PRODROMAL AD – HOW RELIABLE IS THE DIAGNOSIS? ARE WE READY TO START CLINICAL TRIALS? YES

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Alzheimer's disease (AD) is the most common cause of dementia afflicting more than 30 million people worldwide. However, there are still not reliable diagnostic tests for the disorder and definite diagnosis of the disease requires contribution of both, clinical manifestations of dementia and postmortem examinations of the brain for detection of the neuropathological hallmarks of the disease. It is now clear that diagnosis of early (or prodromal) AD is extremely important for testing the efficacy of new drugs and therapies and vital for the identification of the right candidates to benefit from these. Although diagnosis of AD at advanced stages is now relatively reliable based on clinical symptoms, diagnosis of prodromal AD and progression of mild cognitive impairment (MCI) to full-fledged AD is still a challenging task.

MCI is commonly detected by memory tests and lower performance in cognitive domains. The condition may arise from the initial stages of brain neurodegenerative conditions that may develop into AD in a few years, but it is now clear that many MCI patients do not develop dementia of the Alzheimer type. In living NCI patients, evidence of incipient AD neuropathology (prodromal AD) may be provided by a combination of brain imaging and fluid biomarkers. Relevant diagnostic criteria include a number of test and parameters such as cerebral amyloidosis (detected by positron emission tomography (PET)), increased Aβ in cerebrospinal fluid (CSF), imaging of brain atrophy measured by (MRI), evidence of brain hypometabolism by fluorodeoxyglucose (FDG)-PET and CSF tau. It is now believed that presence of some or all of these biomarkers can be predictive of persons with MCI that may progress to AD within a few years. Despite the importance of the above neuropathological indicators, however, a number of questions remain especially when and how are these biomarkers to be used in the design of clinical trials or interventions. Importantly, as increased numbers of clinicians begin to incorporate these measurements into clinical practice, a deeper understanding of their impact and implications on the diagnosis and prediction of AD is of critical importance. In this commentary we will elaborate on the reliability of the MCI diagnostic criteria and whether they can predict subsequent onset of AD. In addition we will comment on their potential use in clinical trials