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Alzheimer's disease: a new prognostic biomarker discovered by a French team in Paris

Alzheimer's disease (AD) is a neurodegenerative disorder, clinically marked by the onset of memory disturbances progressively followed by cognitive deficits. The cause of AD is unknown but according to the "Amyloid Cascade Hypothesis" the accumulation of the amyloid peptide Aβ1-42 in the brain could be at the origin of the neuronal degeneration. Aβ1-42 is able to activate a series of stress kinases in neurons leading to the triggering of cellular toxic pathways. Among these kinases C-Jun-N terminal kinases (JNK) are implicated in various cell functions including neuronal death especially for the JNK3 isoform mainly expressed in the brain.

A French Team led by Prof. Jacques Hugon from the Memory Center at Lariboisiere Hospital in Paris, University Paris Diderot and the Inserm Unit U942, has shown that the protein JNK3 was increased in the brains of 10 AD patients compared to 10 control subjects. JNK3 concentrations correlated with Aβ1-42 concentrations and both molecules we co-expressed in senile plaques, a neuropathological hallmark of AD.

In addition, the cerebrospinal fluid (CSF) levels of JNK3 were statistically increased in 30 AD patients compared to 27 non AD control subjects. AD patients were followed for a period of 1 to 3 years and global cognitive assessment using MMSE was carried out at various intervals. The results showed that JNK3 levels statistically correlated with the cognitive decline of AD patients giving the possibility to predict the rate of cognitive alteration
The French team has previously shown that another stress kinase, PKR, was also a good diagnostic and prognostic CSF AD biomarker.
This work emphasizes the fact that stress kinases including PKR and JKN3 are new potential diagnostic and prognostic biomarkers in AD. Especially, these findings underline that these kinases are new therapeutic targets that could afford neuroprotection and could alter the relentless cognitive decline of AD patients. Preclinical evaluations with kinase inhibitors are currently taking place.

Increased levels of cerebrospinal fluid JNK3 associated with amyloid pathology: links to cognitive decline. Gourmaud et al. Journal of Psychiatry and Neurosciences (in press)

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