

## Signature of three CSF biomarkers for detection of Alzheimer's.

Researchers from a bio-pharmaceutical company in Belgium reported in the August issue of the Archives of Neurology that a signature of three biomarkers might be able to predict patients at risk of developing Alzheimer's disease (AD), and identify patients with AD. The three biomarkers are beta-amyloid protein 1-42, total tau protein, and phosphorylated tau.

It is known that low beta-amyloid levels and high tau protein levels in cerebrospinal fluid (CSF) are a hallmark of dementia and AD; but the pathological process can precede symptoms by 10 years or more.

In their study, the researchers looked at the levels of the three biomarkers in 416 patients from the ADNI (Alzheimer's Disease Neuroimaging Initiative) database to determine clinical usefulness.

The signature was present in 90% of those who had AD, 72% of patients with cognitive impairment, and 36% of healthy controls. Many of the signature-positive healthy controls were ApoE4 carriers (genetic risk factor for late-onset AD).

The researchers verified their results using two other data sets. In one analysis of 68 autopsy-confirmed AD cases, 94% were positive for the signature. In another analysis of 57 patients with mild cognitive impairment followed for five years, the signature showed 100% sensitivity in patients progressing to AD.

The researchers stated that the unexpected presence of the Alzheimer's signature in about one-third of healthy subjects suggests that AD is detectable earlier than thought. They state that the test could be applied when patients present with memory problems, and could help a physician make a distinction whether this was related to ongoing brain disease like AD, or whether some other factor (for example, depression, multi-infarct dementia) was involved. The researchers state that the use of a CSF biomarker profile with a clinical battery would help physicians to identify an AD patient, or a patient who would progress to AD within five to ten years. (They thus imply that these biomarkers need to be included in criteria to diagnose a person with dementia.)

Three of the authors are employees of the company that makes the cerebrospinal fluid assays used in the study. One author was a former employee.

An accompanying editorial states that the study confirms the value of measuring CSF biomarkers in predicting the conversion of mild cognitive impairment to AD. **SMA**

Sources: (1) De Meyer G, et al. Diagnosis-independent Alzheimer disease biomarker signature in cognitively normal elderly people. *Arch Neurol* 2010; 67(8): 949-956. (2) Herskovits AZ, Growdon JH. Sharpen that needle. *Arch Neurol* 2010; 67(8): 918-920.