MS-like conditions are not fully understood. Here, we have used direct in vitro systems and cuprizone induced demyelination in PDGFRa-Cre reporter mice to investigate the role of these pathways in regulating OPC maturation, oligodendrogenesis and remyelination in chronic demyelinating lesions. Our direct in vitrodata show that mTOR inhibition with rapamycin impedes OPC proliferation and maturation and reduces morphological complexity of oligodendrocytes and normal expression of myelin basic protein, which has a major role in myelination. We also identified a significant reduction in OPC proliferation after tunicamycininduction of the UPR, and a decline in OPC differentiation into mature oligodendrocytes and reduced oligodendrocyte arborization. We are currently investigating these pathways in chronic demyelinating lesions of the cuprizone mice. These findings are an interesting starting point for elucidating the role of mTOR and UPR pathways in regulating oligodendrocytes and remyelination in chronic progressive MS.

Funded by the MS Society of Canada.

Disclosure

Nothing to disclose

EP1184

Profiling cognitive-motor interference in cognitively impaired persons with progressive multiple sclerosis

<u>R. Veldkamp^{1,2}, M. D'hooge^{1,2,3}, D. Kos^{3,4}, B.M.</u> <u>Sandroff^{5,6}, J. DeLuca^{5,6}, A. Salter⁷, A. Feinstein⁸, M.P.</u> *Amato^{9,10}, G. Brichetto^{11,12}, J. Chataway¹³, R. Farrell¹³,* N.D. Chiaravalloti^{5,6}, U. Dalgas¹⁴, M. Filippi^{15,16}, J. Freeman¹⁷, R.W. Motl¹⁸, C. Meza⁸, M. Inglese^{19,20}, M.A. Rocca^{15,16}, G. Cutter²¹, P. Feys^{1,2}, On behalf of the CogEx Research Team

¹Hasselt University, REVAL Rehabilitation Research Center, Faculty of Rehabilitation Sciences, Hasselt, Belgium, ²UMSC, Hasselt-Pelt, Belgium, ³National MS Center Melsbroek, Melsbroek, Belgium, ⁴KU Leuven, Department of Rehabilitation Sciences, Leuven, Belgium, ⁵Kessler Foundation, East Hanover, United States, ⁶Rutgers New Jersey Medical School, Department of Physical Medicine & Rehabilitation, Newark, United States, ⁷UT Southwestern Medical Center, Department of Neurology, Section on Statistical Planning and Analysis, Dallas, United States, 8University of Toronto and Sunnybrook Health Sciences Centre, Department of Psychiatry, Toronto, Canada, 9University of Florence, Department NEUROFARBA, Section Neurosciences, Florence, Italy, ¹⁰IRCCS Fondazione Don Carlo Gnocchi, Florence, Italy, ¹¹Scientific Research Area, Italian Multiple Sclerosis Foundation (FISM), Genoa, Italy, ¹²AISM Rehabilitation Service, Italian Multiple Sclerosis Society (AISM), Genoa, Italy, ¹³University College London Queen Square Institute of Neurology, Queen Square MS Centre, Department of Neuroinflammation, London, United Kingdom, 14Aarhus University, Section for Sport Science, Department of Public Health, Aarhus, Denmark,

¹⁵San Raffaele Scientific Institute, Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, and Neurology unit, IRCCS, Milan, Italy, ¹⁶Vita-Salute San Raffaele University, Milan, Italy, ¹⁷University of Plymouth, Faculty of Health: Medicine, Dentistry and Human Sciences, Devon, United Kingdom, ¹⁸University of Alabama at Birmingham, Department of Physical Therapy, Birmingham, United States, ¹⁹University of Genoa, Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), and Center of Excellence for Biomedical Research, Genoa, Italy, ²⁰IRCCS Ospedale Policlinico San Martino, Genoa, Italy, ²¹University of Alabama at Birmingham, Department of Biostatistics, Birmingham, United States

Introduction: Performing cognitive-motor dual tasks (DT) may result in reduced walking speed and cognitive performance in persons with Multiple Sclerosis (MS) and the effect in persons with progressive MS having cognitive dysfunction is unknown.

