12b

Beta Amyloid Imaging

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Molecular imaging with PET and SPECT tracers allows evaluation of the specific pathological processes underlying dementia and will have an increasingly important clinical role in their management. Currently, ^{18}F-FDG PET is available to assist in the diagnosis of AD and comparative studies within the same patients have shown it to be superior to initial expert clinical diagnosis. But FDG PET has limitations. The degree of hypometabolism is proportional to the severity of cognitive impairment so that in very early disease the scans may be normal or equivocal. There are also limitations to the specificity of FDG PET and its accuracy declines in the very elderly patient.

Demand is growing for tools that will permit very early, even preclinical, diagnosis of Alzheimer's disease, the most common cause of dementia in developed countries. Beta amyloid (A□) imaging with PET is a leading contender for such a tool and current progress suggests that an F-18 labelled A□ tracer is likely to be available to clinical practice within the next 3-5 years (1).

A□ deposition in the brain is implicated in the pathogenesis of Alzheimer's disease (AD) and is central to current etiological theories. Neuropathological studies suggest that the characteristic pathological findings of AD are present up to a decade before dementia. The slow development of AD offers great potential for early intervention but current diagnostic criteria and methods do not allow diagnosis until the individual is demented. Clinical distinction of other dementias from AD is frequently incorrect when compared to post mortem findings.

^{11}C-PiB, developed by Chet Mathis and William Klunk at the University of Pittsburgh, has been the most widely used A□ ligand since the first human scan was obtained with this tracer in Uppsala, Sweden in 2002 (2). A myriad of subsequent studies have shown that A□ imaging should provide early detection of Alzheimer's disease and more accurate differential diagnosis of the dementias (3). Increased ^{11}C-PiB binding appears to be predictive of conversion of mild cognitive impairment to AD with a report from Uppsala of a 60% conversion rate over 12 months in the MCI subjects with a positive scan compared to zero per cent when the scan was negative (4). These figures are consistent with our follow-up data at Austin Health Center for PET, Melbourne. Comparison of the diagnostic utility of A□ imaging versus ^{18}F-fluorodeoxyglucose (FDG) PET demonstrates greater accuracy for distinguishing subjects with mild AD from elderly controls (5) and AD from frontotemporal dementia (FTD) as A□ deposition is not present in FTD.

^{11}C-PiB studies have reported positive scans in 20-30% of normal elderly individuals consistent with post mortem studies. Longitudinal studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Australia Imaging, Biomarkers and Lifestyle study of aging (AIBL) will determine whether or not apparently healthy individuals with cortical binding of A□ ligands will develop the clinical features of AD and thus the true specificity of A□ imaging for very early, even preclinical diagnosis of AD.

The next 5 years will see a substantial rise in the use of molecular imaging in the management of neurodegenerative disease, particularly for the very early diagnosis of Alzheimer's disease. The extent of this demand will depend on the effectiveness and safety of specific therapies, many of which are currently in human clinical trials.

References

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