Efficiency of the ratio of cerebrospinal fluid Aβ42/Aβ40 concentrations in detecting Alzheimer’s disease. A step forwards?

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Introduction / Aims
According to its new conceptualization, Alzheimer’s disease (AD) can be diagnosed independently of its clinical symptoms. As a consequence, biomarkers play a crucial role for diagnosing AD, since they are capable to detect AD pathophysiological processes in oligosymptomatic or even preclinical stages of the disease course. Markers of amyloid pathology such as levels of β-amyloid 1-40 (Aβ40) and 1-42 (Aβ42) in the cerebrospinal fluid (CSF) constitute a valuable instrument not only in the field of diagnosing AD, but also of its differential diagnosis.

Methods
The aim of the present investigation was to study the efficiency of the ratio of CSF concentrations of Aβ42/Aβ40 compared to the efficiency of Aβ42, as determined with two new Enzyme-linked Immunosorbent Assays (ELISA), in detecting AD. The ELISA assays have been developed by IBL International GmbH, Hamburg. The clinical diagnosis based on a comprehensive diagnostic workup embodied the gold standard. The study sample consisted of 40 patients fulfilling the National Institute on Aging – Alzheimer Association (NIA-AA) clinical criteria for dementia due to probable AD (pAD) (age in years: 67.55±7.55, 20 men, 20 women) and 43 cognitively healthy elderly individuals (controls) with normal test results and no history of subjective memory complaints and no dependency with regards to their activities of daily living (age in years: 65.74±8.98, 31 men, 12 women). The intraindividual coefficient of variation (CV) was studied in five samples in each of which Aβ42 and Aβ40 were measured twenty times. A receiver operating characteristic (ROC) curve analysis was employed, in order to select the optimal cut-off value of the ratio Aβ42/Aβ40 and the Aβ42 below which an individual has a very high chance of suffering from pAD and to calculate sensitivity and specificity.

Results
The intraindividual CV varied between 3.1-9.1% (mean 4.9%) and 3.7-6.5% (mean 5.0%) for Aβ42 and Aβ40 respectively (Table 1). The Aβ42/Aβ40 optimal cut-off value was 0.05. The sensitivity was 98% and the specificity was 91%, whilst the sensitivity and specificity of CSF Aβ42 levels was 85% and 86%, respectively, based on a cut-off of 640 pg/mL (Table 2).

Conclusions
The results of the present study point to a higher efficiency of the CSF Aβ42/Aβ40 ratio in detecting AD pathophysiological alterations compared to CSF Aβ42 levels and highlight the reliability of the new essays, which can increase our capacity to detect AD. They are in line with the findings of previous studies which indicate that the association of two or three different biomarkers yields higher sensitivity and specificity than each biomarker alone. Nonetheless, further investigations focused on the efficiency of the ratio in the differential diagnosis of pAD and in detecting in AD in oligosymptomatic and preclinical stages are warranted.

Disclosure of relevant financial relationships
The authors serve as consultants of IBL International GmbH

References