Objectives: To profile DT performance during walking in cognitively impaired persons with progressive MS and examine DT performance by disability level.

Methods: Secondary analyses were conducted on baseline data of the CogEX study. Participants, enrolled with SDMT \leq 1.282 SD below normal, performed a single cognitive task (alternating alphabet), single motor task (walking) and a DT (both). Outcomes were walking speed, number of correct answers on the alternating alphabet task, and the DT cost on walking (DTC_{motor}) and cognitive (DTC_{cognitive}) performance. Outcomes were given overall and given and compared by EDSS (<6 vs. \geq 6). Spearman correlations were conducted between the DTC_{motor} with clinical measures and patient reported outcomes.

Results: Overall, participants (n=303, EDSS: 6.0, 4.5-6.5) walked slower and had fewer correct answers on the DT versus ST (both p<0.001), with a DTC_{motor} of 15.7% and DTC_{cognitive} of 2.3%. Participants with lower EDSS walked faster than those with higher EDSS (p<0.001), but did not differ on cognitive performance or DTCs.

Conclusions: DT affects walking and cognitive performance in cognitively impaired persons with progressive MS. This interference did not differ by overall disability level.

Disclosure

Renee Veldkamp has no disclosures to report.

Mieke D'hooge has no disclosures to report.

Anthony Feinstein is on Advisory Boards for Akili Interactive and Roche, and reports grants from the MS Society of Canada, book royalties from Johns Hopkins University Press, Cambridge University Press, Amadeus Press and Glitterati Editions, and speaker's honoraria from Novartis, Biogen, Roche and Sanofi-Genzyme.

Maria Pia Amato received compensation for consulting services and/or speaking activities from Bayer, Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, and Teva Pharmaceutical Industries; and receives research support from Biogen Idec, Merck-Serono, Roche, Pharmaceutical Industries and Fondazione Italiana Sclerosi Multiplav **Giampaolo Brichetto** has been awarded and receives research support from Roche, Fondazione Italiana Sclerosi Multipla, ARSEP, H2020 EU Call.

Jeremy Chataway has received support from the Efficacy and Evaluation (EME) Programme, a Medical Research Council (MRC) and National Institute for Health Research (NIHR) partnership and the Health Technology Assessment (HTA) Programme (NIHR), the UK MS Society, the US National MS Society and the Rosetrees Trust. He is supported in part by the National Institute for Health Research, University College London Hospitals, Biomedical Research Centre, London, UK. He has been a local principal investigator for commercial trials funded by: Actelion, Biogen, Novartis and Roche; has received an investigator grant from Novartis; and has taken part in advisory boards/consultancy for Azadyne, Biogen, Celgene, MedDay, Merck and Roche.

Nancy D. Chiaravalloti is on an Advisory Board for Akili Interactive and is a member of the Editorial Boards of Multiple Sclerosis Journal and Frontiers in NeuroTrauma.

Ulrik Dalgas has received research support, travel grants, and/or teaching honorary from Biogen Idec, Merck Serono, Novartis, Bayer Schering, and Sanofi Aventis as well as honoraria from serving on scientific advisory boards of Biogen Idec and Genzyme. **John DeLuca** is an Associate Editor of the Archives of Physical Medicine and Rehabilitation, and Neuropsychology Review; received compensation for consulting services and/or speaking activities from Biogen Idec, Celgene, MedRhythms, and Novartis; and receives research support from Biogen Idec, National Multiple Sclerosis Society, Consortium of Multiple Sclerosis Centers, and National Institutes of Health.

Cecilia Meza has no disclosures to report.

Peter Feys is editorial board member of NNR, MSJ and Frontiers in Rehabilitation Sciences-section strengthening health systems, provided consultancy to NeuroCompass and was board of advisory board meetings for BIOGEN.

Massimo Filippi is Editor-in-Chief of the Journal of Neurology and Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology, received compensation for consulting services and/or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Eli Lilly, Genzyme, Merck-Serono, Novartis, Roche, Sanofi, Takeda, and Teva Pharmaceutical Industries, and receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Teva Pharmaceutical Industries, the Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA (Fondazione Italiana di Ricerca per la SLA).

