Longitudinal changes in 18F-Flutemetamol amyloid load in cognitively intact APOE4 carriers versus noncarriers: Methodological considerations

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Purpose: Measuring longitudinal changes in amyloid load in the asymptomatic stage of Alzheimer's disease is of high relevance for clinical research and progress towards more efficacious, timely treatments. Apolipoprotein E ε4 (APOE4) has a well-established effect on the rate of amyloid accumulation. Here we investigated which region of interest and which reference region perform best at detecting the effect of APOE4 on longitudinal amyloid load in individuals participating in the Flemish Prevent Alzheimer's Disease Cohort KU Leuven (F-PACK).

Methods: Ninety cognitively intact F-PACK participants (baseline age: 68 (52–80) years, 46 males, 42 APOE4 carriers) received structural MRI and 18F-Flutemetamol PET scans at baseline and follow-up (6.2 (3.4–10.9) year interval). Standardised uptake value ratios (SUVRs) and Centiloids (CLs) were calculated in a composite cortical volume of interest (SUVRcomp/CL) and in the precuneus (SUVRprec), and amyloid rate of change derived: (follow-up amyloid load – baseline amyloid load) / time interval (years). Four reference regions were used to derive amyloid load: whole cerebellum, cerebellar grey matter, eroded subcortical white matter, and pons.

Results: When using whole cerebellum or cerebellar grey matter as reference region, APOE4 carriers had a significantly higher SUVRcomp amyloid rate of change than non-carriers (pcorr = 0.004, t = 3.40 (CI 0.005–0.018); pcorr = 0.036, t = 2.66 (CI 0.003–0.018), respectively). Significance was not observed for eroded subcortical white matter or pons (pcorr = 0.144, t = 2.13 (CI 0.0003–0.008); pcorr = 0.116, t = 2.22 (CI 0.005–0.010), respectively). When using CLs as the amyloid measurement, and whole cerebellum, APOE4 carriers had a higher amyloid rate of change than non-carriers (pcorr = 0.012, t = 3.05 (CI 0.499–2.359)). Significance was not observed for the other reference regions. No significance was observed with any of the reference regions and amyloid rate of change in the precuneus (SUVRprec).

Conclusion: In this cognitively intact cohort, a composite neocortical volume of interest together with whole cerebellum or cerebellar grey matter as reference region are the methods of choice for detecting APOE4-dependent differences in amyloid rate of change.

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