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Metabolism and perfusion studies in evaluation of dementia

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Alzheimer's disease (AD) is the most common cause of dementia (representing about 65 % of all causes), and it is estimated that more than 22 million individuals worldwide will have AD by 2025. One in 10 persons over 65, and nearly half of those over 85 have AD now. Without effective treatments (most of which will be tied to accurate and early diagnosis) and with an anticipated bulge in the elderly population, dementia threatens to overwhelm the world wide health care system (1). Diagnosing AD is a difficult process, and part of the difficulty in accurate differential diagnosis of dementia is that many (less prevalent) conditions other than AD can result in cognitive impairment. Differentiating among these various disorders antemortem is very difficult, particularly when patients are seen relatively early in their symptomatic course. While highly skilled and experienced practitioners can achieve diagnostic sensitivity approaching 90 % in patients meeting clinical criteria for dementia (relative to post-mortem examination of the brain), several studies indicate that the frequency of unrecognized dementia in the general community ranges from 50 % to 90 % (2).

Functional brain imaging provides substantial value in diagnosis and management in the dementias (3, 4). Both Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) assist in the initial diagnosis of dementia and in the differential diagnosis of the specific dementing disorders. These techniques essentially match the sensitivity and specificity of clinical diagnoses in distinguishing Alzheimer's dementia (AD) from age-matched controls, from frontal lobe dementia (FLD), vascular dementia (VD) and even from Lewy Body dementia (LBD). Newer analytic techniques such as voxel-based correlational analyses and discriminant function analyses enhance the power of such differential diagnoses. Functional brain imaging techniques can also significantly assist in patient screening for clinical trials.

The correlation of the observed deficits with specific patterns of cognitive abnormalities permits enhanced patient management and treatment planning and improved longitudinal assessment of outcome. It is also noteworthy that the classic abnormalities of temporoparietal and posterior cingulate hypoperfusion or hypometabolism appear to be present prior to symptom onset. These abnormalities predict progression to AD in the presence of the earliest of symptoms, such as patients with MCI. They are also present even in cognitively normal but at risk subjects, with a severity proportional to the risk status (e.g., greater reductions in subjects with two APOE-4 alleles than for subjects with only one). There are numerous reasons to detect the processes underlying AD early, but the primary motive is to attempt treatment while the damage is still minimal. A substantial number of PET and SPECT studies now address early detection, prediction of progression and longitudinal follow up. Even greater predictive ability for progression to AD is obtained by combining measures of perfusion or metabolism with risk factors, such as tau protein levels, hippocampal N-Acetyl aspartate concentrations, or hippocampal volume measures. These quantitative assessments provide insight into the basic pathology of AD, predict progression and may respond to therapeutic interventions in a manner predictive of cognitive response, in a setting where traditional clinical measures are of limited value.

The modern literature by and large support the notion that the best time to obtain imaging is early in the course of the clinical work-up. The guiding principle for that determination is as follows: a patient who presents with an adverse change in cognition or behavior, which has not been both fully explained and fully reversed following standard diagnostic and treatment approaches, should be considered a candidate for PET or SPECT imaging.

References

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