancement on the post-contrast T1-weighted images (Fig. 1). The diagnosis of infarction was considered. A 5-week later MR examination revealed a lower hyperintensity on long-TR images with a central cavitation of the body of the corpus callosum, with persistent diffusion restriction without mass effect on the lateral ventricle and without contrast enhancement (Fig. 2). Tractography was also performed, displaying a discontinuation at the white matter fibers in left medial side of the body of the corpus callosum with a central malacic area. Spectroscopy study at the lesion of corpus callosum revealed a reduction of Cho, Cr and NAA peaks and an abnormal presence of a Lac peak (Fig.3). The results confirmed the diagnosis of infarction of the body of corpus callosum.

References: Chrysikopoulos H, Andreou J, Roussakis A, Pappas J. Infarction of the corpus callosum: computed tomography and magnetic resonance imaging. Eur J Radiol. 1997 Jul;25(1):2-8.
Yang L-L, Huang Y-N, Cui Z-T. Clinical features of acute corpus callosum infarction patients. Int J Clin Exp Pathol. 2014;7(8):5160-4.
Kasow DL, Destian S, Braun C, Quintas JC, Kagetsu NJ, Johnson CE. Corpus callosum infarcts with atypical clinical and radiologic presentations. AJNR Am J Neuroradiol. 2000 Dec;21(10):1876-80.

CLINICAL EFFICACY AND INCIDENCE OF MOTOR COMPLICATIONS AMONG DIFFERENT L-DOPA ADMINISTRATION MODALITIES IN EARLY PARKINSON'S DISEASE

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Background: It has been suggested that Pulse L-dopa (PLD) stimulation modality in early Parkinson's Disease (PD) may guarantee greater benefit than conventional Intermittent L-dopa (ILD) therapy exploiting the L-dopa Long-Duration Response.
Aims: To evaluate clinical efficacy and incidence of motor complications in early PD treated with different L-dopa administration modalities (PLD or ILD) and Dopamine Agonists (DAs).

Materials and methods: We enrolled de novo PD patients who were stably treated with one of the following treatments: PLD (250 mg once daily), ILD (125 mg three times daily), or DAs. Patients were followed-up every 5 months for 20 months in average. To evaluate clinical efficacy UPDRS - Motor Examination Section (UPDRS-ME) was used. Clinical efficacy was expressed as percent improvement in UPDRS-ME score between "practical-off" state (before taking the first daily dose of the dopaminergic drug after an overnight wash-out) and each follow-up visit. UPDRS-Section IV (UPDRS-IV) item 36 and 32 were used to evaluate incidence rate of wearing-off and dyskinesia over the follow-up period. Abnormal Involuntary Movement Scale (AIMS) was used to assess severity of dyskinesias.

Results: Forty-one de novo PD patients were enrolled: 12 patients were treated with PLD modality, 14 with ILD, 15 with DAs. DAs-treated patients reached a maximum motor improvement of -9.9% after 9 months in average and declining soon after. L-dopa groups reached a similar maximum improvement (-20.6% among PLD versus -19.3% among ILD). However, PLD-treated group maintained such improvement for a longer period of time when compared to ILD-treated group (14.8 ± 1.3 versus 8.8 ± 1.3 months; $p < 0.001$). At the end of the follow-up, a lower risk of motor complications was recorded among DAs-treated patients, while there were no significant differences between PLD and ILD-treated groups.

Conclusion: PLD stimulation modality may guarantee a stable clinical benefit without greater occurrence of motor complications in early de novo PD, representing a potential first line option of treatment.

SEIZURES AND MIGRAINE-LIKE ATTACKS AFTER RADIATION THERAPY (SMART). A NEW MEANING OF AN OLD ACRONYM

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Background: Stroke-like migraine attacks after radiation therapy (SMART) is a late-onset complication of cranial irradiation, characterized by headache, seizures and focal deficits, with suggestive MRI changes. Clinical and neuroimaging findings typically resolve after a few weeks. Seizures or status epilepticus are reported in 69% of SMART patients.
Case reports: We recently observed two patients with SMART presenting with focal status epilepticus and non-migraine headache. Patient 1: a 54-year-old man underwent medulloblastoma resection at 18 years, followed by craniospinal irradiation and chemotherapy. He came for 1-week-history of daily, bilateral, tightening headache and quasi-continuous visual hallucination, associated with left homonymous hemianopia. EEG showed continuous rhythmic spikes over right occipital regions. MRI showed DWI/T2-FLAIR hyperintensity of the right temporo-parieto-occipital cortex with gyral thickening and gadolinium enhancement; post-radiation leukoencephalopathy was also evident. Treatment with carbamazepine and clobazam gave seizure freedom. Hematological and CSF screening was unremarkable. A control MRI 5 days later showed disappearance of DWI restriction. Patient 2: a 23-year-old man underwent medulloblastoma resection at 6 years, then undergoing craniospinal irradiation and chemotherapy. He came for a two-month-history of daily bilateral, tightening headache associated with short-lasting visual elementary hallucinations, with right homonymous hemianopia. EEG showed continuous sharp theta rhythm over left occipital regions. Patient recieved i.v. midazolam with disappearance of visual hallucinations and EEG normalization. Daily levetiracetam determined seizure-freedom. MRI showed post-radiation leukoencephalopathy, DWI/T2-FLAIR hyperintensity of the left occipital cortex, gyral thickening and gadolinium enhancement. A control MRI 3 months later showed spontaneously hyperintense gray matter lesion on T1-weighted sequences (laminar necrosis) in the parieto-occipital cortex (not detectable before) and DWI restriction signal diseppeared.
Discussion and conclusions: These clinical findings emphasize that seizures may be

a key clinical feature of the syndrome. Indeed, we believe that the acronym SMART is inaccurate, since it darkens seizures among clinical features. Moreover, the term "stroke-like migraine attacks" is misleading since it does not fit the features of headaches occurring in described SMART-patients in the literature. The presence of visual hallucinations may have led to a diagnosis of migraine with aura, although in some cases an alternative diagnosis of focal occipital seizures with visual features, supported by ictal EEG recordings, should be considered. In this view, we suggest renaming this entity as "Seizure and Migraine-like Attacks after Radiation Therapy". The new acronym, modified in its meaning but not in its appearance (SMART), better reflects the main clinical features and may allow neurologists to more easily recognize this condition.

HEPATIC MICROABSCESSES DURING CMV REACTIVATION IN A MULTIPLE SCLEROSIS PATIENT AFTER ALEMTUZUMAB TREATMENT

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Background: The anti-CD52 monoclonal antibody alemtuzumab is a highly active treatment for multiple sclerosis (MS) causing rapid depletion of B and T lymphocytes. Opportunistic Cytomegalovirus (CMV) infections have been reported in MS patients treated with alemtuzumab. We report one patient who developed a CMV reactivation with hepatic involvement three weeks after the first cycle of alemtuzumab. This patient achieved a complete recovery with valganciclovir.

Aims: To highlight the risk of CMV reactivation in the first month following alemtuzumab infusion and suggest an appropriate surveillance.

Materials and methods: A 45-year-old caucasian woman, after a left optic neuritis, was diagnosed in 2006 with MS. She started interferon beta-1a subcutaneously, which

she discontinued because of poor efficacy and hypertransaminasemia; then, natalizumab, that was interrupted due to hypertransaminasemia and one pyramidal relapse. In 2014 she started fingolimod which was stopped because of severe lymphopenia and hypertransaminasemia. In September 2016, after three sensorimotor relapses, she began alemtuzumab (12 mg/day intravenously for 5 consecutive days). On the first day of infusion, she started oral prophylaxis for herpes infection (acyclovir 200 mg/twice a day). Three weeks after last alemtuzumab infusion, she developed fever, a modest hypertransaminasemia and an increased C-reactive Protein. The infective and autoimmune panel showed a CMV reactivation with positivity of CMV viral DNA polymerase chain reaction (PCR) (17318 copies/ml), of IgG and negative IgM; the liver ultrasonography demonstrated multiple hepatic microabscesses not detected previously. Oral valganciclovir was administered at dose of 450 mg twice daily for 4 weeks.

Results: The CMV viral load became undetectable 13 days after the beginning of antiviral treatment. Fever, inflammation indexes and hypertransaminasemia resolved in two weeks. Two months later, liver ultrasonography showed regression of the microabscesses. This report suggests that this opportunistic infection should be considered in febrile patients with hepatic markers alteration after alemtuzumab and the need of an appropriate surveillance in order to manage this potential opportunistic infection. Because the acyclovir prophylaxis could be ineffective against the CMV reactivations, patients with fever and hypertransaminasemia, after alemtuzumab, should undergo CMV PCR assay and, in our opinion, liver ultrasonography to demonstrate hepatic involvement.

Conclusions: We suggest performing baseline CMV status before alemtuzumab in MS patients and implementing a weekly monitoring with CMV PCR assay during the first month after infusion. This surveillance would allow a prompt switch from acyclovir to a more specific antiviral treatment (ganciclovir or valganciclovir) in case of CMV reactivation.

References: MacDonald, G.A., Greenson, J.K., DelBuono, E.A., et al., 1997. Mini-microabscess syndrome in liver transplant recipients. Hepatology 26 (1), 192–197.

Clerico, M., De Mercanti, S., Artusi, C.A., et al., 2017. Active CMV infection in two patients with multiple sclerosis treated with alemtuzumab. Mult. Scler. 23 (6), 874–876. http://dx.doi.org/10.1177/1352458516688350. (Epub 2017 Feb 1).

O'Brien, S.M., Keating, M.J., Mocarski, E.S., 2006. Updated guidelines on the management of cytomegalovirus reactivation in patients with chronic lymphocytic leukemia treated with alemtuzumab. Clin. Lymphoma Myeloma 7 (2), 125–130.

A CASE OF MILD NATALIZUMAB-ASSOCIATED PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY WITH A BENIGN COURSE WITHOUT PLASMA EXCHANGE

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Introduction: Natalizuzmab (NTZ) is a monoclonal antibody that inhibits the migration of activated T cells across the blood–brain barrier into the central nervous system. It is widely used as a disease modifying drug in Multiple Sclerosis (MS), but it is associated with an increased risk of Progressive multifocal leukoencephalopathy (PML) due to a reactivation of John Cunningam (JC) virus. Behavioural and cognitive symptoms are the most frequent NTZ-PML's manifestation and positivity to serum JCV antibodies, treatment duration and prior uses of immunosuppressive drugs are risk factors. Magnetic resonance imaging (MRI) is an useful tool in order to reveal an early diagnosis of PML.

Case report: A man was diagnosed with relapsing remitting MS in 2008, at the age of 33. He was treated consecutively with interferon beta 1 b, azathioprine 125 mg daily, glatiramer acetate 20 mg until 2014, without clinical benefits. In July 2014 was administered mitoxantrone 8mg/m2, immediately suspended for adverse events. In December 2014 he started Natalizumab 300 mg monthly, with absence of relapses and new or gadolinium enhancing (GE) lesions during treatment. He was positive for anti JCV serum antibodies (index 1,523). In December 2015, after 11 administration of Natalizumab, he presented a new MRI showing an enlarging FLAIR hyper intense/ T1 hypo intense lesion near the frontal right cortex, without GE. He also referred the presence of concentration difficulties and troubles in identify faces. Natalizumab was immediately interrupted. He underwent a neurocognitive test battery underlining an attention and face-recognizing deficiency (Benton's test). The polymerase chain reaction (PCR) on cerebrospinal fluid (CSF) showed 11 JCV DNA copies/ml. An MRI scan performed after a month showed no modification. The patient was stable and nor plasma exchange (PLEX) or other measures are taken, but only a strict clinical and radiological follow up with monthly brain MRI scans.

Discussion: The patient experienced a definite NTZ associated PML with a very benign clinical course, without signs of immune reconstitution inflammatory syndrome (IRIS). Our case started with unilobar frontal lesion, the most common kind of presentation, especially in asymptomatic course. Our data empathized the role of MRI in showing early PML signs. Recent evidence described no significant benefits in using PLEX in NTZ PML, even if it is widely used; a non-interventional approach could be a valid pathway, preventing IRIS due to an excessively rapid immune reconstitution. Furthermore, deepest cognitive evaluation could be helpful in detecting mild or unusual symptoms.

References: Landi D, De Rossi N, Zagaglia S, Scarpazza C, Prosperini L, Albanese M, Buttari F, Mori F, Marfia GA, Sormani MP, Capra R, Centonze D; Italian PML study group. *No evidence of beneficial effects of plasmapheresis in natalizumab-associated PML*. Neurology. 2017 Mar 21;88(12):1144-1152.
Prosperini L, de Rossi N, Scarpazza C, Moiola L, Cosottini M, Gerevini S, Capra R; Italian PML study group. *Natalizumab-Related Progressive Multifocal Leukoencephalopathy in Multiple Sclerosis: Findings from an Italian Independent Registry.* PLoS One. 2016 Dec 20;11(12).
Dong-Si T, Richman S, Wattjes MP, Wenten M, Gheuens S, Philip J, Datta S, McInnch J, Bozic C, Bloomgren G, Richert N. *Outcome and survival of asymptomatic PML in natalizumab-treated MS patients.* Ann Clin Transl Neurol. 2014 Oct;1(10):755-64.

