Cerebral blood flow, amyloid burden, vascular risk factors, early amyloid accumulation

Introduction

Recent findings indicate considerable overlap between cerebrovascular disease and Alzheimer’s disease (AD), suggesting additive or synergistic effects of both pathologies on cognitive decline [1,2]. As cerebrovascular and Alzheimer’s proteinopathies have previously shown to affect cerebral blood flow (CBF) as well as cognition, CBF could be a potential early hemodynamic biomarker of cognitive decline. Here, we investigated to what extent cardiovascular risk factors and amyloid burden affect CBF in an elderly cognitively unimpaired (CU) population.

Methods

Cognitively unimpaired participants (minimal MMSE ≥ 28) underwent [18F]Flutemetamol PET and arterial spin labeling (ASL) MRI. Cortical amyloid burden was quantified with the Centiloid method globally and for 4 early amyloid accumulation regions of interest (ROIs) (Figure 1). Amyloid-PET scans were visually assessed as negative or positive, upon which participants were grouped based on their longitudinal changes in amyloid positivity (visual read groups). ASL scans were processed and quantified with ExploreASL for total gray matter (GM), and for vascular territories overlapping with the amyloid ROIs (Figure 1).

Results

* While no association between amyloid burden and CBF was observed across the cohort, in participants with a high Framingham vascular risk score, higher amyloid was associated with increased CBF, for most ROIs (Table 1, Figure 2).

* Additionally, preamyloid burden was predictive of CBF change in the corresponding vascular territory (Figure 3). Visual reading shows that subjects with high amyloid burden at baseline had a higher increase of CBF at follow-up (Stable AB+, Figure 4).

Discussion

In an elderly cognitively unimpaired population:

- The effect of amyloid on CBF is dependent on vascular burden, and CBF increases with increased amyloid and Framingham scores, this can be seen as a compensatory mechanism of CBF.
- Only preamyloid Centiloid was predictor of changes in CBF, which is one of the most vulnerable regions for early amyloid accumulation, and responsible for memory and integration of information.
- The group that was already amyloid positive at baseline was the most susceptible and the one where CBF increased the most at follow-up, suggesting again this compensational mechanism of CBF to amyloid accumulation.

Conclusion

Statistical analysis

Associations between CBF and amyloid — with and without the interaction of vascular risk factors (i.e. Framingham score) — were assessed using generalized estimating equations (GEEs), both for baseline and rates of change measurements. Models were adjusted for age, sex, and twin dependency.

References


Contact

Beatriz Padrela
b.estevespadrela@amsterdummc.nl