



The Rationale Behind the New Alzheimer's Disease Conceptualization: Lessons Learned During the Last Decades

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In the last decades, progress in neuroimaging techniques and cerebrospinal fluid assays has enabled the characterization of several Alzheimer's disease (AD) biomarkers. This knowledge has shifted the conceptualization of AD from a clinical-pathological construct, where its diagnosis required the presence of dementia with distinct pathologic features, toward a clinical-biological one that recognizes AD as a pathological continuum with a clinical picture that ranges from normal cognition to a dementia stage. Specifically, AD is now divided into three stages: preclinical (abnormal biomarkers and no or only subtle cognitive impairment), mild cognitive impairment or prodromal AD (abnormal pathophysiological biomarkers and episodic memory impairment), and dementia (abnormal biomarkers and clear cognitive and functional impairment). The possibility of assessing AD pathophysiology in vivo before the onset of clinical symptoms in the preclinical stage provides the unprecedented opportunity to intervene at earlier stages of the continuum in secondary prevention trials. Currently, large cohort studies of cognitively healthy participants are undergoing with the main aim of disentangling the natural history of AD to identify individuals with an increased risk of developing AD in the near future to be recruited in these clinical trials. In this paper, we review how the concept of AD has changed over the years as well as discuss the implications of this conceptual change.

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