CYSTATIN B DODECAMER EXPANSION IN A MILD FORM OF MYOCLONIC EPILEPSY

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Background: Unverricht-Lundborg disease (ULD), progressive myoclonic epilepsy type 1 (EPM1A), is an autosomal recessive inherited neurodegenerative disorder characterized by age of onset from 6 to 16 years, stimulus-sensitive myoclonus, and tonic–clonic epileptic seizures. Some years after the onset ataxia, incoordination, intentional tremor, and dysarthria develop. Depression, anxiety and emotional lability were observed in 40% of patients with EPM1A (Chew et al. Mov Disord 2007).
Aims: To describe a mild form of EPM1A with prominent behavioural features.
Materials and Methods: A 53 years old woman presented to our Epilepsy Centre with a 10-year history of depression and epilepsy. During the adolescence, she developed jerks involving all limbs. EEG recording revealed generalized spikes. At the age of 23 years, she was diagnosed as idiopathic generalized epilepsy and started on valproic acid

(VPA) and levetiracetam (LEV) therapy that gained mild clinical benefits. In the following years, she began to develop a motor slowdown and depression, anxiety symptoms and mild cognitive decline. For this reason, clonazepam and paroxetine were added, while VPA and LEV were suspended. Afterwards, buccal dyskinesia and myoclonic jerks made worse, leading to a difficult gait. We performed a comprehensive clinical and laboratory investigation including EEG and polygraphic video -EEG recording, somatosensory evocated potentials (SEPs), cortical reflex (C reflex) study and 3Tesla brain MRI. The size of the CSTB dodecamer repeat expansion was also determined. Informed consent was obtained according to the protocols approved by the local ethics committee. **Results:** After clonazepam withdrawal, neurological examination revealed severe action myoclonus of upper limbs. EEG recordings showed diffuse spike-waves and a photoparoxysmal response, the polygraphic EEG recording demonstrated myoclonic jerks of upper limbs that were related to spike-waves. SEPs study showed giant potentials. The median nerve stimulation at the wrist highlighted a C reflex with longer latency. Brain MRI displayed cortical atrophy, especially in centro-parietal region, bilaterally. The diagnosis was confirmed by the demonstration of a pathogenic mutation in both alleles of the EPM1 gene.

Conclusions: Our findings emphasize the mild end of the phenotypic spectrum of CSTB mutations. The screening of the CSTB gene in IGE and JME with atypical features should be considered in the genetic diagnosis of epilepsies.

References: Chew NK, Mir P, Edwards MJ, et al. The natural history of Unverricht-Lundborg disease: a report of eight genetically proven cases. Mov Disord 2007; 23: 107-13.

MOVEMENT DISORDERS IN ANGELMAN SYNDROME

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Background and aims: Movement disorders are a common finding in Angelman syndrome (AS), even though there are few reports in literature. Cortical myoclonus with or without electroencephalographic changes has been commonly described, but in small

series only. Despite they represent a hallmark of the disease, abnormal movements in AS are still poorly characterized. The existence of dystonic limb posturing in subjects with AS has been reported in a single study, but its characteristics and prevalence are still unknown. The aim of our study is to evaluate the prevalence and the severity of myoclonus and dystonia in a wide cohort of subjects with AS.

Methods: Patients with AS were included during AS Organisation (OrSA) national conferences; clinical history, neuropsychological evaluation, video-EEG and simultaneous surface EMG with myoclonus activation tasks were performed. We tested: severity, electrophysiological characteristics and neurological examination during myoclonus activating tasks; moreover presence, localization and severity of dystonia were assessed.

Results: Twenty-four patients were included (12 female, median age 19 years, range 3.4-48.3). Eighteen patients (15/18 treated with antiepileptic drugs) presented with spontaneous cortical myoclonus localized at upper limbs, without EEG alterations, increased by activating tasks. Myoclonus was severe (> 1 minute) in 13/18 patients. Twenty-one of 24 patients presented with upper limbs dystonia of different severity (moderate in 12/21, mild in 9/21) and 5/21 with neck dystonia (moderate in 4/5, mild in 1/5).

Discussion and conclusion: Our study involves a large sample of patients with AS. Our findings demonstrate that cortical myoclonus is often severe and rarely associated with EEG alterations. Dystonia more commonly involves upper limbs and it is often of mild/moderate severity.

CONGENITAL MYASTHENIC SYNDROMES: CLINICAL AND MOLECULAR FEATURES IN A COHORT OF ITALIAN PATIENTS

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Background: Congenital myasthenic syndromes (CMS) are a group of heterogeneous inherited disorders caused by mutations in genes encoding proteins, essential for the integrity of neuromuscular transmission. CMS are characterized by fatigable muscle weakness (e.g., ocular, bulbar, limb muscles) with onset at birth or in early childhood; rarely, symptoms may present later. The number of genes known to cause CMS is currently thirty(1). The main proteins involved in the pathogenesis of CMS are: choline acetyltransferase (ChAT), the endplate species of acetylcholinesterase (AChE), 2-laminin, the acetylcholine receptor subunits (CHRNE, CHRND), rapsyn, plectin, Na(v)1.4, the muscle specific protein kinase (MuSK), agrin, downstream of tyrosine kinase 7 (Dok-7), and glutamine-fructose-6-phosphate transaminase 1 (GFPT1)(2). Clinical, electrophysiological and morphological studies are essential for molecular studies, counseling and therapy.
Aims: Aim of this study is to describe clinical and genetic characteristics in a cohort of CMS patients, coming from a great area of Southern Italy, including Sicilia and Calabria, who referred to our Centre.
Materials and methods: In the last 27 years, 19 patients (11 females; 8 males) with CMS were clinically and genetically defined in our Department. The onset of symptoms ranged from birth to 23 years of age. Diagnosis was based on clinical features, laboratory tests (Anti-AChR antibodies, Anti- MuSK), electrophysiological investigations (electromyography , repetitive nerve stimulation , single fiber electromyography), response to treatment with pyridostigmine and genetic analysis. Results: In our cohort we described 5 CMS subtypes: 11 CHRNE, 2 CHRND, 4 GFPT1, 1 DOK-7, 1 CHAT. In two sisters CHRND mutations resulted in a lethal phenotype. Pyridostigmine was the best treatment in CHRNE patients. Salbutamol was effective in DOK-7 and CHRND forms. Ephedrine was used in one CHRNE patient with a clear benefit. Discussion and conclusion: We confirm that,

according to literature(3), CMS due to CHRNE mutation are the most frequent also in our cohort. We described for the first time a new CHAT and DOK-7 mutation. We have also identified a prevalence of T159P and A411P CHRNE mutation among Sicilian patients. In conclusion we underline the main role of genetic analysis as an essential tool to characterize CMS.

References: Nicole S, Azuma Y, Bauché S, et al. Congenital Myasthenic Syndromes or Inherited Disorders of Neuromuscular Transmission: Recent Discoveries and Open Questions. J Neuromuscul Dis. 2017;4(4):269-284. Engel AG. Current status of the congenital myasthenic syndromes. Neuromuscul Disord. 2012 Feb;22(2):99-111.

Engel AG, Shen XM, Selcen D, et al. Congenital myasthenic syndromes: pathogenesis, diagnosis, and treatment. Lancet Neurol. 2015;14(4):420-34.

BISMUTH RELATED ACUTE NEUROTOXICITY AS STROKE MIMIC: A CASE REPORT

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Stroke mimics (SM) are non-vascular conditions that present with an acute neurological deficit simulating acute ischemic stroke. The most common clinical SM includes conversion / functional (psychiatric disorder); seizures and postictal paralysis; toxic-metabolic disturbances; brain tumors; infections, and migraine[1]. Bismuth-based therapies are used in developing countries to treat gastrointestinal (GI) disorder, mostly for eradication of Helicobacter pylori.

We observed a 51-year-old woman arrived to our E.R. with a right facio-brachio-crural moderate hemiparesis with associated ipsilateral hypoesthesia, in the suspicion of acute ischemic stroke. Before admission, the patient had taken 18 tablets of Pylera®140/125/125 mg (Bismuth potassium subcitrate + Metronidazole + Tetracycline hydrochloride) in 20 hours for gastroinstestinal problems. She has been studied in our Neurology department through lab tests, EKG, ultrasound and radiological examinatios, according to the Italian ISO-SPREAD guidelines[2]; all these tests were normal. On the other hand, bismuth's levels resulted much higher than the national recommended standards. Many cases of bismuth related neurotoxicity have been described in literature since 1978, however, so far, no cases of acute Bi neurotoxicity simulating a stroke have

been reported before this case. The Naranjo Algorithm (NA) for adverse drug reactions (ADRs) [3] score was 7 (doubtful 0, possible 1-4, probable 5-8, highly probable ≥ 9). The lesson that can be learnt from this reported experience is that acute focal neurological signs can be due to bismuth intoxication and warning about the real safety of drugs containing bismuth.

References: Vilela P. Acute stroke differential diagnosis: Stroke mimics. Eur J Radiol. 2017 Nov;96:133-144.
Gensini GF, Carolei A, Zaninelli A et al. SPREAD-Stroke Prevention and Educational Awareness Diffusion. Ictus cerebrale: Linee guida italiane di prevenzione e trattamento. In: ISO-spread [online] Available at: www.iso-spread.it. Accessed July 21, 2016.
Naranjo CA, Busto U, Sellers EM et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981 Aug;30(2):239-45.

CAN THE FOAM CELLS AID TO DETERMINATE CLOTS ETIOLOGY?

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Background: The mechanism underling arterial or cardiac thrombus formation is different. The principal factor of clots formation in the arterial vessels is the rupture of atheroma (1). The atheroma is composed by foam cells (FC), which consist of macrophages and smooth muscle cells filled in lipids (2). When the atheroma breaks down, the clot incorporates foam cells. Other clots, due to their different formation, should not contain foam cells. Endovascular thrombectomy provides the opportunity to investigate retrieved thrombi and evaluate the foam cells (FC) presence.
Aims: This is a pilot study that evaluates FC presence in the arterial clot. The principal aim of this study was to demonstrate if foam cells clots group (FCs) had different characteristics in comparison with group without foam cells (NFCs).
Materials and methods: 41 thrombi samples were retrieved by trombectomy and fixed. Slices of samples were obtained and stained with haematoxylin-eosin. Pathologists evaluated the FC presence. Baseline investigation included medical history, neurological examination, brain imaging and blood tests. The patients performed clinical tests to evaluate the presence of atheromatous pathology (ultrasound images or angio-CT).

Continuous data were presented as means with standard deviations (SD±). Categorical data were presented as frequencies and percentages. For statistical significance determination, we used 2 and T Student tests.

Results: On the histopathologic examination, 8 clots presented FC, 33 did not present any FC. The FCs group showed a significant difference in anticoagulant use (60% vs 14% P0.029), in C- reactive protein (CRP) (0.68 vs 2.81 n.v.<0.50mg/dl; P0.01), in white blood cells (WBC) (8*103cell\mm3 vs 10.1*103cell\mm3; P0.025), compared to the NFCs group. The FCs group showed a difference in percentage of presence of large-artery atherosclerosis (100% vs 81%), low HDL cholesterol (100% vs 78%), and hypercholesterolemia (62% vs 31%), compared to NFCs group. No differences in patient age, sex, diabetes, hypertension and smoke use between two groups were found.

Discussion: Data showed different frequencies of anticoagulant use, more used in FCs group. In NFCs group, the anticoagulant use was lower, with INR under range. Moreover, NFCs group had greater CRP and WBC blood values, that could indicate a pro-coagulant inflammatory state, described as possible cardioembolic factor (3). The percentages of large-artery atherosclerosis, low HDL cholesterol and hypercholesterolemia diverged between groups, but did not reach statistical difference due to the low sample size.

References: Peter Libby, Paul M Ridker, Göran K. Hansson. Progress and challenges in translating the biology of atherosclerosis. Nature 2011 May 19. Vol 473.

Tabas I. Macrophage death and defective inflammation resolution in atherosclerosis. Nat Rev Immunol. 2010 Jan;10(1):36-46. doi: 10.1038/nri2675. Epub 2009 Dec 4.

Rose Mary Ferreira Lisboa da Silva. Influence of Inflammation and Atherosclerosis in Atrial Fibrillation. Curr Atheroscler Rep (2017).

METFORMIN AND OUTCOME IN ISCHEMIC STROKE PATIENTS UNDERGOING REPERFUSION THERAPY

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Abstract: The present study looks at the correlations between antidiabetic drugs and the outcome in patients undergoing reperfusion treatments at U.O.S Stroke Unit of Messina University Policlinic, showing a better outcome in metformin users.

Background: Diabetes mellitus is an important risk and negative prognostic factor for ischemic stroke. The use of antidiabetic drugs before stroke is shown to have a relevant role in stroke risk and outcome. 1 Metformin is correlated with the lowest ischemic stroke risk, the lowest admission severity and the best discharge outcome among all antidiabetic drugs.2,3 Currently no study in literature correlates metformin or other antidiabetic drugs with the outcome of patient undergoing reperfusion treatments.

Aims: This study evaluates the relationship between antidiabetic drugs and the outcome in patients with ischemic stroke undergoing reperfusion procedures. The starting hypothesis is that diabetics using metformin before stroke can have a better prognosis due to molecular peculiarities.

Materials and methods: The analysed population is formed by 37 type 2 diabetics who were selected among 209 patients treated with reperfusion therapy at U.O.S Stroke Unit of Messina University Policlinic. These 37 patients were divided according to the class of antidiabetic medications taken, the main groups are: metformin alone (9 patients), metformin alone or in combination (19), sulfonylureas-glinides alone (7), sulfonylureas-glinides alone or in combination (13), insulin alone (9), insulin alone or in combination (11). Outcome is assessed according to discharge National Institute Health Stroke Scale (NIHSS), difference between admission NIHSS and discharge NIHSS (Δ) and intra-hospital death.

