

DEBATE: CAN WE IDENTIFY INCIPIENT AD-DEMENTIA? NO

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In the last decades a lot of progress has been achieved in understanding the pathogenic mechanisms of Alzheimer's disease (AD) but no unifying theory was able to entirely explain the occurrence of neuropathological lesions and the progression of the disease yet. Beside amyloid cascade and tau hyperphosphorylation, many other pathogenic events and factors might be important, such as Inflammation and interleukins, metals, mitochondria-related oxidation processes, cholesterol rafts and vascular factors, to name just a few. Apart from all debates in the field of AD pathogenesis, a continuous effort to agree on new diagnostic criteria goes on in the last years, in order to enable an earlier identification of the disease and a new drug target strategy. With the current criteria, AD patients are diagnosed and treated in an advanced stage of cognitive deterioration, when a widespread brain pathology and a substantial loss of synapses and neurons already occurred. Structural magnetic resonance imaging, molecular PET neuroimaging and cerebrospinal fluid amyloid and tau species are well described biomarkers which are proposed to have their role in the close future for diagnosing AD. However, sensitivity and specificity of these assessment tools remain to be improved by adding new methods and their availability in many centers remains a problem. For instance, hippocampal atrophy evaluated by MRI yields sensitivity and specificity values between 80-90 % in various studies. Combined assessment of A β 42 and total-tau CSF levels showed sensitivities between 85 and 94 % and specificities between 83 and 100 % in AD versus controls, but specificities were much lower for differentiating AD from other dementia types (39-90 %). Still, a great step forward was made by the development of new AD biomarkers in the last decade. CSF Abeta42, amyloid imaging, and CSF tau are good markers of the presence of AD pathology and reliable predictors of progression from prodromal AD to AD dementia. From recent studies it seems that preclinical AD patients can be identified with reasonable sensitivity and specificity by combined analysis of CSF Abeta42, CSF tau, and amyloid imaging. These patients will be the ideal candidates for new clinical studies designed for disease modification purposes.