THE LONGITUDINAL CHANGES OF CSF BIOMARKERS IN ALZHEIMER’S DISEASE - CSF HYPERPHOSPHORYLATED TAU DECREASES IN CONNECTION WITH COGNITIVE DECLINE DURING THE AD PROCESS

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Introduction: Longitudinal changes of Alzheimer’s disease CSF biomarkers have been studied with indefinite results and little is known of their variation in different stages of the disease course.

Aims: To examine the connection between the progression of the cognitive decline and longitudinal CSF biomarker changes.

Methods: 131 memory clinic patients (56 AD, 57 MCI, 10 other neurological disorders, 8 unimpaired) underwent a clinical follow-up with repeated MMSE tests and two lumbar punctures with a median interval of 2.98 years. CSF Aβ42, tau and p-tau-181 concentrations were measured using commercially available ELISA.

Results: 21 subjects progressed to AD and 26 subjects remained stable with MCI.

Subjects with the fastest MMSE decrease rate had the lowest baseline Aβ42, highest tau and highest p-tau-181 CSF concentrations. An annual decrease of -2.20 pg/ml/year in the CSF p-tau-181 concentration of AD-AD patients was noticed. The difference was significant compared to stable MCI-MCI (increase of 1.24 pg/ml/year) and cognitively healthy (increase of 0.84 pg/ml/year) subjects (p for group differences 0.004). The decrease rate of p-tau-181 correlated to MMSE decrease rate (r=0.402, p<0.001). The CSF Aβ42 decreased faster in the AD-AD group (decrease of -11.9 pg/ml/year) compared to MCI-MCI group (increase of 3.42 pg/ml/year). The APOE ε4 allele was associated with a greater decrease of p-tau-181 and a smaller increase of total tau in the follow-up.

Conclusions: Hyperphosphorylated tau decreases in the late stages of the AD process. The decrease of p-tau-181 may correlate to clinical cognitive functioning, probably as a reflector to neuronal loss.