Results: The lowest NIHSS score at discharge (10) is registered in metformin users, the highest is registered in insulin alone users (23,44). Best Δs, both positive, are seen in sulfonylureas-glinides alone group (2,43) and metformin alone group (2,11). The others groups have negative Δs and the lowest is in insulin alone users (-7). The lowest mortality rate is registered in metformin alone users (11%, 1/9) on the contrary the highest is in insulin alone users (44,44%, 4/9).

Conclusion: Metformin use before ischemic stroke could be associated with a better prognosis in diabetic patients with ischemic stroke undergoing reperfusion therapies. Worsening is seen in insulin users. It cannot be excluded that the difference in outcomes among groups could be caused by more severe diabetes and existing comorbidities.

References: Ferrannini E, DeFronzo RA. Impact of glucose-lowering drugs on cardiovascular disease in type 2 diabetes. Eur Heart J. 2015 Sep 7;36(34):2288-96.

Cheng YY, Leu HB, Chen TJ et al. Metformin-inclusive therapy reduces the risk of stroke in patients with diabetes: a 4-year follow-up study. J Stroke Cerebrovasc Dis. 2014 Feb;23(2):e99-105.

Mima Y, Kuwashiro T, Yasaka M et al. Impact of Metformin on the Severity and Outcomes of Acute Ischemic Stroke in Patients with Type 2 Diabetes Mellitus. J Stroke Cerebrovasc Dis. 2016 Feb;25(2):436-46.

ACUTE STROKE TREATMENT IN BASILAR ARTERY OCCLUSION PATIENTS. A MOTHERSHIP CLINICAL SERIES

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Background: Basilar Artery Occlusion (BAO) is responsible for 1-4% of ischemic strokes. In 86-95% of the untreated cases, it results in death because of the vital cerebral structures supplied by the basilar artery. Diagnosis is often delayed because of the unclear and various symptoms and the endovascular treatment is often attempted even beyond 6 hours, sometimes reaching more than 12 hours from the onset of symptoms. Purpose: In this study we report cases of BAO referred from the area of Sicily and Calabria directly to our center in Messina in the so called mothership way. We aim to stress the value of centralization, especially in posterior strokes, and to assess the association between clinical outcome and pc-ASPECTS1, pc-Collateral Score (PC-CS)2, and different endovascular technics used.

Methods: We included consecutive patients with CTA or angiographically confirmed BAO, referred to our Hub center from 2014 to 2017. All the patients underwent CT scan and/or MRI with the purpose to perform endovascular treatment. We assessed the pc-ASPECT on MR images and the PC-CS for every patient.

Preliminary results: The study population consisted of 18 patients (mean age: 66), 13 males and 5 females. 5 patients came from Messina, 1 from Reggio Calabria, the others from different parts of Sicily. The mean NIHSS at admission was 16. 12 patients underwent thrombo-aspiration (unsuccessful in 2 cases): 3 of these were treated with additional intra-arterial thrombolysis (IAT); 1 received intravenous thrombolysis (IVT) before thrombo-aspiration and in 3 cases a stent Neuroform Atlas was placed to treat the underlying stenosis. Mechanical thrombectomy was applied to 3 patients. 1 patient

underwent both thrombo-aspiration and thrombectomy. 2 patients underwent IVT, 1 of these in association with IAT. In 15 patients successful recanalization was obtained, defined as Thrombolysis in Cerebral Infarction (TICI) score 2b-3. The average onset-to-treatment time (OTT) was 7 hours and 5 minutes. The mean pc-ASPECT was 5 and the mean PC-CS was 5. NIHSS > 5 at discharge was reached in 6 patients. Mortality at 3 months was 39%.

Conclusions: Our preliminary results showed a similar rate of death after treatment compared to the data of the literature3 even with a long average OTT, a low pc-ASPECT and PC-CS. We suggest adopting centralization especially for BAO patients, taking into account the delayed diagnosis and the extensive OTT. Mothership system may allow a wide recruitment of patients that otherwise would be destined to a poor prognosis.

References: Tei H, Uchiyama S, Usui T, Ohara K. "Posterior circulation ASPECTS on diffusion-weighted MRI can be a powerful marker for predicting functional outcome". J Neurol. 2010 May; 257(5):767-73.
Van der Hoeven EJ, McVerry F, Vos JA, Algra A, Puetz V, Kappelle LJ, Schonewille WJ; BASICS registry investigators. "Collateral flow predicts outcome after basilar artery occlusion: The posterior circulation collateral score". Int J Stroke. 2016 Oct; 11(7):768-75.
Singer OC, Berkefeld J, Nolte CH, Bohner G, Haring HP, Trenkler J, Gröschel K, Müller-Forell W, Niederkorn K, Deutschmann H, Neumann-Haefelin T, Hohmann C, Bussmeyer M, Mpotsaris A, Stoll A, Bormann A, Brenck J, Schlamann MU, Jander S, Turowski B, Petzold GC, Urbach H, Liebeskind DS; ENDOSTROKE Study Group. "Mechanical recanalization in basilar artery occlusion: the ENDOSTROKE study". Ann Neurol. 2015 Mar;77 (3):415-24.

WHEN THE PFO SHOULD NOT BE CLOSED

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Patent Foramen Ovale (PFO), a common congenital cardiac abnormality, consists in a dynamic tunnel between the atria of the heart. PFOs are found in approximately 20-30% of the general population, in up to 40% of all cryptogenic strokes and 60% of all migraine-with-aura patients[1]. Current treatments range from medical therapy (MT) using anticoagulant and/or antiplatelet agents, endovascular PFO closure (PFO-C) by meshed devices, or even surgical closure[1]. The latest meta-analyses showed a better protective

effect of PFO-C plus MT on stroke recurrence in selected patients, compared to medical therapy with an NNT of 33[2]. PFO-C plus MT did not show minor incidence of major bleeding (MB), serious adverse events (SAEs) or mortality rate (MR) compared to MT. Nevertheless, meta-analyses showed a major risk of atrial fibrillation (AF), with a global NNH of 49. Subgroup analyses did not show any benefit of PFO-C plus MT in small shunt size group versus MT alone. It is important to underline that only a 91% of patients achieved a successful device implantation and at 6 months only 82% of patients met criteria for effective closure[2]. This means that, in order to reach 33 successful PFO-C, about 39 patients underwent to implantation procedure. Another key point is that PFO-C groups were treated with dual antiplatelet therapy after device implantation up to 6 months, followed by monotherapy with either aspirin, Clopidogrel, or aspirin with dipyridamole, without indications about the end of MT. PFO-C then exposed patients to risks of surgery, without reducing significantly the risks of adverse effects of antiplatelet therapy. Today there are no trial available comparing PFO-C to anticoagulant therapy, especially to the non-vitamin-k oral anticoagulants (NOACs). Oral anticoagulants showed superior efficacy to antiplatelet therapy in stroke prevention, effective venous thrombosis prevention, less bleeding risk, and greater convenience of use than warfarin. Another emergent use of PFO-C is to reduce attack of migraine with aura (MA). Although early trials suggested benefit to PFO closure, these were of poor quality, and subsequent randomized trials have failed to yield positive results. Three major trials have been completed today[3]. The trials did not reach statistical significance for headache cessation in PFO closure and PFO-C have a higher incidence of SAEs[3]. There is a significant reduction in days per month of median total migraine headache in the PFO-C group, but all patients took double antiplatelet therapy, which might have contributed to some improvement in symptoms.

References: Lattanzi S, Brigo F, Cagnetti C. et al. Patent Foramen Ovale and Cryptogenic Stroke or Transient Ischemic Attack: To Close or Not to Close? A Systematic Review and Meta-Analysis. Cerebrovasc Dis. 2018 Apr 12; 45(5-6):193-203.

Volker S, · Yingfeng, Athanasios K. et al. Patent foramen ovale closure or medical therapy for cryptogenic ischemic stroke: an updated meta-analysis of randomized controlled trials. Clin Res Cardiol. 2018 Mar 2 22:1-11.

Hildick-Smith D, Williams TM. Patent Foramen Ovale and Migraine Headache. Interv Cardiol Clin. 2017 Oct;6(4):539-545.

ISOLATED INSULAR STROKE: CLINICAL PRESENTATION AND MANAGEMENT

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Background: The symptoms related to insular dysfunction has been the object of several studies in patients affected by stroke, but they are often intermingled with concomitant symptoms. Isolated insular strokes (IIS) are rarely seen without involvement of adjacent structures supplied by the middle cerebral artery (MCA). The insula is vulnerable to ischemia due to thromboembolic vascular occlusion of the M1 MCA segment and the two main branches of the MCA (M2), where they abruptly arise from the main stem at a right angle. This topographical and anatomical characteristic could enable an embolism, especially due to atrial fibrillation (AF), to occlude in the transition region between the M1 and M2, while the proximal origin of vascular supply protects the insula from ischemia due to hemodynamic factors.
Aims: The aim of our study is to characterize the clinical presentation of acute ischemic strokes in patients with a first event stroke restricted to the insular territory with specific attention to atypical manifestation of insular dysfunction.
Materials and methods: We found 233 patients with a first event stroke involving the insular territory and 13 cases of ISS, from the stroke registry of the "G. Martino" Polyclinic Hospital, University of Messina, between the 28th February 2014 and the 10th May 2017. IIS patients showed CT/MRI lesions restricted to the insular region. Exclusion criteria were: coexisting neurological diseases, structural brain lesions, extension to the subinsular area > 50% of the total infarct volume.
Results: We identified 13 IIS patients (mean age 74 years), with one or a combination of typical symptoms - motor deficits (13/15), sensory impairment (6/13), speech disorder (11/13) - and atypical symptoms - hemispatial inattention (2/13), sleepiness (2/13), confusion (2/13), vestibularlike syndrome (5/13), auditory (1/13), transient dysphagia (3/13), space-time disorientation (1/13), confusion and agitation (1/13), weeping tendency (1/13) and anxiety (1/13), autonomic disturbance (11/13), cardiac disturbances (11/13, newly-detected AF, atrioventricular blocks and an increased ectopic beats, hystory of AF).
Discussion and conclusion: IIS were described only in few previous studies and their incidence is not well defined. IIS results in multimodal deficits combining motor and

somatosensory, speech or language, vestibular-like, autonomic and cognitive disturbances. AF detected after acute ischemic stroke may be short-lasting and an autonomic epiphenomena of insular infarctions. Early and accurate identification of stroke patients at high risk for AF is important for cardiac monitoring.

References: Nieuwenhuys R. The insular cortex: a review. Brain Struct Funct. 2013 Mar;218(2):303-52.
Kang J, Hong JH, Jang MU, Kim BJ, Bae HJ, Han M. Cardioembolism and Involvement of the Insular Cortex in Patients with Ischemic Stroke. PLoS One. 2015 Oct 21;10(10):e0139540.
Lemieux F, Lanthier S, Chevrier MC, Gioia L, Rouleau I, Cereda C, Nguyen DK. Insular Ischemic Stroke: Clinical Presentation and Outcome, Cerebrovasc Dis Extra 2012;2:80-87.

IVIG VS STEROID IN CIDP: OUR EXPERIENCE ON IMMUNOGLOBULIN TREATMENT

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Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic progressive or relapsing autoimmune neuropathy. Symptoms typically include symmetrical, proximal and/or distal weakness and sensory loss. Intravenous immunoglobulin (IVIg) and steroids are both used as initial treatment of CIDP. Corticosteroids carry the long-term risk of serious side effects. IVIg have side effects such as transient cutaneous rash, headache, hypertensions and cardiac overload, usually related to infusion speed. We describe a cohort of 25 patients with CIDP (7 F and 18 M) defined according to the EFNS/PNS criteria. All patients were evaluated at baseline and every 6-month. Clinical follow-up included: the Overall Neuropathy Limitation Scale (ONLS) to assess disability, MRC sum-score to evaluate muscle strength, and the Life Quality Index questionnaire (LQI) as a quality of life measures. A therapeutic shift from intravenous to subcutaneous immunoglobulin was performed in 11/25. We observed a maintenance of clinical efficacy in our CIDP population, except in 2 patients. Transient adverse events were observed in two cases. A global personal satisfaction as well as a significant improvement of the quality of life measures in SCIg were observed. Our experience strongly confirms the long term tollerability of immunoglobulin and the positive effects on maintenance of muscle strength and functionality.

NON CONVULSIVE STATUS EPILEPTICUS PRESENTING AS MIGRAINOUS ATTACK

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Abstract: We report the case of a young male patient suffering from migraine who presented an attack of severe cephalic pain, mental blurring, psychomotor agitation, dysphasia and episode amnesia during which the EEG showed continuous epileptiform discharges on both the posterior temporal regions.

Background: The term "epileptic headache" (EH) refers to an episode of cephalic pain caused by an ictal epileptiform discharge. This is a rare disorder. To our knowledge only 32 patients with EH have been reported and only 12 patients had headache attacks lasting hours or days. Among these, 8 patients were also affected from obvious epileptic seizures, whereas in 4 patients the sole type of seizure was represented by prolonged headache, associated with continuous epileptiform discharges on the posterior regions, occipital or parieto-occipital [1].

Aims: To report a new case of long lasting EH configuring an unusual type of non-convulsive status epilepticus (NCSE).

Patient: 16-years-old boy, with normal neurologic examination and MRI, suffering from migraine with and without aura. He never had epileptic seizures. The migraine attacks occurred every two or three months, usually were responsive to analgesic drugs and ceased after 1-2 hours. Prophyilactic treatment first with Topiramate and thereafter with Lamotrigine 100mg/day, was not effective. During an attack presenting with severe pain, mental blurring, psychomotor agitation, dysphasia and episode amnesia, the EEG showed continuous epileptiform discharges on both the posterior temporal regions. The attack ceased spontaneously after 6 hours, roughly.

Discussion and conclusion: The presence of continuous epileptiform discharges on the EEG recorded during the migraine attack led to the diagnosis of EH. This is a rare and underdiagnosed disorder. Only 32 cases are reported in the literature. The majority

showed short-lasting headache attacks (seconds-minutes) that could be or not followed by obvious epileptic manifestations. Long-lasting attacks (hours- days) of EH, whose sole or main symptom was headache, occurring in patients without other types of epileptic seizures, have been reported only in four cases and could be classified as NCSE with.

References: Cianchetti C, Dainese F, Ledda MG, Avanzini G. Epileptic headache: A rare form of painful seizure. Seizure 2017; 52: 169–75.

NEURO-BEHÇET'S DISEASE PRESENTING AS AN ISOLATED PROGRESSIVE COGNITIVE AND BEHAVIORAL SYNDROME

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Background: Behçet's disease (BD) is a chronic disease manifesting as a vasculitis that affects arteries and veins of any size. Neurological dysfunction, defining neuro-Behçet's disease (NBD), can be present in up to 44% of patients. It is usually characterized by a progressive or relapsing multifocal neurological syndrome, similar to other acquired leukoencephalopathies, often associated with impairments in cognitive functions and behavior. In this report, we describe an elusive case of NBD presenting exclusively with progressive cognitive and behavioral deterioration.
Materials and methods: Patient's clinical history subacutely started at age 42 with memory disturbances, non-fluent speech and tendency to disinhibition, with relentlessly progressive course, thus severely impairing social skills and daily life activities in the following months. During the entire disease course, the patient underwent extensive clinical, instrumental and laboratory evaluations, including neuropsychological examinations, brain MRI, cerebral FDG-PET, lumbar puncture and, finally, cerebral biopsy.
Results: The first MRI scan showed T2/FLAIR hyperintense lesions in right medial thalamus and right cortico-spinal tract, with enhancement after gadolinium administration. Follow-up MRI scans evidenced a progression of lesion burden, with involvement of bilateral supratentorial white matter including the genu of corpus callosum. FDG-PET revealed hypometabolism in right mesiofrontal and left temporal cortex, bilateral caudate nuclei, left putamen and both cerebellar hemispheres. CSF examination showed mild pleocytosis (lymphocytic and histiocytic-monocytic elements); oligoclonal bands, 14.3.3 protein, anti-NMDA and anti-cerebellum antibodies were absent. All microbiological assays resulted negative. The patient's neuropsychological profile was characterized by impairment in attentional-executive functions, mild short- and long-term memory deficits and behavioral disorders with prevailing apathetic conducts. Only partial and transient response was achieved after steroidal treatment. The cerebral biopsy revealed gliosis and perivascular inflammatory infiltrates. After a thorough interview, the patient revealed

that he had been affected by erythema nodosum and painful, relapsing oral and genital ulcers up to three years before the onset of neurological symptoms. The presence of HLA-B51 allele and the positivity of the skin pathergy test corroborated the diagnosis of BD.

Discussion and conclusions: Cognitive and behavioral features of NBD usually develop simultaneously to focal neurological signs and systemic manifestations of BD, reflecting disease activity. In our case the typical neurocognitive profile, associated with highly suggestive imaging findings, developed largely independently from the other BD features, thus hampering the correct diagnosis. Therefore, we recommend to include BD among the possible alternative diagnoses of acquired leukoencephalopathies, in order to promptly start an appropriate treatment.

References: Monastero R, Camarda C, Pipia C, et al. Cognitive impairment in Behçet's disease patients without overt neurological involvement. Journal of the Neurological Sciences 2004;220:99-104.
Gündüz T, Emir O, Kürtüncü M, et al. Cognitive Impairment in Neuro-Behcet's Disease and Multiple Sclerosis: A Comparative Study. International Journal of Neuroscience 2012;122:650-656.
Mazzoccoli G, Matarangolo A, Rubino R, et al. Behçet syndrome: from pathogenesis to novel therapies. Clinical and Experimental Medicine 2016;16(1):1-12.

MOTOR, BEHAVIOURAL, AND COGNITIVE CORRELATES OF FATIGUE IN EARLY, DE NOVO PARKINSON'S DISEASE PATIENTS

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Background: Fatigue is one of the most common and disabling non-motor symptoms in Parkinson's disease (PD).

Aims: The objective of this study was to determine prevalence and motor, behavioural, and cognitive correlates of distressing fatigue in early, de novo PD patients.

Methods: Eighty-one consecutive de novo PD patients (64% men; mean age 65.73 ± 8.26 years) underwent a comprehensive examination, including Parkinson's disease

Fatigue Scale (PFS), Epworth Sleepiness Scale (ESS), Parkinson's Disease Sleep Scale (PDSS), Beck Depression Inventory (BDI), Parkinson's Anxiety Scale (PAS), and Apathy Evaluation Scale (AES). Moreover, all patients underwent a detailed neuropsychological evaluation exploring attention and working memory, executive functions, memory, visuospatial abilities and language. Score of patients with or without distressing fatigue (defined as a PFS score 8) were compared by Student's t-test or Pearson's chi-square test. Logistic regression analyses were performed to search for motor and non-motor features independently associated with presence of distressing fatigue.

Results: Twelve (15%) patients presented distressing fatigue. Logistic regression identified sleepiness (p ¼ 0.04), "episodic anxiety" subscale of PAS (p ¼ 0.005), and "cognitive apathy" subscale of AES (p ¼ 0.017) as the main factors associated with distressing fatigue. No significant association was found between diagnosis of Mild Cognitive Impairment and distressing fatigue (p ¼ 0.745).

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

COPING STRATEGIES ASSOCIATED TO INCREASED CLINICAL ACTIVITY IN RELAPSING REMITTING MS

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Background: Very few studies have evaluated which coping strategies are associated with the risk for relapse in Multiple Sclerosis (MS) revealing that patients in exacerbation favoured Emotion-Focused strategies. However, the finding might have been influenced by the inclusion of depressed patients.

Aims: The present study was performed to better investigate the coping strategies in people with MS (pwMS) without clinically relevant depression and to examine the potential role of coping skills on MS activity.
Materials and methods: Sixty-seven relapsing-remitting pwMS and 67 healthy subjects (HS) underwent Coping Orientation to Problems Experienced (I-COPE) and Coping Inventory for Stressful Situation (CISS) and Beck Depression Inventory-II (BDI-II). pwMS underwent MRI section to evaluate lesion load and scales assessing cognitive status and physical disability. We also calculated a "Relapse Index" (RI), representing MS activity.
Results: The two groups did not differ on demographic variables and BDI-II scores. pwMS showed lower scores than HSs on social support and turning to religion subscales of the I-COPE and on Emotion dimension of the CISS. Multiple linear regression revealed that, in pwMS, higher "RI" score was related to higher positive attitude and lower score on the turning to religion subscale of I-COPE.
Conclusions: The present study revealed a less exploitation of emotion-based coping strategies in pwMS. A scarce use of faith for support and a frequent adoption of a positive attitude were associated with an increase of MS activity in terms of relapses. The evaluation of coping strategies should be included in clinical routine to better assess the patient's behavioral profile and risk for relapse.

References: Brown RF, Tennant CC, Sharrock M, et al. Relationship between stress and relapse in multiple sclerosis: Part I. Important features. Mult Scler 2006; 12: 453-464.
Farran N, Ammar D, Darwish H. Quality of life and coping strategies in Lebanese Multiple Sclerosis patients: A pilot study. Mult Scler Relat Disord 2016;6:21-27.

AN ATYPICAL LANGUAGE DISORDER AS VARIANT ONSET OF ALZHEIMER'S DISEASE

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Abstract and Background: Alzheimer's Disease (AD) is the most common neurodegenerative dementia in the elderly. AD's clinical signature is a memory deficit of

hippocampal type; however some atypical presentations, featuring early language, visuo-spatial or dysexecutive-behavioural aspects have been widely recognized, especially in not so aged individuals. Here we report on a peculiar progressive language disorder not completely satisfying any of the Primary Progressive Aphasia (PPA) criteria, probably due to AD pathology.

Presentation and history: Our patient is a 69-year-old woman who presented a language disorder insidiously started two years before, mainly characterized by anomia, circumlocutions, neologisms, passepartout words and phonemic paraphasias, with spared comprehension. This clinical picture progressively worsened and episodic memory deficits, apathy, anhedonia and lack of insight appeared thereafter. The patient underwent a complete clinical, neuropsychological and instrumental evaluation at our ward including EEG, brain MRI, cerebral 18FDG-PET and lumbar puncture with analysis of biomarkers of neurodegeneration (Aβ, tau and phospho-tau).

Materials and methods: Neurological examination: Epstein sign. Neuropsychological profile MMSE: 25.39/30; FAB: 14/18. Language assessment showed semantic more than phonological deficits, impaired written and oral naming, dyscalculia and impaired word-digit conversion. Repetition, as well as listening and reading comprehension were spared. Labolatory values TSH, FT3, FT4, Folic acid and B12: normal, TPHA: negative. CSF clear and colorless; Glucose normal, Protein: 46 mg/dl; Cell count: 1.2 cells/ml, Aβ42: 399 pg/mL, Total Tau: 722 pg/mL, P181-Tau: 96 pg/mL. Neuroimaging Brain MRI and cerebral 18FDG-PET(Figure 1 and 2).

Discussion and conclusions: PPA has been classified into three main variants: Progressive Non Fluent Aphasia (PNFA), Semantic Dementia (SD) and Logopenic-Phonological Aphasia (LPA). While it is evident that the first two entities are part of the Fronto-Temporal Lobar Degeneration (FTLD) spectrum, LPA has been recognized as an atypical AD variant, being usually associated with AD biomarkers and pathology. Our patient displays a language disorder with prevailing word-retrieval and naming defects, but the sparing of repetition doesn't allow a diagnosis of LPA. Neither SD can be the final diagnosis due to semantic deficits, as comprehension is largely unaffected. The pattern of glucose metabolism and CSF biomarkers are strongly evocative of AD. Thus we believe this case to be of particular interest as it broadens the spectrum of language disorders associated with AD, even in absence of left hemisphere prevalent alterations.

GENDER-SPECIFIC PATTERN OF SENSORI-MOTOR NETWORK CONNECTIVITY IN DE NOVO PARKINSON'S DISEASE PATIENTS

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Background and aim: Clinical and epidemiological evidences support the presence of sex-specific expression of Parkinson's disease (PD), from the early to the late stages. In the present study, we aimed to investigate the potential sex-difference effect on the spontaneous neuronal activity within the sensori-motor network (SMN) in early untreated PD patients, using the amplitude of low-frequency fluctuation (ALFF) and its correlation with baseline and longitudinal clinical features.

Methods: Fifty-six de novo PD patients and 23 matched healthy controls (HC) were enrolled in the study. Whole brain structural and functional imaging was performed on a 3T GE MR scanner. Functional data were analyzed using BrainVoyager QX software. Linear logistic regression was used to investigate whether functional imaging data at baseline were predictors of motor impairment over a 2-years follow-up period.

Results: Compared with female PD patients and HC, male PD patients showed an increased ALFF connectivity within the SMN in the 5-slow band. No ALFF differences were detected between male and female HC and within female PD patients and HC. Male PD patients showed a higher risk to develop axial symptoms at 2-years follow-up. Functional abnormalities within the SMN at baseline showed to be an independent predictor of axial impairment overtime in the PD group.

Conclusions: Our findings revealed that the organization of the intrinsic functional connectivity within the SMN in PD differs between genders. We hypothesize that this specific pattern may be related to the presence of a gender-specific nigro-striatal dopaminergic pathway and might predict PD progression and development of motor complications over the disease course.

APATHY IS CORRELATED WITH WIDESPREAD DIFFUSION TENSOR IMAGING (DTI) IMPAIRMENT IN AMYOTROPHIC LATERAL SCLEROSIS

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Apathy is recognized as the most common behavioural change in several neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS), a multisystem neurodegenerative disorder where apathy may severely impact prognosis. However, brain microstructural substrates of this behavioural symptom, reported as the most common in ALS, have not been completely elucidated. Using a tract-based spatial statistics (TBSS) diffusion tensor imaging (DTI) approach, we aim to explore the potential association between brain microstructural damage and apathy score in the early stages of ALS. Twenty-two consecutive ALS patients, in King's clinical stages 1 or 2, and 19 age- and sex-matched healthy controls (HCs) underwent magnetic resonance imaging and neuropsychological examination. When compared to HCs, ALS patients exhibited a decreased fractional anisotropy (FA) ($p<.05$, corrected) in the corpus callosum and bilateral anterior cingulate cortices. Apathy Evaluation Scale (AES) scores were positively correlated with measures of mean (MD) and radial (RD) diffusivity ($p<.05$, corrected) in widespread white matter (WM) areas, including several associative fiber tracts in frontal, temporal and parietal lobes. Moreover, between-groups comparisons did not show any significant difference of cognitive and behavioural performances. Our results point towards an early microstructural degeneration of brain areas biologically involved in behaviour regulation, although the significant correlations described between clinical scores of apathy and DTI measures in several brain areas may suggest the involvement of more widespread circuits in determining behavioural disturbances prior to their clinical appearance.

