Opinion

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Biomarkers in Alzheimer´s Disease

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ABSTRACT

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Opinion

The World Health Organization (WHO) in coordination with the United Nations has defined a biomarker as "any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease" [1]. For Alzheimer's Disease (AD) the established criteria to determine a biomarker are as follows: to describe the physiopathological processes occurring in the brain, to recognize the initial stage of the disease and to monitor its progression, to reflect the therapeutic effectiveness after drug administration, to be highly sensitive (> 85% of the patients) and specific (>85% of individuals who do not have the disease and which are correctly identified), and to produce reproducible results [2,3]. The three biomarkers currently established for the diagnosis of AD are: amyloid β protein, tau protein and phosphorylated tau protein [2,4,5]. When obtained from the CNS, these biomarkers exhibit >95% sensitivity and >85% specificity [2].

Amyloid β Protein

Aβ depositions are widely used to characterize AD. Analysis of Cerebrospinal Fluid (CSF) of AD patients demonstrates a clear reduction of Aβ, due to the formation of aggregates in the brain, which can be detected in patients with mild cognitive impairment as well as in those who are in the preclinical stages of the disease [6]. Amyloid β proteins can also be measured in plasma but their correlation with cerebral amyloid pathology is very small when evaluated by immunological methods probably due to the influence exerted by platelets and other extra-cerebral structures on their secretion [6]. Several studies have shown a clinically significant correlation between amyloid β plasma concentration and AD using mass spectrometry [6-9]. Other studies show that several plasma proteins (pancreatic polypeptide Y, immunoglobulin M, chemokine ligand 13, nterleukin 17, vascular cell adhesion protein 1, α2-macroglobulin, apolipoprotein A1) are associated with the levels of Aβ42 in the brain with independence of the clinical state of the patient [6,10,11].

Tau Protein

Tau protein is one of the specific biomarker for AD since it is present in increased concentrations in the CFS of AD patients being a major component of abnormal intraneuronal aggregates forming in the disease. It can be detected post-mortem by both immuno-histochemical, and biochemical techniques and recently sensitive assays have been developed for its quantification in CSF [6].

Phosphorylated tau: Hyperphosphorylated tau proteins are the main component of neurofibrillary tangles in AD. They intervene in the stabilization and union of the microtubules of the axons of neurons, a process that is inhibited when they are phosphorylated. This condition of phosphorylated tau protein appears in nearly 39 possible sites with position 181 acting as a biomarker in AD when compared to controls [2]. To date there are no adequate blood biomarkers that relate to neurofibrillary tangles in AD but recent studies have shown an increase in the concentration of phosphorylated P-tau in exosomes transmitted by blood representing a promising approach to the diagnosis of the disease [12].

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