Jennifer Freeman has been awarded research grants from the NIHR, UK

Matilde Inglese is Co-Editor for Controversies for Multiple Sclerosis Journal; received compensation for consulting services and/or speaking activities from Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme; and received research support from NIH, NMSS, the MS Society of Canada, the Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, H2020 EU Call. **Robert W. Motl** has no disclosures to report.

Maria Assunta Rocca received speaker honoraria from Bayer, Biogen, Bristol Myers Squibb, Celgene, Genzyme, Merck Serono, Novartis, Roche, and Teva and research support from the Canadian MS Society and Fondazione Italiana Sclerosi Multipla. Brian Sandroff has no disclosures to report.

Gary Cutter is a member of Data and Safety Monitoring Boards for Astra-Zeneca, Avexis Pharmaceuticals, Biolinerx, Brainstorm Cell Therapeutics, Bristol Meyers Squibb/Celgene, CSL Behring, Galmed Pharmaceuticals, Horizon Pharmaceuticals, Hisun Pharmaceuticals, Mapi Pharmaceuticals LTD, Merck, Merck/ Pfizer, Opko Biologics, OncoImmune, Neurim, Novartis, Ophazyme, Sanofi-Aventis, Reata Pharmaceuticals, Teva pharmaceuticals, VielaBio Inc, Vivus, NHLBI (Protocol Review Committee), NICHD (OPRU oversight committee). He is on Consulting or Advisory Boards for Biodelivery Sciences International, Biogen, Click Therapeutics, Genzyme, Genentech, GW Pharmaceuticals, Klein-Buendel Incorporated, Medimmune, Medday, Neurogenesis LTD, Novartis, Osmotica Pharmaceuticals, Perception Neurosciences, Recursion/Cerexis Pharmaceuticals, Roche, TG Therapeutics. Dr. Cutter is employed by the University of Alabama at Birmingham and President of Pythagoras, Inc. a private consulting company located in Birmingham AL.

Amber Salter is a statistical editor for Circulation: Cardiovascular Imaging.

Daphne Kos received consulting and/or educational support from Roche, Novartis, Biogen, Merck, Sanofi Genzyme, Almirall.

EP1185

SPMS diagnosis: a Canadian practice audit

R. Vosoughi¹, M. Baharnoori², J. Bakker³, W. Berger⁴, A. Gagnon⁵, T. Lad⁶, R. Leckey⁷, S. McKenzie¹, A. Morinville⁸, D. Rivest⁹, G. Vorobeychik¹⁰ ¹St. Michael's Hospital, Neurology, Toronto, Canada, ²Kingston Health Sciences Centre, Neurology, Kingston, Canada, ³Red Deer Regional Hospital, Neurology, Red Deer, Canada, ⁴London Health Sciences Centre, Neurology, London, Canada, ⁵Clinique Neuro-Outaouais, Gatineau, Canada, ⁶Joseph Brant Hospital, Burlington, Canada, ⁷Dalhousie University, Medicine, Halifax, Canada, ⁸Novartis Pharmaceuticals Canada Inc., Dorval, Canada, ⁹Clinique Neuro-Lévis, Lévis, Canada, ¹⁰Fraser Health MS Clinic Burnaby Hospital, Burnaby, Canada

Introduction: An estimated 50% of relapsing-remitting multiple sclerosis (RRMS) patients develop secondary-progressive disease (SPMS) within 15-20 years of MS onset; average age at onset is 45 years (Tremlett 2008,Tutuncu 2013). The lack of consensus on diagnostic criteria contributes to clinician uncertainty and a considerable diagnostic delay (Katz Sand 2014).

Objectives: To examine the clinical characteristics of potentially transitioning RRMS and SPMS populations in the Canadian practice setting.

Methods: A retrospective chart review was completed in Canadian MS specialized centres and community neurology practices of MS patients with EDSS 3.0-6.5 who received an RRMS diagnosis 10-20 years ago.

Results: Data were collected for 708 patients at 15 centres (59% from 10 MS clinics, 41% from 6 community practices). A majority were aged >50 years (58%). The average duration of MS was 15.2 years (range 13.3-17.1 years). The SPMS group (n=223) was older (76% aged >50 years vs. 49%), had a higher current