References: A. Chiò, A. Ilardi, S. Cammarosano et al., "Neurobehavioral dysfunction in ALS has a negative effect on outcome and use of PEG and NIV," Neurology, 2012, vol. 78, pp. 1085-1089.

F. Agosta, S. Galantucci, G. Magnani et al., "MRI signatures of the frontotemporal lobar degeneration continuum," Human Brain Mapping, 2015, vol. 36, pp. 2602-2614.
R. Radakovic, L. Stephenson, J. Newton et al., "Multidimensional apathy and executive dysfunction in amyotrophic lateral sclerosis," Cortex, 2017, vol. 94, pp. 142-151.

PARENTHOOD DESIRE AND DECISION-MAKING IN PEOPLE WITH MULTIPLE SCLEROSIS: AN EXPLORATIVE WEB-BASED STUDY

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Background: Multiple Sclerosis (MS) affects young adults during the reproductive age. Its unpredictable course can make parenthood decisions challenging. Improved knowledge on pregnancy in MS has led to risk minimization through pregnancy and breastfeeding planning. However, in people with MS (pwMS), little is known about the putative influence of disease consciousness on parenthood motivation.
AIMS: Our aim was to assess the impact of diagnosis on parenthood decision-making, in a large cohort of pwMS who filled out an on-line survey.
Materials and methods: PwMS were recruited on http://www.SMsocialnetwork.com/ and completed a 26 items-questionnaire. The 5 main interest areas of the questionnaire were: 1) social and clinical status 2) parenthood desire 3) external influences during the elaboration phase of family desire 4) pregnancy outcomes 5) abortions and adoptions. Results Of 519 participants we considered 395 surveys (excluding who refused parenthood for reasons not MS-related and incomplete questionnaires): 15.8% of responders were discouraged about parenthood, mainly by neurologists. Nevertheless only 8.5% refused to become parent because of MS ("anti-parenthood pw MS"). At

decision time (between 21 and 35 years-old), of 362 patients who were pro-parenthood, 47% ("pro-parenthood-pwMS") had already received the diagnosis and 53% ("pro-parenthood unaware") had not. Respectively, 77% in first and 92% in second group had at least one son ($p<0.001$); the first at a later age than the second ($p<0.001$). Who desired a child despite the diagnosis (170 patients) had a lower age at disease onset ($p=0.016$) and diagnosis ($p<0.001$) compared to whom refused parenthood because of MS (33 patients). A higher age at diagnosis was associated with a lower propensity to parenthood (OR 0.90, CI 95% 0.85-0.96, $p=0.001$). Moreover, the percentage of "pro-parenthood pwMS" was higher in the relapsing subgroup than in the not relapsing one (49% vs 27% $p=0.001$) and the percentage of "pro-parenthood unaware UD" was higher in not relapsing pwMS, than in relapsing ones (62% vs 44% $p=0.012$).

Discussion and conclusion: In our sample pwMS expressing the desire for parenthood after the diagnosis had children later and in a lower percentage than those who expressed the desire before the diagnosis. Early diagnosis increased the propensity to parenthood, probably allowing pwMS longer time to adapt/react to the disease remaining in the temporal range of parenthood choices. Moreover, the parenthood desire seems to be higher in patients who present a relapsing course of disease.

References: Janssens AC et al. Impact of recently diagnosed multiple sclerosis on quality of life, anxiety, depression and distress of patients and partners. Acta Neurol Scand. 2003.
Sepúlveda M et al. Impairment of decision-making in multiple sclerosis: A neuroeconomic approach. Mult Scler. 2017.
Alwan S et al. Reproductive decision making after the diagnosis of multiple sclerosis (MS). Mult Scler. 2013.

CLINICAL AND NEURORADIOLOGICAL CORRELATIONS BETWEEN CEREBRAL MICROBLEEDS AND DIFFERENT SUBTYPES OF MILD COGNITIVE IMPAIRMENT

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Objectives: Cerebral Microbleeds (CMBs) are small hypointense lesions seen in specific Magnetic Resonance Imaging (MRI) sequences, corresponding histologically to focal accumulations of hemosiderin-containing macrophages. They are commonly considered

expression of impaired small vessel integrity, due to either hypertensive vasculopathy or cerebral amyloid angiopathy. Previous studies have investigated the relationship between CMBs and Mild Cognitive Impairment (MCI) in terms of prevalence and risk of progression to dementia, but little or no data are available about the specific subtypes of MCI. The aim of this study is to explore the clinical and neuroradiological correlations between the presence and location of CMBs and the different subtypes of MCI.

Patients and methods: Our cohort consisted of 20 patients with suspected MCI who underwent a diagnostic protocol including neurological evaluation, extensive laboratory assays, EEG, functional (18FDG-PET) neuroimaging. The extensive neuropsychological assessment confirmed the diagnosis and defined the MCI subtype. For each patient, we then performed a brain MRI scan including T2* Gradient-Recalled Echo (GRE) and Susceptibility-Weighted Imaging (SWI) sequences to identify CMBs. Microbleed Anatomical Rating Scale (MARS) was used to assess CMBs burden and location (lobar and deep/infratentorial).

Results: Neuropsychological evaluation showed, in relation to the number of cognitive domains involved, 10 multiple domain (MD) and 10 single domain (SD) MCI. Considering the specific cognitive domain involved, 14 subjects were amnestic (aMCI) and 6 non-amnestic (naMCI). CMBs were present in 9 patients (CMBs+) and absent in 11 patients (CMBs-). In the CMB+ group, 6/9 patients were MD (66.6%), whereas in the CMBs- group only 4/11 patients were MD (26.4%). In both CMBs+ and CMBs- groups the prevalence of aMCI was higher than naMCI. All CMBs+ patients had lobar CMBs, coexisting with deep CMBs in only 3 cases.

Discussion and conclusions: The number of patients is too small to outline definitive conclusions, but some interesting observations can still be made. The lobar location of all CMBs+ cases confirms that, in MCI patients, amyloid deposition in the wall of small vessels has probably a greater role than cardiovascular risk factors in determining CMBs formation. Another more interesting observation, never reported in the literature, is that CMBs seems to have a higher prevalence in MD subtypes. This latter aspect could be intriguing if confirmed, since it indicates that the presence of CMBs may extend the cognitive spectrum of MCI. However, additional patients will need to be enrolled to establish a greater correlation between CMBs and subtypes of MCI.

References: Barnaure I, Montandon ML, Rodriguez C et al. Clinicoradiologic Correlations of Cerebral Microbleeds in Advanced Age. AJNR Am J Neuroradiol. 2017 Jan;38(1):39-45.

Gregoire SM, Chaudhary UJ, Brown MM et al. The Microbleed Anatomical Rating Scale (MARS): reliability of a tool to map brain microbleeds. Neurology. 2009 Nov 24;73(21):1759-66.
Gauthier S, Reisberg B, Zaudig M et al. Mild cognitive impairment. Lancet. 2006 Apr 15; 367(9518):1262-70.

MICROSTRUCTURAL CORRELATES OF EDINBURGH COGNITIVE AND BEHAVIOURAL ALS SCREEN (ECAS) CHANGES IN AMYOTROPHIC LATERAL SCLEROSIS

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Background: Edinburgh Cognitive and Behavioural ALS Screen has been specifically designed for testing patients with amyotrophic lateral sclerosis, as it allows to assess impairment of several cognitive domains while compensating for physical disability. It includes a range of tests sensitive to impairment of cognitive domains, more specifically involved in ALS, and an assessment of ALS non-specific functions. However, brain microstructural correlates of ALS-specific and non-specific cognitive abnormalities have not been completely elucidated.
Aims: Using a whole-brain tract-based spatial statistics diffusion tensor imaging approach, we aim to explore the potential association between brain microstructural damage and ECAS scores in early stages of ALS.
Materials and methods: Forty consecutive ALS patients in King's clinical stages 1 or 2, cognitively assessed by ECAS, and 35 age-, sex- and education-matched healthy controls underwent magnetic resonance imaging at 3 Tesla. DTI TBSS analysis was performed to measure fractional anisotropy and axial, radial and mean diffusivities for between-groups comparisons and correlations between DTI metrics and ECAS scores.
Results: ALS patients exhibited a decreased FA ($p<.05$, corrected) in bilateral cortico-spinal tracts, corpus callosum and superior longitudinal fasciculi and an increased RD in the rostral part of the right cortico-spinal tract and in the midbody of CC. ECAS total score, including both ALS-specific and non-specific scores, were significantly related to measures of FA, MD and RD ($p<.05$, corrected) in widespread white matter areas, including several motor and extra-motor fiber tracts in frontal, temporal and parietal

lobes. With regard to ALS-specific scores, verbal fluency was associated to RD in the splenium of CC. The total score from all ALS non-specific tests was significantly related to FA decrease in the right cortico-spinal tract, the body of CC, the fornix, the left inferior fronto-occipital fasciculus and bilateral superior longitudinal fasciculi, with more widespread areas of correlation, extended also to bilateral superior longitudinal fasciculi, considering the memory subscore alone.

Discussion and conclusion: Our results point towards an early microstructural degeneration of brain areas in ALS, with significant relationships between DTI metrics and ALS-specific and non-specific ECAS scores in several motor and extra-motor fiber tracts. In particular, WM abnormalities of the splenium of CC was found related to verbal fluency, while a more widespread cerebral microstructural impairment was found associated to ALS non-specific performances, especially to memory.

CEREBELLAR AND ADVANCED VISUAL NETWORK HYPERRESPONSIVENESS DURING TRIGEMINAL NOCICEPTION IN MIGRAINE WITH AURA

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Aims: To investigate the functional response of neural pathways associated with trigeminal noxious stimulation in patients with migraine with aura (MwA). Methods: eleven patients with MwA and ten patients with migraine without aura (MwoA) underwent whole-brain blood oxygen level–dependent (BOLD) fMRI during trigeminal heat stimulation (THS). The functional response of neural pathways to this stimulation in patients with MwA was compared with ten age- and sex-matched patients with MwoA and healthy controls (HC). Secondary analyses explored associations between BOLD signal change and clinical features of migraine in patients.

Results: We observed a robust cortical and subcortical pattern of BOLD signal change in response to THS across all participants. Patients with MwA showed a significantly

increased activation in the advanced visual network (AVN) and cerebellum in comparison with both patients with MwoA and HC. The magnitude of cerebellar activation was correlated with disease duration of patients with MwA. Furthermore, a positive correlation between the activity in cerebellum and cerebral regions constituting the AVN was observed. Conclusions: We provide novel evidence of a cerebellar modulation of AVN functional response to THS in patients with MwA, suggesting that mechanisms underlying MwA could affect multisensory integration between trigeminal pain network and visual network.

References: Hougaard A, Amin FM, Hoffmann MB et al. Interhemispheric differences of fMRI responses to visual stimuli in patients with side-fixed migraine aura. Hum Brain Mapp. 2014; 35(6):2714-23.
Moulton EA, Schmahmann JD, Becerra L, Borsook D. The cerebellum and pain: passive integrator or active participator? Brain Res Rev. 2010; 5;65(1):14-27.
Mehnert J, May A. Functional and structural alterations in the migraine cerebellum. J Cereb Blood Flow Metab. 2017 Jan 1:271678X17722109.

ADEM-LIKE ONSET OF LARGE B-CELL PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: A CASE REPORT AND NEUROPATHOLOGICAL CORRELATES

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Background: Primary CNS Lymphoma (PCNSL) is an uncommon malignancy of the central nervous system (CNS), which accounts for <2-3% of all brain tumors [1]. We describe an atypical neuropathologically-confirmed case of PCNSL with an Acute Disseminated Encephalomyelitis (ADEM)-like onset.
Materials and methods: A 58 year-old immunocompetent and otherwise healthy male presented with a subacute onset of dizziness, headache and vomiting, preceded by a remittent fever. During the first hospitalization, our diagnostic protocol included serum and cerebrospinal fluid (CSF) assays, extensive screening for autoimmune and infectious diseases, contrast-enhanced brain magnetic resonance imaging (MRI) and oncohematologic assessment for hidden malignancies. Because of a successive rapid

deterioration of the patient's neurological conditions, a complete diagnostic re-evaluation became necessary. Histological and Immunohistochemical studies on brain biopsy specimen were finally performed.

Results: At first admission, general examination and routine laboratory screening did not disclose any significant finding. Neurological examination showed slight postural and gait unsteadiness, mild apathic syndrome and sub-confusional state. CSF analysis revealed not-neoplastic lymphocytic pleiocytosis, elevated protein level and an increased IgG index. MRI showed multifocal areas of FLAIR-T2w hyperintensity within the white matter of frontal and occipital lobes. The extensive screening for infectious, autoimmune, oncological and hematologic diseases was normal. A diagnosis of ADEM was initially made and the patient's neurological deficits completely regressed with corticosteroid therapy. Nevertheless, a periodical clinical follow-up revealed a subsequent rapid neurological worsening, finally leading to coma and then death four months after the onset. At second admission to our clinic, the patient appeared markedly neurologically deteriorated. CSF analysis revealed similar abnormalities while MRI showed a significant progression with the appearance of perivascular contrast-enhancement and the extension of the FLAIR-hyperintense lesions to nucleus-capsular regions, white matter of both hemispheres and brainstem; a moderate restriction in the DWI study suggested high cellularity. Histopathological examination showed atypical lymphoid cells with enlarged round nuclei, which were immunopositive for CD-20, BCL-2 and MUM-1. A diagnosis of large B-cell lymphoma, non-germinal center pattern was made.

