GENOME-WIDE LINKAGE AND ASSOCIATION ANALYSES IN NONDEMENTED HYPERTENSIVE INDIVIDUALS SUGGEST ASSOCIATION OF PSEN2 WITH PLASMA AMYLOID BETA

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Introduction: Plasma amyloid beta (abeta) is an easily obtained marker for abeta load in brain, which is highly correlated with hippocampal atrophy, a biomarker for early stages of late-onset Alzheimer disease.

Aims: The aim of this study was to find genetic variants associated with plasma abeta levels.

Methods: This study included 128 nondemented hypertensive subjects 55 to 75 years old from the Erasmus Rucphen Family (ERF) study. Quantitative trait linkage analysis was performed for non-fasting plasma abeta levels (AB40, AB42, and truncated forms ABn40 and ABn42) in MERLIN. Regions with at least suggestive evidence of linkage were followed up with association analysis using linear mixed model in GenABEL. All analyses were adjusted for age and sex.

Results: Linkage analysis revealed two regions with LOD scores >1.9, both for AB40: 1q41 (LOD = 2.07) and 11q14.3 (LOD=2.97). For the region on chromosome 1, strong association was observed at the PSEN2 gene (p-value 2.5x10^-4). There is suggestive evidence for association to chromosome 11q14-21 (p-value 3.1x10^-3)

Conclusions: Our combined results from linkage and association indicate an association between PSEN2 and plasma AB40. The high LOD region on chromosome 11 for AB40 is close to region 11q25 found to be associated with depressive disorder (1), with autism (2) and with late-onset Alzheimer's disease (3). This region is therefore of particular interest for further research.

References: