Abstract Number: [1906]

Abstract Title: Brain-age association with clinical and neuropsychological biomarkers in progressive multiple sclerosis patients

Abstract Category: Imaging and non-imaging biomarkers - 32 - Big data and artificial intelligence

Preferred Presentation Type: Oral or poster presentation

Ermelinda De Meo*1, Charles Willard2, Amy Jolly1, Licinio Craveiro3, Marco Ganzetti3, Agne Kazlauskaitė3, Corrado Bernasconi3, Arman Eshaghi1, Frederik Barkhof1, Declan Chard1, James Cole4

1University College London, Neuroinflammation, London, United Kingdom, 2QSA, London, United Kingdom, 3Hoffmann-La Roche, Basel, Switzerland, 4University College London, Computer Science, London, United Kingdom

Introduction:
The difference between individual’s age and age predicted from neuroimaging data using machine-learning methodologies, the so-called brain-predicted age difference (brain-PAD) has recently been proposed as an age-adjusted index of brain health.

Objectives/Aims:
To assess the role of brain-PAD as potential biomarker for clinical disability and neuropsychological performance in people with progressive multiple sclerosis (PMS) enrolled in the phase IIIb CONSONANCE study (NCT03523858).

Methods:
Predicted brain age was estimated with a neural network algorithm that was previously trained (80%), tested (10%) and validated (10%) on T1-weighted MR images of 3752 healthy subjects obtained from publically available datasets (UK biobank, OASIS, IXI, HCP). In the present analysis, brain-PAD was computed at baseline for the first 633 people with PMS (309 primary PMS [PPMS] and 324 secondary [SPMS]) who enrolled in the study. Each clinical variable (Expanded Disability Status Scale [EDSS], Timed 25-Foot Walk Test [T25FW], 9-Hole-Peg Test [9HPT], Symbol Digit Modalities Test [SDMT] and Brief Visuospatial Memory Test [BVMT]) was separately predicted using an independent LASSO regression model. Independent variables included in these models were brain-PAD and regional brain volumes of the brainstem, pons, deep gray matter, cerebellum, temporal lobe, frontal lobe, limbic cortex, parietal lobe, occipital lobe, optic chiasm. These regional volumes were extracted using GIF (University College London). Additional covariates included in the models were age, gender, education status and clinical phenotype.

Results:
People with SPMS had higher brain-PAD than people with PPMS (mean±SD 4.18±10.99 years vs 0.46±11.01 years, p=0.005). Only brain-PAD significantly associated with EDSS, T25FW, BVMT (p<0.001), whereas both brain-PAD and temporal lobe volume were associated with 9HPT and SDMT (p<0.001). No other associations between volumetric MRI outcomes and clinical variables were observed. These results indicate that a positive brain-PAD (actual age>predicted age) was associated with higher EDSS, worse performance on T25FW, 9HPT, SDMT and BVMT.

Conclusion:
Compared to conventional volumetric measures, brain-PAD may provide greater contribution in explaining clinical disability. Future work interrogating longitudinal brain-PAD trajectories will assess brain-PAD as a potential biomarker for disease monitoring.

**Disclosures:**
- Ermelinda De Meo: nothing to disclose
- Charles Willard: nothing to disclose
- Amy Jolly: nothing to disclose
- Licinio Craveiro: is an employee of and shareholder in F. Hoffmann-La Roche Ltd
- Marco Ganzetti: is a contractor for F. Hoffmann-La Roche Ltd.
- Agne Kazlauskaite: is an employee of and shareholder in F. Hoffmann-La Roche Ltd
- Corrado Bernasconi: is a contractor for F. Hoffmann-La Roche Ltd.
- Arman Eshaghi: has received research grants from the Medical Research Council (MRC), National Institute for Health and Care Research (NIHR), Innovate UK, Biogen, Merck, and Roche. He serves as an advisory board member of Merck Serono. He is the founder and equity stake holder in Queen Square Analytics Limited. He serves on the editorial board of Neurology (American Academy of Neurology).
- Frederik Barkhof: is supported by the NIHR Biomedical Research Centre at UCLH and is a consultant to Biogen, Combinotics, IXICO, Merck, and Roche. NDeS is a consultant for Biogen, Merck, Novartis, Sanofi, Roche, and Teva; has grants or grants pending from FISM and Novartis, is on the speakers’ bureaus of Biogen, Merck, Novartis, Roche, Sanofi, and Teva; and has received travel funds from Merck, Novartis, Roche, Sanofi, and Teva.
- Declan Chard: is a consultant for Biogen and Hoffmann-La Roche. He has received research funding from the International Progressive MS Alliance, the MS Society, and the National Institute for Health Research (NIHR) University College London Hospitals (UCLH) Biomedical Research Centre

**Travel / Abstract Grant Application and Young Scientific Investigators’ Session:** I wish to apply for Travel Grant and/or Young Scientific Investigators’ Session

**Which one would you like to apply to:** I wish to apply for Travel / Abstract Grant and Young Scientific Investigators’ Session

**Date of Birth:** 29/04/1989