S49.3

CSF tau phosphorylated at threonine 231, total tau and neuronal thread protein in the diagnosis of Alzheimer's disease

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Background: One of the major neuropathological hallmarks of Alzheimer's disease (AD) are neurofibrillary tangles composed of paired helical filaments (PHF). The principal protein subunit of PHF is abnormally hyperphosphorylated tau (p-tau). An elevation of the unspecific total tau protein level (t-tau) in the cerebrospinal fluid (CSF) has been reported in AD. However, there is still considerable overlap of values between AD and relevant controls. Promising efforts are under way to establish biological markers to improve diagnostic accuracy of AD. A major line is combining tau with other disease related proteins and analysing the more specific p-tau in CSF. Phosphorylation of tau at threonine 231 (p-tau231) appears specific and very early in AD and preceeds paired helical filament assembly.

Methods: For t-tau, gp130 and AD7C-NTP we used a commercially available enzyme-linked immunosorbent assay (ELISA)(1–3). P-tau was measured by a newly developed ELISA specific for tau phosphorylated at threonine 231 (4).

Results: T-tau was increased in AD compared to HC. Based on a previously established cut-off of 260 pg/ml, the discriminative power of t-tau was higher in the young old than in the old old subjects. ROC-analysis revealed a higher correct classification rate in the young old (1). A stepwise multivariate discriminant analysis showed that t-tau and solublegp130 maximized separation between groups (2). The combined evaluation of t-tau and AD7C-NTP with discriminant analysis raised specificity (3). CSF levels of p-tau231 significantly improved separation compared to t-tau. P-tau231 was highly increased in AD compared to healthy age-matched controls, other neurological disorders and relevant dementia disorders with high sensitivity and specificity (4). We found a linear decrease only for p-tau231 during the course of AD. In addition, p-tau231 was inversely correlated with the MMSE-score at baseline, accelerating with AD progression (5). Interestingly, the majority of subjects with mild cognitive impairment showed p-tau231 levels above the cutoff that discriminated best between AD and HC.

Conclusion: Diagnostic accuracy could be improved by combining t-tau with age and additional proteins. CSF p-tau231 was particularly useful in early detection, differential diagnosis and mapping disease progression in subjects at risk and AD patients.

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S49.4

Tau, phospho-tau and Ab42 in cerebrospinal fluid in Alzheimer's disease

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The possibility to provide Alzheimer's disease (AD) patients symptomatic treatment with AChE inhibitors has made patients seek medical advice very early in the course of the disease, when symptoms are vague and difficult to distinguish from memory problems associated with normal aging. This has created a great need for biochemical diagnostic markers of AD. Forthcoming disease-arresting drugs (e.g. β/γ-secretase inhibitors) will make this need even larger.

Numerous studies have found an increase in CSF total tau (T-tau) and a decrease in CSF Aβ42 in AD, with sensitivity figures ≈90%. The specificity is also high against normal aging, depression, and Parkinson's disease, but lower against other dementias. The addition of phospho tau (P-tau) increases the specificity, since increased levels are not found in other dementias (e.g. frontotemporal dementia). These CSF-markers are positive in patients with mild cognitive impairment whom will progress to AD.

We use CSF-tau and CSF-Aβ42 in clinical routine in our laboratory. CSF samples are sent for diagnostic purposes from clinicians all over Sweden and ELISAs are run each week as clinical neurochemical routine analyses. Also in this setting, the analytical variation is within the range expected for immunoassays, and we find high sensitivity and specificity figures also in unselected community-based patients.

CSF biomarkers may also be useful to monitor the biochemical effect of new potential therapeutic compounds. Catching the clinical effect of "disease-arresting" drugs that partly may slow down the degeneration will need very large patient materials and extended treatment periods. The biochemical effect may be identified much earlier and in much smaller patient samples, by analyzing specific CSF biomarkers before and after a shorter period of treatment. Data will be presented on the performance of these CSF-markers after treatment of AD patients with drugs, including AChE inhibitors and cholesterol-lowering agents (statins).

S49.5

Aβ42 plasma in the diagnosis of Alzheimer's disease

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No abstract was available at the time of printing.

S50. Culture and refugee trauma

Chairs: M. Fernandez (S), A.J. Marsella (USA)

S50.1

Culture, trauma and refugees

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This presentation will review the current global situation regarding the growing numbers of international refugees and the complex

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