Amyloid-PET imaging predicts functional decline in clinically normal individuals

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Abstract:

Background: There is good evidence that elevated amyloid-β (Aβ) positron emission tomography (PET) signal is associated with cognitive decline in clinically normal (CN) individuals. However, it is less well established whether there is an association between the Aβ burden and decline in daily living activities in this population. Moreover, Aβ-PET Centiloids (CL) thresholds that can optimally predict functional decline have not yet been established.

Methods: Cross-sectional and longitudinal analyses over a mean three-year timeframe were performed on the European amyloid-PET imaging AMYPAD-PNHS dataset that phenotypes 1260 individuals, including 1032 CN individuals and 228 participants with questionable functional impairment. Amyloid-PET was assessed continuously on the Centiloid (CL) scale and using Aβ groups (CL < 12 = Aβ-, 12 ≤ CL ≤ 50 = Aβ-intermediate/Aβ± , CL > 50 = Aβ+). Functional abilities were longitudinally assessed using the Clinical Dementia Rating (Global-CDR, CDR-SOB) and the Amsterdam Instrumental Activities of Daily Living Questionnaire (A-IADL-Q). The Global-CDR was available for the 1260 participants at baseline, while baseline CDR-SOB and A-IADL-Q scores and longitudinal functional data were available for different subsamples that had similar characteristics to those of the entire sample.

Results: Participants included 765 Aβ- (61%, Mdnage = 66.0, IQRage = 61.0–71.0; 59% women), 301 Aβ± (24%; Mdnage = 69.0, IQRage = 64.0–75.0; 53% women) and 194 Aβ+ individuals (15%, Mdnage = 73.0, IQRage = 68.0–78.0; 53% women). Cross-sectionally, CL values were associated with CDR outcomes. Longitudinally, baseline CL values predicted prospective changes in the CDR-SOB (bCL*Time = 0.001/CL/year, 95% CI [0.0005,0.0024], p = .003) and A-IADL-Q (bCL*Time = -0.010/CL/year, 95% CI [-0.016,-0.004], p = .002) scores in initially CN participants. Increased clinical progression (Global-CDR > 0) was mainly observed in Aβ+ CN individuals (HRAβ+ vs Aβ- = 2.55, 95% CI [1.16,5.60], p = .020). Optimal thresholds for predicting decline were found at 41 CL using the CDR-SOB (bAβ+ vs Aβ- = 0.137/year, 95% CI [0.069,0.206], p < .001) and 28 CL using the A-IADL-Q (bAβ+ vs Aβ- = -0.693/year, 95% CI [-1.179,-0.208], p = .005).

Conclusions: Amyloid-PET quantification supports the identification of CN individuals at risk of functional decline.

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