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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

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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-weigthed 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.

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