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Examining cross-sectional relationships of optical coherence tomography, cervical cord MRI and disability in secondary progressive MS

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Background: There is a major need to develop interim markers of disability in progressive MS. Optical coherence tomography (OCT) and spinal cord MRI (SC-MRI) have significant promise.

Aim: To assess the cross-sectional relationships of OCT, SC-MRI and clinical measures of disability in a large cohort of patients with secondary progressive MS (SPMS).

Methods: MS-SMART (NCT01910259) is an ongoing UK multi-centre, multi-arm, double-blind, placebo-controlled phase IIb randomised controlled trial that has enrolled 445 SPMS patients aged 18-65, with EDSS 4.0-6.5. An embedded single-centre study was pre-planned to assess OCT and SC-MRI. For this sub-study, we excluded patients with ocular disease, high refractive errors (> ±6.0 dpt), history of bilateral optic neuritis (ON), or possible subclinical ON (i.e. interocular OCT differences > 20%). For patients with no previous ON, we averaged the OCT measures from both eyes; with a history of unilateral ON, we only included the fellow eye with no history of ON. We collected Expanded Disability Status Scale (EDSS), Symbol Digit Modalities Test (SDMT), MS Functional Composite (MSFC), mean upper cervical cord area (MUCCA), and 3 OCT measures (peripapillary retinal nerve fibre layer [pRNFL], ganglion cell layer [GCL] volume, total macular volume [TMV]). We calculated Kendall's tau correlation coefficients between the clinical variables, MUCCA, and OCT. Subsequently, we divided the cohort in quartiles and performed multiple linear regression analyses, with adjustment for gender, age, and disease duration.

Results: OCT data were available for 112 participants, MUCCA for 146, and both OCT and MUCCA were available for 95. EDSS was moderately correlated with MUCCA (N=146, t: -0.307, p< 0.001), but not with the three OCT measures. SDMT was weakly correlated with MUCCA (N=145, t: 0.202, p=0.015), pRNFL (N=111, t: 0.262, p< 0.001), GCL (N=112; t: 0.259, p< 0.001), and very weakly with TMV (N=112, t: 0.138 p=0.034). MSFC was moderately correlated with MUCCA (N=146, t: 0.328, p< 0.001), but not with the three OCT measures. There was no significant correlation between MUCCA and any OCT measure. Regression analyses confirmed these findings.

Conclusions: This cross-sectional analysis may suggest that MUCCA and OCT measure complementary dimensions of neurodegeneration in SPMS. Ongoing longitudinal analysis will clarify these findings.

Disclosure:

F.D.A., A.G.G., R.P., D.P., A.D., J.S., S.H.P., C.W., P.C. N.S., C.H., B.S, S.C. have nothing to disclose.

F.B. serves on the editorial boards of Brain, European Radiology, Journal of Neurology, Neurosurgery & Psychiatry, Neurology, Multiple Sclerosis, and Neuroradiology, and serves as consultant for Bayer Shering Pharma, Sanofi-Aventis, Biogen-Idec, TEVA Pharmaceuticals, Genzyme, Merck-Serono, Novartis, Roche, Synthon, Jansen Research, and Lundbeck.

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D.H.M. has received honoraria through payments to UCL Institute of Neurology, for Advisory Committee and/or Consultancy advice in multiple sclerosis studies from Novartis and Mitsubishi Pharma Europe and compensation through payments to UCL Institute of Neurology for performing central MRI analysis of a multiple sclerosis trial from Novartis.
G.G. is a steering committee member on the daclizumab trials for AbbVie, the BG12 and daclizumab trials for Biogen-Idec, the fingolimod and siponimod trials for Novartis, the laquinimod trials for Teva, and the ocrelizumab trials for Roche. He has also received consultancy fees for advisory board meetings for oral cladribine trials for Merck-Serono, Genzyme-Sanofi, and in relation to DSMB activities for Synthon BV, as well as honoraria for speaking at the Physicians' summit and several medical education meetings. He is also the co-chief editor of Multiple Sclerosis and Related Disorders (Elsevier).
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