longitudinal observations in normal persons years in advance of clinical deterioration. There is the problem of long-term stability and availability of the imaging instrumentation. Finally, there are issues related to the precision of the sampling of the anatomical-pathology in relatively healthy brains. These factors have hindered accumulation of normal samples of adequate size (considering the low incidence of these clinical transitions), limited repeat observations, and resulted in image analysis solutions with limited anatomical-pathological validity. In a series of longitudinal studies that began approximately 14 years ago with new MRI and PET instrumentation, we initiated longitudinal studies of normal elderly subjects. In this presentation we will describe anatomically validated methods for hippocampal imaging that produced three independent demonstrations that imaging can predict MCI/AD up to nine years in advance [1-3]. These data show that metabolic compromise and atrophy of hippocampal formation structures is increased during a normal aging phase that precedes decline to MCI.

IM-08 FMRI FEATURES OF AD: DISTINGUISHING ALZHEIMER'S DISEASE FROM NORMAL AGING AND OTHER DEMENTIAS WITH FMRI

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Functional magnetic resonance imaging (fMRI) is a non-invasive neuroimaging technique that can be used to study the neural correlates of complex cognitive processes, such as learning and memory. FMRI is an indirect measure of neural activity that exploits the intrinsic contrast properties of changes in levels of de-oxygenated hemoglobin and blood flow. FMRI has already been used to investigate the alterations in function that occur in Alzheimer's disease. These studies have consistently reported that, compared to older control subjects, patients with clinical AD show decreased fMRI activation in the hippocampus and related structures within the medial temporal lobe, during the encoding of new memories. More recently, fMRI studies of subjects at risk for AD, by virtue of their genetics or evidence of mild cognitive impairment (MCI), have yielded variable results. Some of these studies, including our own, suggest that there may be a phase of paradoxically increased activation early in the course of prodromal AD. FMRI may prove particularly useful in the assessment of pharmacological agents, as a marker of hippocampal response to amyloid modifying therapies. Further studies to validate fMRI in these populations are needed, particularly longitudinal studies to investigate the pattern of alterations in functional activity over the course of prodromal AD.

IM-09 IMAGING ALZHEIMER'S DISEASE AND OTHER DEMENTIAS WITH PET

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Background: Positron emission tomography with 18-F-fluorodeoxyglucose (FDG-PET) is a molecular imaging method that provides clinicians unique information about the location and severity of neuronal and synaptic loss in dementing diseases. Alzheimer's disease (AD) and other dementias cause distinctive changes in glucose metabolism that can be exploited to aid diagnosis and treatment decisions. Medicare and other insurers have recently decided to reimburse FDG-PET for the specific indication of distinguishing AD from frontotemporal dementia (FTD). **Objective(s):** Review strategies to best use FDG-PET in the evaluation and management of dementia. **Methods:** Review of the literature and presentation of illustrative case examples. **Conclusions:** Using FDG-PET is particularly useful in deciding whether a patient has AD or FTD. These two disorders can share similar symptoms, but have contrasting patterns of hypometabolism: AD causes abnormalities predominantly in posterior temporoparietal cortex and posterior cingulate gyrus, while in FTD they are most evident in frontal and anterior temporal regions. Recent studies have indicated that visual interpretation of FDG-PET images can be reliable after training and highly accurate when compared to autopsy findings. Clinicians need to be aware of the limitations of this imaging technique. FDG-PET cannot determine whether a patient has dementia; this only can be determined reliably with a clinical evaluation that includes an assessment of mental status and functional abilities. FDG-PET also has not been validated to determine individual future risk of dementia, even though changes have been identified in groups at increased risk of AD. Furthermore, scan findings must be interpreted with full consideration of many technical factors that can affect scan results, and the findings on clinical examination and structural imaging studies. Many other potential applications of FDG-PET currently are being evaluated and offer the hope that it can further improve physician confidence and accuracy in dementia diagnosis.

IM-10 THE APPLICATION OF AMYLOID-IMAGING TO THE DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE

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Background: Deposition of the amyloid-beta (Aβ) peptide in the form of plaques and cerebrovascular amyloid is one of the key pathologic features of Alzheimer's disease (AD). Evidence, including compelling data from human genetic studies, has accumulated that strongly implicates alterations in Aβ metabolism as a key event in the pathogenesis of AD. Aβ metabolism has thus become an important therapeutic target in the pharmaceutical development of drugs for the treatment of AD. **Objective(s):** Discuss the role of amyloid imaging in the diagnosis and treatment of AD. **Methods:** Given the central role that Aβ deposition plays in the diagnosis and pathophysiology of AD, our group has spent over a decade developing in vivo imaging agents for the detection and quantitation of amyloid deposition in humans. The goal of this work is to detect amyloid deposition prior to the onset of clinical symptoms and follow the natural history of amyloid deposition as a baseline to detect changes in that natural history induced by anti-amyloid therapies. **Conclusions:** This presentation will review the preclinical development of benzothiazole amyloid imaging agents such as Pittsburgh Compound-B (PIB) and describe the initial human studies with this agent. Recent work in mild cognitive impairment patients will be reviewed. The results obtained from studies of post-mortem samples from the Aβ active immunization study (AN-1792) will be discussed in terms of the potential for this technology to detect the effects of anti-amyloid therapies.