EMIF Deliverable 4.1: Report on cross-validated plasma, genetic, CSF, MRI markers for diagnosis for predementia of AD

Executive summary

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The objective of this deliverable is to report the work done: 1. To cross-validate the new plasma, CSF, genetic and MRI markers from WP 3 or related biomarker discovery studies in an independent cohort, and to estimate variability resulting from inter-biobanking samples collection procedures. 2. To investigate the relation between genetic risk factors and amyloid pathology on neuropathological examination. 3. To investigate the relation between new AD plasma and CFS biomarkers and long-term cognitive decline in the general population.

Relation between two candidate biomarkers discovered in the WP3 (Ficolin-2 and Fibrinogen gamma) was investigated in an independent cohort and compared to the four CSF biomarkers (Aβ1-42, Aβ42/40, Tau, and pTau181.

Neurogranin (Ng), YKL40, and NfL were validated against amyloid status and clinical diagnosis in the preclinAD cohort, SNAP cohort and ADNI study. Relation between plasma NfL concentrations and the four CSF AD biomarkers (incl. Aβ42/40) in MCI, AD-type dementia, and controls was investigated. Plasma NfL was also validated in terms of preanalytical sample handling procedure.

A cross-validation study was performed testing concordance of two CSF biomarkers - a well established one (Aβ1-42) and a candidate (Aβ42/40 ratio) with the Aβ-PET results; it was shown that Aβ42/40 correlates better with the PET findings than Aβ1-42.

The genomics team has generated novel data for EMIF-AD cohort within WP3 and generated validation results using the genomics and corresponding phenotype data in ADNI.

We replicated the effect of amyloid pathology on brain atrophy in MCI in the Amsterdam Dementia Cohort. In subjects with MCI, both abnormal amyloid CSF and decreased gray matter volume were associated with future progression to dementia. The spatial pattern of decreased gray matter volume associated with progression to dementia was consistent for amyloid-positive and amyloid-negative subjects.

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