
Notes: In the past 8 years, both the International Working Group (IWG) and the US National Institute on Aging-Alzheimer's Association have contributed criteria for the diagnosis of Alzheimer's disease (AD) that better define clinical phenotypes and integrate biomarkers into the diagnostic process, covering the full staging of the disease. This Position Paper considers the strengths and limitations of the IWG research diagnostic criteria and proposes advances to improve the diagnostic framework. On the basis of these refinements, the diagnosis of AD can be simplified, requiring the presence of an appropriate clinical AD phenotype (typical or atypical) and a pathophysiological biomarker consistent with the presence of Alzheimer's pathology. We propose that downstream topographical biomarkers of the disease, such as volumetric MRI and fluorodeoxyglucose PET, might better serve in the measurement and monitoring of the course of disease. This paper also elaborates on the specific diagnostic criteria for atypical forms of AD, for mixed AD, and for the preclinical states of AD.


Notes: Neuroimaging in the early differential diagnosis of dementia has gained considerable interest over the last decade. From being used for exclusive purposes only, neuroimaging is now in the forefront of aiding in the diagnosis of Alzheimer's disease (AD), frontotemporal dementia, vascular dementia, and dementia with Lewy bodies (DLB). With the exception of dopamine transporter single photon-emission computed tomography imaging in DBL, imaging has not yet been incorporated into the diagnostic criteria for the various dementia syndromes, but that will soon change. The recently formulated research criteria for early AD recently formulated by Dubois et al explicitly mention magnetic resonance imaging and positron emission tomography for AD, and are an example of a new diagnostic process developing. In this review, the various imaging techniques will be highlighted, with an emphasis on their ability to diagnose Alzheimer's disease and separate it from other entities.


Notes: Department of Neurology, Free University Hospital, Amsterdam, The Netherlands In a prospective magnetic resonance imaging (MRI) study we evaluated the prevalence and severity of white matter changes in 29 patients with Alzheimer's Disease (AD) and 24 age-matched healthy elderly, all without cerebrovascular risk factors. The AD patients were divided into two groups according to age at onset of symptoms, one with presenile onset AD (n = 13) and one with senile onset AD (n = 16), who were matched for dementia severity. Signal hyperintensities were rated using a semiquantitative scoring method, separately in the periventricular region (PVH) and in the lobar white matter (WMH), as well as in the basal ganglia (BGH) and in the infratentorial region (ITFH). Cortical atrophy as a parameter of grey matter involvement was rated on a 0 (absent) to 3 (severe) scale. We found PVH, WMH and BGH scores to be significantly higher in senile onset AD patients than in age-matched controls. By means of multiple linear logistic regression we found that PVH, WMH and BGH scores were significantly dependent on the diagnosis of senile onset AD, while the PVH score also showed a significant age dependency. Cortical atrophy did not differ significantly between presenile onset AD and senile onset AD patients. These results indicate that presenile onset AD and senile onset AD patients differ with respect to white matter involvement, but not with respect to grey matter involvement on MRI. Since cerebrovascular risk factors were excluded these findings may
indicate that senile onset AD patients display more small vessel involvement (arteriolosclerosis) than presenile onset AD patients, suggesting additional (microvascular) factors for the dementia syndrome in senile onset AD. Our data lend support to the growing body of evidence that AD is heterogeneous, consisting of at least two types. Based on our findings two forms can be distinguished: (i) a ‘pure’ form of the disease, usually with early disease onset, and no more white matter changes than normal for age; (ii) a ‘mixed’ form, usually with disease onset later in life, and showing more white matter changes on MRI than normal for age.