Discussion and conclusion: The diagnosis of PCNSL is frequently missed, due to the rarity of this condition and to the absence of specific clinical and radiological signs. So, neuropathology should be an essential step to consider in the investigation of atypical clinical cases, as it offer a definite confirmation of the diagnosis and allow for targeted therapeutic protocols.

References: Lukas RV, Stupp R, Gondi V, Raizer JJ. Primary Central Nervous System Lymphoma-PART 1: Epidemiology, Diagnosis, Staging, and Prognosis. Oncology (Williston Park). 2018 Jan 15;32(1):17-22. Review.

AN UNUSUAL PRESENTATION OF SYNE1 MUTATION (ARCA1 - BEAUCE ATAXIA - SCAR8): HYPOGONADISM AND INTELLECTUAL DISABILITY

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Introduction, background and aim of the study: to describe the atypical phenotype in two patients from a consanguineous marriage carrying a homozygous truncating mutation in SYNE1/nesprin1 gene.
Patients and methods: 21 ataxic patients who tested negative for pathological expansions in SCA1, 2, 3, 6, 7, 17 and for the intronic GAA expansion in FXN were analyzed using a customized targeted next-generation sequencing (NGS) panel able to investigate the coding regions of 82 genes linked to ataxia. NGS data were analyzed using Ingenuity Variant Analysis software. Probable and possible pathogenetic mutations were confirmed by traditional Sanger sequencing. RESULTS: A definite diagnosis was reached in 1/3 of the patients. One patient from a consanguineous marriage carried a homozygous mutation c.4609C>T (p.R1537*) in the SYNE1/nesprin1 gene. Segregation was studied in the family by Sanger sequencing. Both parents were carriers and the affected brother was homozygous for the mutation c.4609C>T (p.R1537*). The mutation is not previously reported. The proband was 36-year-old woman with onset 24. She has slight ataxia, marked dysarthria, brisk knee jerks, normal nerve conduction study and marked cerebellar atrophy. She also had low beta-estradiol and increased LH and FSH in some occasions. The 39-year-old brother had psychomotor retardation. He showed very mild ataxia, intellectual disability (IQ = 45), testosterone low level with normal gonadotropin, normal nerve conduction study and marked cerebellar ataxia.
Discussion: SYNE1/nesprin1 gene is one of the biggest genes in the human genome and includes 146 exons. The screening of the gene is difficult with traditional sequencing. NGS made easier testing the gene. ARCA1 has been originally described as a pure form of cerebellar ataxia but recent studies broadened the phenotype and showed that only 20% of the patients have a pure phenotype.
Conclusions: SYNE1/nesprin1 gene should be considered in the screening of hereditary ataxia. Mental retardation is rarely reported, and hypogonadism is never been reported.

References: “Mutations in SYNE1 lead to a newly discovered form of autosomal recessive cerebellar ataxia”, F. Gros-Louis, N.Dupre, P. Dion, M. A. Fox, S. Laurent, S. Verreault, J.R. Sanes, J.-Bouchard,G A R -Nature genetics 2007 Jan;39(1):80-5.
”Next generation sequencing for molecular diagnosis of neurological disorders using ataxias as a model”, AH. Ne meth, A. C. Kwasniewska, S.Lise, R. P. Schnekenberg, E. B. E. Becker, K. D. Bera, M. E. Shanks, L. Gregory, D. Buck, M. Z. Cader, K. Talbot R. de Silva, N. Fletcher, R. Hastings, S. Jayawant,P. J. Morrison, P. Worth, M. Taylor, J. Tolmie, M. O’Regan, UK Ataxia Consortium, R Valentine, E. Packham, J Evans, A Seller and Jiannis Ragoussis - Brain 2013 Oct;136(Pt 10): “SYNE1 related cerebellar ataxia presents with variable phenotypes in a consanguineous family from Turkey” E. Yucesan, S. A. Ugur Iseri, B. Bilgic, Z. Gormez, B. Bakir Gungor, A. Sarac, O. Ozdemir, M. Sagiroglu, H. Gurvit, H. Hanagasi, U. Ozbek, Neurological science 2017 Dec;38(12):2203-2207.

REVERSIBLE VALPROATE-INDUCED SUBACUTE ENCEPHALOPATHY ASSOCIATED WITH A MT-ATP8 VARIANT IN THE MITOCHONDRIAL GENOME

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Introduction: There are several reported cases of patients developing motor and cognitive neurological impairment under treatment with valproic acid (VPA). We describe a woman who developed a subacute encephalopathy after VPA intake, harboring a mitochondrial DNA variant, previously described as causing VPA sensitivity in one pediatric patient (1).
Material and methods: A 65-year old woman developed a progressive, severe neurological deterioration after a three-month treatment with valproate sodium, 800 mg daily. Magnetic resonance spectroscopy (MRS), muscle histochemical analysis and assay of mitochondrial enzymatic activities, and mitochondrial DNA sequencing were performed.
Results: Neurological examination showed drowsiness, vertical gaze palsy, inability to either stand or walk, diffuse weakness, increased tendon reflexes. Blood lactate was increased, EEG showed diffuse theta and delta activity, MRI subcortical atrophy and leukoencephalopathy, MRS marked reduction of the NAA spectrum, with a small signal compatible with presence of lactate. Muscle biopsy evidenced a significant variability of the fiber caliber with hypotrophic fibers, presence of ragged red fibers (20%) and reduced COX reactivity. Assay of the muscle enzymatic activities showed multiple deficiencies of

the electron transport chain. The nt.8393C>T variant in the MT-ATP8 gene was found in homoplasmy. The patient considerably improved after valproate withdrawal. **Conclusion:** The mutation we found has been reported both as a polymorphism and related to the valproate-induced encephalopathy. The present case is the first bearing this mutation in homoplasmy. In case of neurological symptoms after starting VPA therapy, once hyperammonemia and liver failure have been ruled out, mtDNA abnormalities should be considered (2).

References: Galimberti CA et al., Brain pseudo-atrophy and mental regression on valproate and a mitochondrial DNA mutation. Neurology 2006; 67:1715-1717.
Gerstner T et al., Valproic acid induced encephalopathy-19 new cases in Germany from 1994 to 2003-a side effect associated to VPA-therapy not only in young children. Seizure 2006;15:443-8.

NEW DIAGNOSTIC CRITERIA AND THE COSTS FOR TREATING MULTIPLE SCLEROSIS

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Introduction and Aim of the study: National healthcare systems are confronted by soaring costs for disease-modifying treatments (DMTs) in multiple sclerosis (MS). We aim to assess whether the introduction of new diagnostic criteria is associated with higher costs for treating MS, as a consequence of early diagnosis and increased number of people with MS eligible to DMTs. Methods: The present cohort study retrospectively included 2229 RRMS patients (42.1±11.2 years; female 63.3%), prospectively followed up from 1997 to 2017. Costs for DMT administration and management were calculated, and referred to each year of observation (annual costs). An interrupted time-series analysis was employed to assess whether the introduction of new diagnostic criteria (2001, 2006, and 2011) had an impact in modifying the average annual patient cost for treatment. The DMT cost variable was log-transformed to reduce data skewness. To account for repeated measurements within each patient over the study period, a mixed-

effect log-linear regression model was employed, with the covariates age, gender, disease duration, DMT type, year of treatment start and baseline EDSS included as fixed effects in the model.

Results: Average annual cost per patient was 12356.50±6198.45 euros. We observed a 0.6% increase in the average annual cost per patient after the introduction of 2001 criteria (Coeff=0.006; 95%CI=0.003/0.009; p>0.001), no significant variations after 2006 criteria, and a 0.3% decrease after 2010 criteria (Coeff=-0.003; 95%CI=-0.006/-0.001; p=0.045). When we did not adjust for DMT type, average annual cost per patient increased by 7.9% after 2010 criteria (Coeff=0.079; 95%CI=0.059-0.099; p<0.001).

Discussion and conclusion: In RRMS, average annual costs per patient are mainly driven by the introduction of more effective and expensive DMTs in recent years. Costs have otherwise remained stable over time independently from the introduction of new criteria. Profiling RRMS patients towards the most appropriate treatment is needed to control DMT-related costs.

References: Hartung DM, Bourdette DN, Ahmed SM, Whitham RH. The cost of multiple sclerosis drugs in the US and the pharmaceutical industry: Too big to fail? Neurology. 2015;84(21):2185-92.
Moccia M, Palladino R, Lanzillo R, Triassi M, Brescia Morra V. Predictors of the 10-year direct costs for treating multiple sclerosis. Acta Neurol Scand. 2017;135(5):522-528.
Moccia M, Palladino R, Lanzillo R, Carotenuto A, Russo CV, Triassi M, Brescia Morra V. Healthcare Costs for Treating Relapsing Multiple Sclerosis and the Risk of Progression: A Retrospective Italian Cohort Study from 2001 to 2015. PLoS One. 2017;12(1):e0169489.

LONGITUDINAL STUDY OF A COHORT OF MSA-C PATIENTS IN SOUTH ITALY: SURVIVAL AND CLINICAL FEATURES

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Abstract: Multiple system atrophy is a progressive fatal neurodegenerative disorder. Two major forms of the disease are recognized, the parkinsonian (MSA-P) and the cerebellar(MSA-C). Factors predicting survival are not fully established. We conducted a retrospective study to determine the median time to loss of independent walk, to become wheel-chair bound, and to death and determinants.

Background: Twelve mainly retrospective studies are available. Mean age at onset varied from 52.5 to 60 years, the median time to wheel-chair varied from 5 to 6.7 years, and the median time to death varied from 6.2 to 10 years. A recent meta-analysis identified as unfavorable predictors of survival severe dysautonomia and early development of combined autonomic and motor features but not MSA phenotype, early falls but not sex. There was conflicting evidence regarding the prognostic effect of aging, age at onset and stridor.
Aim of the Study: To evaluate clinical features, disease progression and survival and to identify variables that may modify the rate of disease progression in an ethnically homogeneous sample of Italian Multiple System Atrophy (MSA-C) patients.
Materials and methods: We investigated a cohort of 60 patients (31 F, 29 M), 51 with diagnosis of probable, 9 of possible MSA-C. Cerebellar impairment was estimated using the Inherited Ataxia Clinical Rating Scale, non-cerebellar features using UMSARS and MMSE. MRI, PET, DAT-SCAN, NCV were performed when required.
Results: Mean age at onset was 56.4 years (±7.8), mean age at examination was 61.9 (±7.1). The most frequent features were: ataxia (98.3%), dysarthria (88.3%), urinary incontinence (86%), sexual dysfunction in males (85%), RBD (78.6 %), increased tendon reflexes (76.7%), dysphagia (72.7%), tremor (73.3%). MRI scan detected hot cross bun sign (HBS) in 58.2% patients and pontine atrophy in 75%, putamen rim hyperintensity in 14.3%. 35 patients lost independent gait, median time was 5 years, at 61.2 years. 25 patients were confined to wheelchair, median time 10 years, at 63.1 years; 17 patients died, median time 10 years, at 64.5. Increased tendon reflexes, RBD, parkinsonism, nystagmus, and HBS at MRI were associated with a shorter survival.
Discussion and conclusion: MSA is a progressive adult-onset neurodegenerative disorder causing parkinsonism, cerebellar ataxia, autonomic, and pyramidal dysfunction in various combinations. Subtype C is predominantly characterized by cerebellar ataxia, subtype P predominantly by parkinsonism. MSA typically shows onset in middle age, disease course is faster than in Parkinson disease, with reduced life expectancies. In our study mean survival (10 years) was in agreement with previous studies and some clinical features predicted faster progression to death. The last finding should be replicated on a large population.

References: Wenning et al. The natural history of multiple system atrophy: a prospective European cohort study. Lancet Neurol 2013; 12:264-74.
Low et al. Natural history of multiple system atrophy in the USA: a prospective cohort study. Lancet Neurol. 2015; 14:710-9.
Filla et al. Prevalence of hereditary ataxias and spastic paraplegias in Molise, a region of Italy. J Neurol 1992; 239:351.

SIX-MINUTE WALK TEST AS RELIABLE AND OBJECTIVE TOOL TO MEASURE IMPROVEMENTS IN FATIGUE FOR CIDP PATIENTS

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Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disabling disease with monophasic, chronic or relapsing course. CIDP patients frequently complain about fatigue during a relapse or progressive deterioration of their clinical condition, together with sensory and motor symptoms. Clinical evaluation and clinimetric tests are based on qualitative evaluation or self-administered scale, not so sensitive in capturing minimal variations. Our aim is to test six-minute walk test (6MWT) as a quantitative measure of clinical improvement and set a minimum cut off to consider therapy as efficacious (Minimal Clinically Important Change Score – MCID). We performed an extensive assessment on 34 CIDP patients before and after therapy (one month) through a battery of outcome measures as modified version of the Inflammatory neuropathy cause and treatment (INCAT) scale, Overall neuropathy limitations Scale (ONLS), Rasch-built overall disability scale (RODS), modified Rankin scale (mRS), Medical research Council (MRC) scale, 10 meters walking test (10mwt) and 6MWT. In order to set MCID we performed both anchor-based method and distribution-method. Response to therapy was evaluated through patients interview and by performing Wilcoxon signed-rank test. Logistic regression model was applied to evaluate the correlation among outcome measuring tools. We found a significant relationship between 6MWT and ONLS, RODS, 10mwt, mRS and MRC score ($p>0.000$), not with INCAT scale. Mean velocity in 6MWT significantly increased at each time point after therapy ($p>0.000$). Anchor-based and distribution-based method showed a value of 15-meter (MCID) as cut-off to consider significantly improved the 6MWT. Our data suggest that 6MWT is a useful and reliable clinical measure in CIDP. Moreover, MCID for 6MWT can be fixed at 15-meter improvement.

