

waves of both these longitudinal studies are underway to assess the predictive power of plasma biomarkers for cognitive decline from MCI to AD.

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PLASMA BETA-AMYLOID CORRELATES WITH COGNITION AND BRAIN VOLUMETRICS IN MILD COGNITIVE IMPAIRMENT

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Background: A β peptides are hallmark features of Alzheimer's disease (AD), and their potential for use as biomarkers of disease onset, progression, response to treatment or population based screening is of considerable interest. While A β expression in CSF over the course of AD is reasonably well established, levels in plasma and their relevance to cognitive and brain volumetric changes are less well defined, particularly at prodromal stages such as amnesic mild cognitive impairment (aMCI). We report plasma A β 1-40 and A β 1-42 levels in a population based cohort study, to determine whether: (1) plasma A β peptide levels correlate cross-sectionally with brain volumetrics and cognitive performance in elderly individuals with and without aMCI, (2) there is a differential effect of plasma A β peptide levels in APOE e 4 carrier vs non-carrier subjects. **Methods:** Subjects with aMCI (n = 89) and controls (n = 126) were drawn from wave 1 of the Sydney Memory and Aging Study (MAS), a population based study of nondemented 70-90 year old adults. AD patients (n=39) were included from a memory disorders clinic. MAS participants underwent brain MRI scans and were assessed on 10 cognitive tests. Plasma levels of A β 1-40 and 1-42 were quantified using sandwich ELISA and comparisons corrected for age, sex, education and APOE e 4 carrier status. **Results:** Baseline plasma levels of A β 1-42 and A β 1-42/1-40 ratio were reduced in aMCI and AD, and were positively associated with cognitive performance, total grey matter volume and hippocampal volume and negatively with white matter hyperintensity volume. Baseline levels of A β 1-40 were also lower in aMCI and AD but significant associations with general cognition and brain volumetric measures only appear in APOE e 4 carriers. By contrast the effects of A β 1-42 are predominantly expressed in non-carriers of the e 4 allele. **Conclusions:** These data show that plasma A β 1-42 and the A β 1-42/A β 1-40 ratio reflect the trends predicted by the A β sink model of pathology, and may serve as blood biomarkers of AD at a pre-dementia stage. Significant cognitive and brain volumetric associations were observed with A β 1-40 in APOE e 4 carriers and with A β 1-42 in APOE e 4 non-carriers.

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THE COMPARISON OF OLIGOMERIC BETA-AMYLOID AND TOTAL BETA-AMYLOID IN PEOPLE WITH ALZHEIMER'S DISEASE AND COGNITIVELY NORMAL INDIVIDUALS

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Background: Amyloid- β (A β) peptide is the main component of amyloid plaques that is recognized as a neuropathological hallmark of Alzheimer's disease (AD). Studies on total A β in plasma as biomarkers for AD have been contradictory. Here, we have compared level of A β oligomers as major toxic species of AD, with total A β . **Methods:** For evaluation of A β oligomers, Multimer Detection System (MDS) was used. In MDS, epitope-overlapping N-terminal A β antibodies were used for capturing and detecting of antigen. Using this system, we tested A β oligomers in samples from 20 patients with clinically diagnosed AD and 20 healthy normal. For quantitation of total A β in samples, a commercially available kit was used. **Results:** We confirmed A β oligomers differentiated AD and healthy normal clearly in comparison to total A β in the samples. On the other hand, data did not show clear difference in concentrations of total A β between healthy normal group and AD patients. **Conclusions:** In comparison of total A β levels and A β oligomers levels between AD patients and healthy normal, our findings show that the level of A β oligomers is more effective in differentiation of AD patients from healthy normal, possibility of serving as a more powerful biomarker for AD diagnosis than total A β in samples.

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VALIDATION OF BETA-AMYLOID TEST AS A RELIABLE TOOL FOR QUANTIFYING BETA-AMYLOID 1-40 AND BETA-AMYLOID 1-42 IN BLOOD

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Background: Owing to the urgent requirement of easily accessible biomarkers for a wide-population screening of people at risk of suffering Alzheimer's disease (AD), there is increasing interest in blood AD biomarkers. The aim of this study was to validate two ELISA tests, ABtest40 and ABtest42, as reliable and sensitive tools for the quantification of A β 1-40 and A β 1-42 at levels as low as those present in blood. **Methods:** Inter and intra-assay precision was evaluated by repeated testing of 3 samples covering the whole range of quantification within 3 independent runs. Sensitivity of the assay was assessed by the estimation of the LLOQ (lower limit of quantification) and specificity was established by confirming absence of cross-reactivity with other A β species. Evaluation of relative error (RE) in quantification at LLOQ and ULOQ (upper limit of quantification) allowed the test accuracy assessment. **Results:** Intra and inter-assay coefficients of variation were below 8% for both ABtest40 and ABtest42. The estimated LLOQ was 4.68pg/ml regarding ABtest40 and 11.95pg/ml for ABtest42. Accuracy of A β 1-40 and A β 1-42 quantification at LLOQ and ULOQ provided a relative error below 16% in all cases. Assays demonstrated very high affinity for their target analytes; cross reactivity was less than 3.35% for all the similar A β species tested at the ULOQ (N-terminal specificity assessed using A β 2-40 and A β 3-40 and C-terminal with A β 1-38, A β 1-43 and either A β 1-40 or A β 1-42). **Conclusions:** ABtest40 and ABtest42 proved to be accurate, specific and sensible enough to give a reliable quantification of low levels of A β 1-40 and A β 1-42.

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THE EFFECT OF ANTICOAGULANT AND SAMPLE PREPARATION METHOD ON BETA-AMYLOID OLIGOMER DETECTION IN BLOOD

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Background: Recent studies suggest that soluble amyloid- β (A β) oligomers are major toxic species responsible for Alzheimer's disease (AD)