BETA-AMYLOID OLIGOMERS IN CSF ARE ASSOCIATED WITH COGNITIVE DECLINE IN PATIENTS WITH ALZHEIMER'S DISEASE

A.N. Santos¹, M. Ewers², A. Simm¹, R.-E. Silber¹, K. Blennow³, O. Hansson⁴, H. Hampel²

¹Department of Cardiothoracic Surgery, Martin-Luther-University Halle-Wittenberg, Halle, Germany,
²Trinity College Dublin, Dublin, Ireland, ³University of Göteborg, Sahlgrenska University Hospital,
Göteborg, ⁴Clinical Memory Research Unit, Lund University, Malmö, Sweden

Background: Oligomers of the amyloid b peptide (Ab) are thought to be the most toxic form of Aβ and are linked to the development of Alzheimer’s disease (AD).

Methods: 30 CSF samples from patients suffering from AD (n = 14) and other neurological disorders (non-demented n= 12; Lewy bodies dementia n = 2; vascular dementia n = 1; primary progressive aphasia n = 1) were analyzed for the presence of Ab-oligomers by flow cytometry. The CSF levels of Total tau (t-tau), phosphorylated Tau (p-Tau) and Ab₁₋₄₂ were determined using ELISA.

Findings: The amount of Ab-oligomers in AD patients was elevated in comparison to the non-AD group (p = 0.08). Using the ratio Ab-oligomers/Ab₁₋₄₂ a significant discrimination between the AD and non-AD groups was achieved (p = 0.001). Most important, there was a negative correlation between the amount of Ab-oligomers and the MMSE (r = -0.51; p = 0.004), indicating that cognitive decline in Alzheimer patients are accompanied by an increase in Ab-oligomers in CSF.

Interpretation: The detection of Ab-oligomers using flow cytometry analysis seems to be useful in assessing the Alzheimer’s disease progression. This is a novel and important finding as none of the currently used CSF biomarkers are clearly associated with the decline of the cognitive function. Furthermore, the measurement of Ab-oligomers in CSF could be a tool for assessing the effects of new AD treatments on oligomeric Ab load in humans.