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NEUROIMAGING

The Link between Brain age and Alzheimer's Disease development using different neuroimaging modalities

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Abstract

Background: Brain age (BA) provides a proxy of general brain health through the prediction of chronological age (CA) from neuroimaging data of healthy individuals. During aging, the adult brain undergoes changes both on the morphological and metabolic level. Here, we compare the link between BA predicted from morphology (structural MRI) or metabolism (^{18}F-FDG-PET) and cognitive function, as well as pathophysiological measures of Alzheimer's disease (AD) in cognitively normal individuals (CN) and patients with mild cognitive impairment (MCI).

Method: Several machine learning algorithms were trained to predict BA from 256 matched MRI or ^{18}F-FDG-PET scans of CN from the Alzheimer's Disease Neuroimaging Initiative. Trained algorithms were then used to predict BA in a test sample of CN (n = 123) and MCI (n = 621). Partial spearman correlations between brain-predicted age difference (BA – CA; BPAD) and composite scores of cognitive function (memory: ADNI-MEM; executive function: ADNI-EF), as well as pathophysiological measures of AD (amyloid (cerebrospinal fluid (CSF) and PET) and tau pathology (CSF tau and p-tau)) were subsequently calculated in these test samples correcting for sex.

Result: ^{18}F-FDG-PET- and MRI-predicted brain age showed a mean absolute error of 2.77 and 1.81 years in CN, respectively.

ADNI-MEM scores declined with increasing ^{18}F-FDG-PET-BPAD, while ADNI-EF scores declined with increasing MRI-BPAD in CN.

Higher BPAD was significantly associated with worse cognitive function in MCI in both modalities, while stronger associations were found for MRI-BPAD and cognitive function.

^{18}F-FDG-PET-, but not MRI-BPAD was correlated with CSF amyloid load in CN.

In MCI, higher BPAD from both modalities was associated with more amyloid and CSF p-tau pathology, while only MRI-BPAD was significantly associated with an increase of CSF tau pathology. Associations of MRI-BPAD and pathology were generally stronger.

Conclusion: Brain age can be reliably predicted on the basis of ^{18}F-FDG-PET and MRI. Amyloid-neuropathology, predisposing for AD, as well as initial memory decline is related to features of advanced BPAD in ^{18}F-FDG-PET ahead of clinical onset of

disease. Onset of tau-related neurodegeneration and of objective cognitive decline is more strongly associated with signals of increasing BPAD on MRI.