

## Quantification of baseline amyloid PET in individuals with subjective cognitive decline can identify risk of amyloid accumulation and cognitive worsening the FACEHBI study

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### Abstract:

**Purpose:** Amyloid PET imaging is capable of measuring brain amyloid load in vivo. The aim of this study is to assess the relationship of the baseline amyloid with its accumulation over time and with cognition in individuals with subjective cognitive decline (SCD), giving a focus on those below A $\beta$  positivity thresholds.

**Methods:** 118 of 197 individuals with SCD from the Fundació ACE Healthy Brain Initiative underwent three [18F]florbetaben scans and the remaining 79 underwent two scans in a 5-year span. Individuals were categorised based on baseline Centiloid values (CL) into amyloid positive (A $\beta$ +, CL > 35.7), Grey Zone (GZ; 20 < CL  $\leq$  35.7), and amyloid negative (A $\beta$ -, CL  $\leq$  20). Relationship between conversion to mild cognitive decline (MCI) and baseline amyloid levels was assessed. Then, to focus on sub-threshold individuals with amyloid accumulation, the A $\beta$ -group was split into two groups (N1 (CL  $\leq$  13.5) and N2 (13.5 < CL  $\leq$  20)), A $\beta$  accumulation was determined, and a parametric image analysis of the A $\beta$  accumulators in the N1 group was performed.

**Results:** At baseline, 20 individuals were A $\beta$ +, 8 GZ, 160 N1, and 9 N2. Higher A $\beta$  load, older and less educated individuals presented increased risk of MCI-conversion. Longitudinally, 19% of N1 individuals were accumulators despite very low A $\beta$  burden at baseline. Meanwhile, 89% of the N2 group accumulated A $\beta$  as well as all GZ individuals (which had the highest rate of amyloid accumulation, 5.1 CL/year). In the parametric image analysis of N1 accumulators, a region within the precuneus was linked to increased A $\beta$  over time.

**Conclusion:** Baseline amyloid levels differentiate individuals who accumulate amyloid over time and that are at risk for cognitive decline, including those at sub-threshold levels of A $\beta$ . This can be valuable to identify pre-clinical AD in a SCD population.

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