THE NEW CHALLENGE OF THE MOLECULAR DIAGNOSIS IN HEREDITARY PERIPHERAL NEUROPATHIES: NEXT-GENERATION SEQUENCING AND WHOLE EXOME SEQUENCING

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Background: Hereditary peripheral neuropathies (HPN) represent a large group of genetic diseases, consisting in Charcot-Marie-Tooth disease (CMT), Hereditary Sensory Autonomic Neuropathy (HSAN) and distal Hereditary Motor Neuropathy (dHMN), with a wide spectrum of gene-disease. In recent years, the use of the next-generation sequencing (NGS) and the whole exome sequencing (WES) was led to the identification of many previously unknown involved genes and to the expansion of the patho-mechanisms of genetic defects already known to cause neuropathies.1

AIMS To report the experience about the use of NGS and WES by the center of neuromuscular disorder of University of Naples "Federico II".

Materials and methods: We report four cases of HPN. All cases underwent neurological evaluation, electrophysiological characterization and a stepwise genetic diagnostic approach for the more frequent genes. Then, two cases underwent NGS and the other two underwent WES.

Results: The case 1 is a female of 43 years with electrophysiological findings of dHMN. Genetic tests for HSPB1 and HSPB8 were negative and NGS discovered a mutation in the MYH14 gene (c.1994C>T, p.Ser665Leu).

The case 2 belonged to a large family with a mild disability and axonal phenotype, confirmed by nerve biopsy in the proband. No mutation was found by the genetic testing of the common genes accountable of CMT type 2 (MPZ, GJB1, MFN2, GDAP1). Through a NGS-based panel, a variant in the EGR2 gene (c.1235>G, p.Glu412Gly), segregating in the others affected member of family, was found.

The case 3 belonged to a family characterized by three male siblings affected by a severe HSAN with ulcers and amputations. Sequence of the WNK1 gene was negative.

WES analysis allowed to identify a compound heterozygous mutations in the DST gene (c.616C>T, p.R206W and c.68711G>A, p.K229fs), segregating in the family.2 The case 4 belonged to a large family with mild-moderate phenotype and with electro-physiological feature of an intermediate form of CMT. No mutation was found in MPZ, GJB1, NEFL, DNM2, GDAP1, MFN2. WES indentified a mutation in the ATP1A1 gene (c.1798C>G, p.Pro600Ala), allowed to discover a new gene-disease.3

Conclusion: NGS and WES approaches represent a successful perspective able to expand the phenotype of already known HPN-genes and to discover new gene-disease.

References: Eggermann K, Gess B, Häusler M, Weis J, Hahn A, Kurth I. Hereditary Neuropathies. Dtsch Arztebl Int. 2018 Feb 9;115(6):91-97.

Manganelli F, Parisi S, Nolano M, Tao F, Paladino S, Pisciotta C, Tozza S, Nesti C, Rebelo AP, Provitera V, Santorelli FM, Shy ME, Russo T, Zuchner S, Santoro L. Novel mutations in dystonin provide clues to the pathomechanisms of HSAN-VI. Neurology. 2017 May 30;88(22):2132-2140.

Lassuthova P, Rebelo AP, Ravenscroft G, Lamont PJ, Davis MR, Manganelli F, Feely SM, Bacon C, Brožková DŠ, Haberlova J, Mazanec R, Tao F, Saghira C, Abreu L, Courel S, Powell E, Buglo E, Bis DM, Baxter MF, Ong RW, Marns L, Lee YC, Bai Y, Isom DG, Barro-Soria R, Chung KW, Scherer SS, Larsson HP, Laing NG, Choi BO, Seeman P, Shy ME, Santoro L, Zuchner S. Mutations in ATP1A1 Cause Dominant Charcot-Marie-Tooth Type 2. Am J Hum Genet. 2018 Mar 1;102(3):505-514.

ABNORMAL PATTERN OF INTRACORTICAL FACILITATION IN EPISODIC MIGRAINE WITHOUT AURA: RESULTS OF A PAIRED-PULSE TMS STUDY

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Introduction: Paired-pulse TMS paradigms can be used to test connectivity within the primary motor cortex in human subjects. [1]Aim of the present study was to provide additional information on short intracortical inhibition (SICI), long intracortical inhibition (LICI) and intracortical facilitation (ICF) using different intensities of the test stimulus (TS) in patients suffering from migraine without aura (MwoA).

Methods: We enrolled 24 patients suffering with episodic MwoA and 24 healthy subjects. Both patients and controls were randomly assigned to two groups: the first group underwent assessment of SICI and LICI, whilst in the second group we evaluated ICF. We assessed SICI, LICI and ICF at three different suprathreshold intensities of the TS (110%, 130% and 150% of the resting motor threshold). Interstimulus intervals (ISI) of 2 ms and 100 ms were used for testing SICI and LICI respectively, whilst ICF was carried out by using 10 msISI.[2]

Results: When testing ICF, maximum increase in conditioned MEP amplitude was observed in migraineurs at the lower stimulation intensity of the TS. This intensity was indeed unable to induce significant facilitation in the healthy subjects, where maximum facilitation was observed at the higher stimulation intensities. No significant differences were observed between patients and healthy subjects as regards SICI and LICI.

Conclusion: Our results strengthen the notion of altered tuning of cortical excitability in migraine. [3] In particular, we provide evidence of hyperresponsivity of the glutamatergic intracortical circuits that could be revealed only by using a low stimulation intensity.

References: Ziemann U, Rothwell JC, Ridding MC. Interaction between intracortical inhibition and facilitation in human motor cortex. J Physiol. 1996;496 (Pt 3):873-81.

Sanger TD, Garg RR, Chen R.Interactions between two different inhibitory systems in the human motor cortex.J Physiol. 2001;530(Pt 2):307-17.

Cosentino G, Fierro B, Vigneri S, Talamanca S, Palermo A, Puma A, Brighina F. Impaired glutamatergic neurotransmission in migraine with aura? Evidence by an input-output curves transcranial magnetic stimulation study. Headache. 2011;51(5):726-33.

VISUAL CORTICAL EXCITABILITY IN PEDIATRIC MIGRAINE: A STUDY WITH SOUND-INDUCED FLASH ILLUSIONS

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Introduction: Sound-induced flash illusions (SIFI) are related with the level of visual cortex (V1) excitability (1). In adults migraineurs, in response to SIFI, V1 is hyperexcitable(2). Susceptibility to SIFI in children is increased because during childhood acoustic dominance switch to a visual (3). We evaluate by SIFI the V1 excitability in children with migraine to assessing also age-related differences in audio-visual perception. Twenty-six migraine children (examined interictally), fifteen children and twenty-four healthy adults with no familiarity for migraine were tested.
Methods: Visual(flash) and sound(beep) stimuli are presented with different combinations: multiple flashes with a single beep causes perception of less flashes (fusion illusion) while multiple beeps and single flash, induce perception of more flashes (fission illusion). Each combination was randomly presented and the subject had to indicate the number of the flashes seen.
Results: Children see more illusions than adults. Children with migraine do not differ from age matched control in the illusory percept, but they perceive more flashesin multiple flash trials.
Conclusions: Children see a greater number of SIFI than adults, this is due to the higher propensity of visual stimulation to be driven by auditory stimulus. Even if no difference in the illusory percept between controls and patients emerge, the migraine children have an increased ability to perceive flashes, even outside migraine attack, that reveal a hyper-functional visual cortex in migraine also in pediatric age. The SIFI can be used in pediatric migraine for testing the responsivity of V1.

References: Bolognini N, Rossetti A, Casati C, Mancini F, Vallar G. Neuromodulation of multisensory perception: a tDCS study of the sound-induced flash illusion. Neuropsycologia2011, 49:231-237.
Brighina F, Bolognini N, Cosentino G, Maccora S, Paladino P, Baschi R, Fierro B. Visual cortex hyperexcitability in migraine in response to sound-induced flash illusions.Neurology 2015 84: 2057-2051.
Nava E, Pavani F. Changes in Sensory Dominance During Childhood: Converging evidence From the Colavita Effect and the Sound induced Flash Illusion. Child Development. 2013, 84: 604-616.

MENSTRUAL CYCLE AND CORTICAL EXCITABILITY IN FEMALES WITH MIGRAINE AND IN HEALTY CONTROLS: A STUDY BY CROSS MODAL SOUND INDUCED FLASH ILLUSIONS

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Introduction: the sound-induced flash illusions (SIFI) represent an example of multisensory integration, and provide a tool to indirectly explore the excitability state of the visual cortex. Aim of the present study was to evaluate SIFI perceptions in healthy women and patients with menstrual migraine and to describe the effects of cyclical change of steroid hormones and cortical responsiveness.

Materials and methods: nineteen women (11 affected with menstrual migraine, 8 healthy controls) were enrolled. Serum determination for sexual hormones (estradiol, progesterone) and a SIFI trial were performed in all participants in two different sessions on the 14th and 27th day of menstrual cycle.

Results: healthy women showed more illusions in the premenstrual (27th day) than in the luteal phase (14° day) ($p < 0.01$). Migraine patients did not show any difference during the two phases of menstrual cycle; they saw significantly less fissions illusions ($p < 0.001$) with respect to healthy women at 27th, but not at 14th day of menstrual cycle.

Conclusions: In healthy subjects during late follicular phase, the increase of estradiol could determine visual cortex hyperexcitability corresponding to a reduction of SIFI. Conversely, premenstrual fall of estradiol would account for restored illusions. In migraine patients, instead, there is a persistence of a reduced illusory susceptibility in both phases of menstrual cycle. This effect probably would underlie a reduced responsivity of visual cortex to hormonal fluctuation in migraine.

CLINICAL EFFECTS OF MOTOR CORTEX tRNS ON TWENTY FIBROMYALGIA PATIENTS: RESULTS OF A RANDOMIZED SHAM-CONTROLLED TRIAL

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Background: Fibromyalgia syndrome (FMS) is a complex clinical picture characterized by widespread musculoskeletal pain, chronic fatigue, cognitive deficit (so-called fibrofog), sleep and mood disorders.
Pharmacological therapy, mainly based on painkillers, myorelaxant and antidepressants drugs, is often ineffective and/or not well tolerated and the need remains for alternative therapeutic tools.
In the last years, non-invasive brains stimulation by direct currents (transcranial direct current stimulation: tDCS) showed therapeutic effects in FMS. Primary motor cortex (M1) tDCS was able to reduce pain while targeting of dorsolateral prefrontal cortex (DLPFC) improved mood and cognitive impairment (1). More recently, a new transcranial electrical stimulation approach based on randomly changing alternating currents (tRNS) showed interesting effect on working memory and pain in limited series of patients with multiple sclerosis (2). Here we explored the effects of M1 tRNS treatment on the complex clinical picture of FMS.
Materials and methods: Twenty women with FMS between the ages of 26 and 67 were randomized into two treatment groups undergoing daily stimulation sessions for two weeks (weekend free): one received active, real tRNS and the other one sham, placebo tRNS. Each patient was evaluated, before and after treatment, through Visual Analogue Scale (VAS), Fibromyalgia Impact Questionnaire (FIQ), Mini-Mental State Examination (MMSE), Hospital Anxiety and Depression Scale (HADS) and other specific neuropsychological tests, such as Trail Making Test (TMT), Rey Auditory Verbal Learning Test (AVLT), Forward and Backward Digit Span, FAS verbal fluency test. FMS patients without cognitive deficit and with other neurological or psychiatric disease were ruled out.

Results: M1 active tRNS, compared to sham, induced a general improvement of FMS clinical picture: pain, depression, anxiety, FIQ scores reduced significantly. Even TMT A, AVLT and FAS scores showed significant improving.

Discussion and conclusions: Our findings suggest that M1 tRNS can have an important role in relieving cognitive, mood and pain symptoms of fibromyalgia.

Differently from motor cortex tDCS, tRNS seems able to reduce not only pain but also mood and cognitive impairment in these patients. Even if the reason for such manifold therapeutic effect remain to be cleared, it could follow to the mechanism suggested for tRNS known as stochastic resonance. According to this, tRNS could amplify subthreshold neural activities, so bringing to a synchronization of neural firing that could account for its more spreading and lasting effects.

References: Hou WH, Wang TY, Kang JH. The effects of add-on non-invasive brain stimulation in fibromyalgia: a metaanalysis and meta-regression of randomized controlled trials. Rheumatology (Oxford). 2016; 55: 1507-17.

Palm U, Chalah MA, Padberg F, Al-ani T, Abdekaoui M, Sorel M, Dimitri D, Creange A, Lefaucheur JP, Ayache SS. Effects of transcranial random noise stimulation (tRNS) on affect, pain and attention in multiple sclerosis. Restor Neurol Neurosci. 2016;34:189-99.

AGE AND SEX RELATED FUNCTIONAL HEMISPHERIC ASYMMETRIES IN HEALTHY SUBJECTS AS REVEALED BY SOUND INDUCED FLASH ILLUSIONS

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Objectives: Generally left hemisphere is specialized for language, while the right one is competent for visuospatial processing. These asymmetries change with sex (men show more visuospatial ability)1 and age (less hemispheric specialization in the elderly)2. Interhemispheric asymmetries play a role in a cross-modal perception, but little is known about sound-induced flash illusion (SIFI). Here, multiple flash with a single beep cause the perception of less flashes, “fusion illusions” while multiple beeps with single flash, induce perception of more flashes, “fission illusion”. It has been shown that the grey

matter volume in the visual cortex predicts the susceptibility to SIFI.3 Here we aimed to investigate how interhemispheric asymmetries affect SIFI mechanisms evaluating also the role of gender and age-related changes.

