



Title: The β -amyloid pool in blood helps to distinguish between prodromal AD (probable MCI and other MCI).

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Abstract:

Introduction: Current biomarkers of amyloid-beta (CSF and PET amyloid imaging) primarily reflect conical amyloid fibrils deposition which could characterize stage I of preclinical Alzheimer's disease (AD, Sperling at al. *Alzheimer's & Dementia* (2011) 1-13). However, as circulating oligomeric forms of amyloid may be critical in the pathological cascade, it might be possible to find still earlier biomarkers that would allow detecting the true onset of the pathological process. We have reported that several blood A β markers, including the calculated total A β 40 + A β 42 (pool in blood), discriminated between healthy people and mild cognitive impairment (MCI) patients with high sensitivity and specificity.

Objectives: The present work was aimed to validate those results in a new population sample with a special focus in the comparison between probable-MCI (equivalent to prodromal AD) and possible-MCI. **Material and methods:** We measured A β 40 and A β 42 free in plasma (FP), total in plasma (TP) and cell bound (CB) in groups (n=16 each) of healthy controls (HC) 45-54, HC 55-64 and HC>65 years old, probable-MCI, possible-MCI and AD patients by ELISA sandwich (ABtest40 and ABtest42. Araclon Biotech Ltd. Zaragoza, Spain).

Results: In agreement with our previous work, we found that all A β blood markers increased in probable-MCI with regard to HC>65 (except CB A β 40). These differences reached statistical significance for TP A β 40, CB A β 42, total A β 42 and the total pool in blood. **Discussion:** Interestingly, we also found that total A β 42 and the total pool in blood measurements were significantly higher in probable-MCI, considered the prodromal stage of AD, than in possible-MCI, considered to have less chance to convert to AD. Not significant increments were found in any marker neither between probable-MCI and mild-AD patients nor between possible-MCI and aged matched HC.

Conclusion: These results reinforce the interest of blood A β markers for early diagnostic of A β pathology, screening of participants and assessment of efficacy in clinical trials of A β -targeted drugs.