Redefining Alzheimer’s disease

Advances in our understanding of disease pathology and progression have triggered a review of how AD is diagnosed, resulting in the definition of three phases. Traditionally, an AD diagnosis was based on clinical symptoms complemented by neuropsychological tests. Patients could only be diagnosed with “probable AD”, with a definitive diagnosis made postmortem. With the development of biomarkers, we now understand that AD pathology does not always correlate with clinical symptoms and that disease development (including cognitive deficiency) is progressive. The National Institute of Aging and Alzheimer’s Association (NIA-AA) has recently used disease pathophysiology to define three contiguous stages of AD. The first phase is preclinical AD, in which AD pathology is detectable in asymptomatic patients. Because patients with preclinical AD may never actually develop clinical symptoms, this phase is currently relevant only for research purposes. The second phase is mild cognitive impairment (MCI) due to AD, in which there is symptomatic predementia. Patients are typically still functionally independent but report progressive cognitive decline that is not a normal part of aging. MCI is often the phase during which people seek medical attention, and in the absence of a diagnostic laboratory test, it is important for physicians to know how to diagnose it. Finally is the clinical dementia, the phase during which cognitive, functional, and behavioral symptoms disrupt the routine of daily life. Given the progressive nature of the disease, the boundaries between these three phases overlap and should be considered a continuum. The diagnosis and evaluation of patients may be facilitated by the use of biomarkers. Biomarkers are measurable biological characteristics that can serve as indicators of disease states, and may be used to evaluate disease progression and treatment efficacy. The NIA-AA recommends that biomarkers may be used to identify patients with preclinical AD, in whom clinical symptoms are absent or subtle, which is important for research purposes. In MCI and dementia patients, biomarkers are optional and serve to complement the clinical diagnoses. In contrast, the International Working Group (IWG) for New Research Criteria for the Diagnosis of AD incorporates biomarker use in their diagnostic criteria. For example, they refer to MCI due to AD as “prodromal AD”, for which the clinical criteria are memory impairment without dementia coupled with biomarker evidence of pathology. The current understanding of the amyloid cascade and how it has driven the development of diagnostic and therapeutic strategies will be described. Further research initiatives will also be reviewed including the development of tau biomarkers. Given that diagnosis is missed or delayed in half of all AD patients, we need to improve our diagnostic accuracy, particularly with respect to MCI, and to incorporate biomarkers when possible, based on our understanding of AD pathology.

Biography

Eric G Tangalos is Professor of Medicine at the Mayo Clinic in Rochester, Minnesota. He was Chair of Primary Care Internal Medicine from 1997 to 2006. He received his undergraduate training from the University of Michigan. He is a graduate of the Loyola University Stritch School of Medicine in Chicago, and was a resident and fellow in Internal Medicine at Mayo. He is a past president of the American Medical Directors Association (AMDA) and is a fellow and past governor of the American College of Physicians. He is a past director of the American Geriatrics Society and serves on their Foundation for Health in Aging. He served eight years on the national board of the Alzheimer’s Association and was a member of their executive committee. He has served as Director and Co-Director of Education for the Mayo Clinic Alzheimer’s Disease Research Center and has been continuously funded by the National Institutes of Health since 1987. He is one of the original authors to first describe Mild Cognitive Impairment and recruited the 4, 500 normal volunteers that were observed over time to progress toward disease.

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