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Serum neurofilament light levels in relation to the Brain-Age Paradigm in normal ageing

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Background: Serum neurofilament light (sNfL) is an easy accessible biomarker that increases upon neuro-axonal injury and neurodegeneration. Previous studies have shown that sNfL levels rise in normal ageing, which was further correlated to brain volume changes. The Brain-Age paradigm is a machine learning approach which predicts brain-age from neuroimaging data. We assessed whether brain-predicted age differences (brain-PAD) correlated with sNfL levels in a community-dwelling cohort.

Method: We included 328 neurologically normal individuals participating in a community-dwelling cohort study free of a history of previous stroke or dementia. There were 193 females. Age ranged from 38 to 85 years, with a median of 68.11 (IQR: 55.90 73.18) years. Brain-PAD was measured using neuroimaging data attained from T1-weighted MRI, and sNfL was quantified by a single molecule array (Simoa) assay.

Results: sNfL correlated with chronological age ($r=0.73$, $p<0.001$) and brain-predicted age ($r=0.65$, $p<0.001$). However, sNfL was unrelated to brain-PAD ($r=0.038$, $p=0.50$). Further analyses revealed no differences in brain-PAD comparing individuals within the lowest and the highest sNfL quartile ($p=0.57$), with a mean brain-PAD of 0.79 ± 6.03 and 1.42 ± 7.97 years respectively.

Conclusion: Although sNfL correlated with chronological and brain predicted age, no correlation was found regarding brain-PAD. This could be due to a lower brain-PAD variation in our community-dwelling cohort. Moreover, factors apart from neurodegeneration such as reduced protein turn-over in higher age may be associated with the age-related increase in sNfL, which may have hampered to find associations between sNfL and brain-PAD.