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Role of biological markers and MR-based assessment in Alzheimer's Disease

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Objectives: The pathophysiologic process leading to neurodegeneration in Alzheimer's disease (AD) is thought to begin long before clinical symptoms develop. Existing therapeutics for AD improve symptoms, but increasing efforts are being directed toward the development of therapies to impede the pathologic progression of the disease. Although these medications must ultimately demonstrate efficacy in slowing clinical decline, there is a critical need for biomarkers that will stratify pre-clinical and clinical patient populations for trials, indicate whether a candidate disease-modifying therapeutic agent is actually altering the underlying degenerative process.

Methods and Results: A number of in vivo neurochemistry and neuroimaging techniques, which can reliably assess aspects of physiology, pathology, chemistry, and neuroanatomy, hold promise as biomarkers (1). These neurobiological measures appear to relate closely to pathophysiological, neuropathological and clinical data, such as hyperphosphorylation of tau, abeta metabolism, rate of atrophy and cognitive decline, as well as risk of future decline (2-5). As this work has considerably matured, it has become clear that biological measures may serve a variety of potential roles in early clinical and pre-clinical diagnosis, clinical trials of candidate therapeutic agents for AD, depending in part on the question of interest and phase of drug development.

Conclusions: In this presentation, the conceptual framework of current multimodal magnetic resonance imaging (MRI) – as well as neurochemistry – based biomarker research is reviewed, as well as data related to the range of core feasible neurochemical, as well as neuroimaging markers of AD and potential applications of these techniques in future clinical practise and in clinical studies, particularly with respect to early diagnosis, patient stratification, classification, prediction, as well as the monitoring of disease progression in trials of disease-modifying therapies.

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