The Role of Neuroimaging in the Assessment of the Cognitively Impaired Elderly

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KEYWORDS

• Brain imaging • MRI • CT • PET • SPECT • Dementia

KEY POINTS

- Dementia is defined as a progressive loss of cognition and several distinct causes have been identified.
- Different causes of dementia are associated with unique patterns of symptoms and abnormalities within the brain.
- Brain imaging can provide an essential window into the pathologic processes occurring in vivo within the brain of a patient experiencing cognitive complaints and potentially aid in the differential diagnosis of dementia.

INTRODUCTION

Elderly individuals often experience issues with memory. For many, such cognitive complaints reflect the normal process of aging and are characterized by relatively minor changes in brain structure and function. For some, cognitive complaints can reflect other issues, such as hypothyroidism or medication side effects, dictating the need to run additional tests to rule out these causes. However, for others, cognitive complaints may reflect an ongoing neurodegenerative process that can lead to an increasing trajectory of worsening in both cognition and daily function, as well as, perhaps difficulty with motoric abilities. Therefore, memory complaints may indicate a propensity for the future development of dementia.

According to the latest *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* criteria, dementia is classified as a major neurocognitive disorder interfering

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with both cognitive function and performance of everyday activities. Cognitive function refers to memory, speed, language, judgment reasoning, planning, and other thinking abilities.[1] Several distinct causes of dementia have been identified[2,3] (**Table 1**). Alzheimer disease (AD) is a degenerative brain disease and is the most common cause of dementia. Estimates of the frequency of dementias include AD, 60% to 80%; vascular dementia (VaD), 15% to 20%; dementia with Lewy bodies (DLB), 10% to 30%; and frontotemporal lobar degeneration (FTLD), other rarer causes, and occasionally reversible conditions (5%).[4,5] Of interest, several studies report that individuals with dementia can have brain abnormalities associated with more than a single cause of dementia, a condition termed mixed dementia, which is particularly common in the extreme elderly.[6–9] In most cases, AD is combined with VaD with rates ranging from 2% to 58%,[6] although a lower percentage of patients can also show evidence for combinations of AD with DLB, and AD with VaD and DLB. Different causes of dementia are associated with unique patterns of symptoms and abnormalities within the brain, and several of these causes are summarized in **Table 2**.[10,11]

AD is characterized by the abnormal accumulation of beta-amyloid (Aβ) neuritic plaques and neurofibrillary tangles (NFT) containing hyperphosphorylated tau identified in the brain on autopsy.[12] Several studies have shown that these changes begin in individuals 20 or more years before symptoms appear.[13–15] Mild cognitive impairment (MCI) is thought to serve as a potential precursor to AD and is defined as a loss of cognitive function that exceeds common age-associated changes but does not meet the diagnostic criteria for dementia (eg, everyday activities are preserved).[16] Although MCI is largely regarded as defining a population at-risk for AD, MCI can develop for reasons other than AD and not all patients diagnosed with MCI will go on to develop dementia. More recently, significant interest has been focused on understanding the earliest preclinical or prodromal phase of AD.[17,18] The revised criteria and guidelines for AD diagnosis[19–22] identify 2 stages: (1) MCI due to AD and (2) dementia due to AD. In addition, for research purposes, the guidelines also propose a preclinical phase of AD that occurs before symptoms develop, such as memory loss, during which biomarkers of amyloid deposition and/or neurodegeneration can be identified.

The differential diagnosis of dementia is predominantly based on clinical criteria and neuropsychological testing. The evaluation of a patient with cognitive complaints typically involves several steps: (1) obtaining a detailed medical history, (2) running blood tests to rule out other causes of cognitive impairment, (3) performing neuropsychological tests to assess deficits in cognition and functioning, and (4) structural brain imaging. However, a number of clinicians describe patients who have overlapping symptoms that complicate a clear diagnosis of dementia based on clinical criteria alone.[23,24] Moreover, several reviews of published studies report a relatively low sensitivity and specificity of neuropsychological evaluations for identifying pathologically confirmed AD dementia.[25,26] In the more recent study, Beach and colleagues reviewed 23 studies regarding current clinical AD diagnostic methods and reported sensitivity estimates ranging between 41-100% (median of 87%) and specificity estimates ranging between 37-100% (median of 58%).[26] In addition, using clinical and neuropathological data from the National Alzheimer's Coordinating Center (2005-2010), these authors reported sensitivity estimates ranging from 70.9-87.3% and specificity estimates ranging from 44.3-70.8% for clinical diagnosis of "probable" or "possible" AD in identifying AD histopathology across 4 levels of neuropathological criteria.[26] Thus, in this latter study, up to 30% of patients who were thought to have AD did not show evidence of postmortem histopathology consistent with AD, while at least 40% of patients diagnosed with non-AD dementia did show characteristic