Materials and methods: We examined two groups of healthy subjects: 20 young (<30 years) and 15 older (>50yrs), matched by sex. Combinations of 1-4 flashes and 0-4 beeps were presented. Visual stimuli were presented centrally or 10° to the left or right. Subjects were asked to count the number of flashes seen.

Results: Fission-illusions were significantly more frequent in women (vs men) and in the older (vs young) subjects($p<.01$). Conversely, in unimodal trial (flashes without beeps) significantly more flashes were reported in men and in the younger($p<.01$). No difference at all emerged for SIFI in the two hemifields.

Discussion: Functional hemispheric asymmetries seem to be reflected by the different performance of the groups. Women are more susceptible to SIFI than men, who have a bigger V1, show more visuospatial ability and so less proneness to auditory driven illusions. The reduction of interhemispheric asymmetries and the loss of visual-cortical influence with age, can explain the illusions increase in the older subjects. However, these subjects show an optimal multi-sensory integration system: beeps increase, more than in younger, the perception of flashes. This could compensate for the lower flash perception in uni-modal (flash only) trials with respect to younger. Finally, the symmetrical bilateral extension of V1 can likely explain the lack of differences for lateralized presentations in right and left hemifield.

Conclusion: SIFI are sensitive to sex- and age-related changes in interhemispheric asymmetries. They confirm a greater visuospatial ability in men that is lost in the elderly. SIFI is somewhat related with the cortical volume (especially of visual area) and could represent a tool to study neurodegenerative disease.

References: Weiss EM, Kemmler G, Eberhard A. Deisenhammer Fleischhacker WW, Delazer M. Sex differences in cognitive functions. Personality and Individual Differences. 2003: 863–875.

Dolcosa F, Ricea HJ, Cabezaa R, Hemispheric asymmetry and aging: right hemisphere decline or asymmetry reduction. Neurosci. Biobehav Reviews 2002, 26: 819–82,5.

de Haas B, Kanai R, Jalkanen L, Rees G. Grey matter volume in early human visual cortex predicts proneness to the sound-induced flash illusion. Proc. R. Soc. B 2012, 279: 4955–61.

VISUAL CORTEX HYPEREXCITABILITY IN CLUSTER HEADACHE: A PILOT STUDY WITH SOUND INDUCED FLASH ILLUSION PARADIGM

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Objectives: Pathophysiological mechanisms underlying cluster headache (CH) largely remain to be cleared. We recently observed increased motor cortical excitability in episodic CH patients both outside and inside bout[1]. The sound-induced flash illusions (SIFI) represent an example of multisensory integration, and provide a tool to indirectly explore the excitability state of the visual cortex. In SIFI, multiple flash with a single beep cause the perception of less flashes, “fusion illusions” while multiple beeps with single flash, induce perception of more flashes, “fission illusion”(2). In a recent study we showed visual cortical hyperexcitability by SIFI in migraine (3) On such bases, here we used SIFI to explore excitability of visual cortex in CH patients.

Materials and methods: SIFI were examined in ten untreated patients with episodic CH and in twelve age- and sex-matched healthy volunteers. Visual stimuli were presented centrally or 10° to the left or right Five out of the ten patients were evaluated both inside (in the interval between two pain attacks) and outside bout. Visual stimuli were accompanied by beeps in different combinations of 1-4 flashes and 0-4 beeps were presented to evaluate both fission illusion and fusion illusion.

Results: The fission but not the fusion illusion was significantly reduced in CH patients with respect to healthy controls. No significant differences in perception of SIFI were observed between bout and outside bout phases or in the two hemifields in patients evaluated both in the ictal and interictal state. Although intercritical patients perceived more flashes in the ipsilateral hemisphere side of pain,regardless of SIFI.

Discussion: The present results provide evidence of increased visual cortical excitability in CH not only during the bout, but also in the pain-free period. This is in agreement with previous findings by our group showing increased motor cortex excitability in CH inside and outside bout (1).

Conclusions: These results strengthen the relevance of an abnormal cortical excitability state in CH. Moreover, findings in CH patients are very similar to those observed in

migraine with aura patients(3).The lack of perception abnormalities during the critical phase requires further clarification to evaluate possible fluctuations of cortical excitability in the phases that precede pain.

References: Cosentino 1. G, Brighina F, Brancato S, Valentino F, Indovino S, Fierro B: Transcranial magnetic stimulation reveals cortical hyperexcitability in episodic cluster headache. J Pain. 2015, 16: 53-9.
Shams L, Kamitani Y, Shimojo S: Illusions. What you see is what you hear. Nature. 2000, 408 (6814): 788-10.1038/35048669.
Brighina F, Bolognini N, Cosentino G, Maccora S, Paladino P, Baschi R, Vallar G, Fierro B: Visual cortex hyperexcitability in migraine in response to sound-induced flash illusions. Neurology. 2015, 84 (20): 2057-61.

THE RIGHT SIDE OF THE BRAIN IS NOT MERELY A SILENT VIEWER IN TERMS OF LANGUAGE

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Introduction: The left brain dominance for language is a not completely solved matter. Although the left hemisphere is crucial for language, the clinical, behavioral and neuroimaging research suggest that the right hemisphere also contributes to language processing. In particular, figurative language may be one kind of linguistic skill that preferably engages right hemisphere regions (1, 2). Furthermore, the right hemisphere participates in linguistic and correct phonological processing, consisting of syllabic order within a word (3).
Objective of the study: The objective of the present study is to explore the possible contribution of the right hemisphere, involved in spatial perception, in the segmental processing of language.
Materials and methods: Twelve healthy subjects performed a pseudoword learning task during anodal tDCS of the right and left temporo-parietal junction and during a control session with sham (placebo) tDCS. The task included a learning phase of image-

pseudowords associations and a second phase of recognition of the same, in which the images were associated simultaneously with the correct pseudoword (previously learned) and with an alternative, incorrect pseudoword. Two types of errors were analyzed: error of transposition of syllables within the learned pseudoword and identity error.

Results: The number of transposition errors is significantly reduced during right anodal stimulation, whereas the left anodal stimulation reduces the number of identity errors, compared to the placebo condition.

Conclusion: The right hemisphere has a competence in spatial perception, and the segmental processing of the language could represent a spatial operation where right hemisphere could play a critical role. The evidence that the stimulation of the right cortical areas reduces the number of errors of transposition of letters within the learned pseudowords could suggest a role of the spatial competences of the non-dominant hemisphere in the segmental processing of language. This is in line with the evidence about the right hemisphere role for the understanding of the overall linguistic context and could represent the underpinning mechanism for such contribution. A right brain damage can cause inability to understand the prosodic features of language or even result in language impairment. Moreover, lateralization can be switched in order to adapt to loss or damage (1). The left-right brain cross-talk appears an essential requirement for language.

References: Lindell AK. In your right mind: right hemisphere contributions to language processing and production. Neuropsychol Rev. 2006 Sep;16(3):131-48.

Diaz MT, Eppes A. Factors Influencing Right Hemisphere Engagement During Metaphor Comprehension. Front Psychol. 2018 Mar 28;9:4143.

Hartwigsen G, Baumgaertner A, Price CJ, Koehnke M, Ulmer S, Siebner HR.Phonological decisions require both the left and right supramarginal gyri. ProcNatl Acad Sci U S A. 2010 Sep 21;107(38):16494-9.

TRANSCRANIAL DIRECT CURRENT STIMULATION IN POST-STROKE APHASIA REHABILITATION: BILATERAL VS UNILATERAL ONLINE STIMULATION

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Abstract: Aphasia is a very limiting cognitive disorder acquired after stroke and current approaches to its treatment are not entirely efficient yet. Here, we aim to evaluate the efficacy of multiple sessions of tDCS combined to behavioral therapy in post stroke aphasic patients. Our study revealed that both dual and single tDCS montages have positive effects in post stroke aphasia recovery, compared to sham.

Background: Aphasia is the most common post-stroke cognitive disorder and it severely compromises activities of daily living and social interactions. tDCS recently showed good results in post-stroke aphasia rehabilitiation, even if no agreement at now exists about the stimulation parameters to employ to achieve the best rehabilitative outcome [1].

Aims: Here we aim to evaluate the efficacy of repeated sessions of tDCS as additional treatment to standard behavioral rehabilitation in post-stroke aphasic patients, comparing bilateral with unilateral left-sided and sham-tDCS.

Matherials and methods: We enrolled twenty-two patients with single left-brain lesion at CT or MR scan. Aphasia was investigated through selected subitems of Aachener Aphasie Test (AAT), used as outcome measures. Patients were randomly assigned to 3 groups: bilateral-tDCS (7); unilateral-tDCS (8); sham-tDCS (7). Anode was placed over the left inferior frontal gyrus (IFG), while cathode was positioned over contralateral supraorbital area (unilateral-tDCS) or over the right-IFG (bilateral-tDCS). The direct current (1.5 mA for 20 min) was delivered during a picture naming task (online) in daily sessions. The procol lasted two consecutive weeks for each patient (weekend-free) for a total of 10 stimulations.

Results: A repeated measures ANOVA showed as both dual and single-tDCS lead to significant improvements in outcome measures as compared to baseline evaluation and

sham-tDCS. A Post Hoc Duncan's test highlighted how the most significant AAT score improvement concerned naming subitem, followed by the others. Discussion and Conclusion: tDCS represents a useful tool for aphasia rehabilitation, both in single and dual montage. It is well tolerated and IFG stimulation (left anodal-tDCS or both left-anodal and right-cathodal) lead patients to significant naming and general speech improvements, compared to sham. Since there are several variables to consider yet, such as time distance from stroke and rehabilitation and size of the lesion, further studies are required for a standardized clinical application.

References: De Aguiar V, Paolazzi CL, Miceli G. tDCS in post-stroke aphasia: the role of stimulation parameters, behavioral treatment and patient characteristics. Cortex. 2015; 63:296-316.

COGNITIVE IMPAIRMENT: EVALUATION OF CEREBROSPINAL FLUID BIOMARKERS IN COMBINATION WITH CLINICAL, NEUROIMAGING AND NEUROPSYCHOLOGICAL ASSESSMENT: OUR EXPERIENCE

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Objective: This study was aimed to evaluate the impact of CSF biomarkers on the diagnosis of dementia subtype in our population.
Background: The Recommendations from the National Institute on Aging-Alzheimer's Association (NIA-AA) incorporate the evaluation of fluid biomarkers for diagnosis of various stages of Alzheimer Disease.
Methods: We retrospectively selected 32 patients (14 M, 18 F; age 69.5 ± 6.5 SD) with clinical evidence of cognitive decline who underwent a CSF dosage of amyloid-β (A), total Tau (Tau) and phosphorylated Tau (p-Tau). All procedures for CSF collection and proteins measurement was made according to international recommendation. Each patient was submitted to an extensive clinical evaluation including a structured cognitive evaluation (81.2% of total), structural neuroimaging evaluation (CT or MRI, 87.5% of total) and to a 18-FDG PET scan (62.5% of total).

Results: We assigned diagnosis on basis of clinical evaluation and FDG-PET scan: 1 SCD (subjective cognitive disorder), 7 MCI (mild cognitive impairment) due to AD, 2 amnestic MCI, 2 MCI unlikely due to AD, 6 MCI, 10 AD (Alzheimer disease), 2 VCI (vascular cognitive impairment), 1 bvFTD (behavioural variant of Fronto-Temporal dementia). 29 out of 32 (90.6%) diagnosis were confirmed by CSF biomarkers: 1 Preclinical AD, 3 MCI unlikely due to AD, 9 MCI due to AD, 9 AD, 2 VCI and 8 SNAP (Suspected non-amyloid disease pathophysiology). In a case of suspected bvFTD, who had a FDG-PET Scan's abnormal pattern with hypometabolism in temporal and frontal lobes and behavioural disorders with multiple cognitive domains compromised, we find low level of Aβ, total Tau and p-Tau at CSF analysis and so we have changed our diagnosis to AD with severe behavioural symptoms. In two other cases of suspected AD, we find normal levels of amyloid-β biomarker and abnormal lever of neurodegeneration's biomarkers, so we assigned them a diagnosis of SNAP.

Conclusions: We showed a significant degree of concordance between clinical criteria, NPS assessment, fluid biomarkers and neuroimaging. Given obvious limitations for small cohort of our study, we have found eight patients with border-line biomarkers values (8/32: 25%) and we used caution into those intrinsic validity. Discussion. Standardization of analytical procedures and further harmonization of CSF biomarker measurements are needed. Moreover, CSF AD biomarkers informations may help with an early diagnosis of MCI because of AD, in the way to offer them the possibility of participating in clinical trials with new potentially disease-modifying drugs and in non-pharmacological interventions.

References: Guy M. McKhann, et all. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & Dementia. DOI: 10.1016/j.jalz.2011.03.005, 2011, Vol. 7, 263–269.

Marilyn S. Albert, et all. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & Dementia. DOI: 10.1016/j.jalz.2011.03.008, 2011, Vol. 7, 270-279.

Anja Hviid Simonsen, et all. Recommendations for CSF AD biomarkers in the diagnostic evaluation of dementia. Alzeimer's & Dementia. DOI: http://dx.doi.org/10.1016/j.jalz.2016.09.008, 2017, Vol. 13, 174-284.

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