



MRI Measures of Neurodegeneration as Biomarkers of Alzheimer's Disease

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MRI Measures of Neurodegeneration as Biomarkers of Alzheimer's Disease

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Abstract:

Alzheimer's disease (AD) is the most common age-related neurodegenerative disease. Many researchers believe that an effective AD treatment will prevent the development of disease rather than treat the disease after a diagnosis. Therefore, the development of tools to detect AD-related pathology in early stages is an important goal. In this report, MRI-based

markers of neurodegeneration are explored as biomarkers of AD. In the first chapter, the sensitivity of cross-sectional MRI biomarkers to neurodegenerative changes is evaluated in AD patients and in patients with a diagnosis of mild cognitive impairment (MCI), a prodromal stage of AD. The results in Chapter 1 suggest that cross-sectional MRI biomarkers effectively measure neurodegeneration in AD and MCI patients and are sensitive to atrophic changes in patients who convert from MCI to AD up to 1 year before clinical conversion. Chapter 2 investigates longitudinal MRI-based measures of neurodegeneration as biomarkers of AD. In Chapter 2a, measures of brain atrophy rate in a cohort of AD and MCI patients are evaluated; whereas in Chapter 2b, these measures are assessed in a pre-MCI stage, namely older adults with cognitive complaints (CC) but no significant deficits. The results from Chapter 2 suggest that dynamic MRI-based measures of neurodegeneration are sensitive biomarkers for measuring progressive atrophy associated with the development of AD. In the final chapter, a novel biomarker for AD, visual contrast sensitivity, was evaluated. The results demonstrated contrast sensitivity impairments in AD and MCI patients, as well as slightly in CC participants. Impaired contrast sensitivity was also shown to be significantly associated with known markers of AD, including cognitive impairments and temporal lobe atrophy on MRI-based measures. The results of Chapter 3 support contrast sensitivity as a potential novel biomarker for AD and suggest that future studies are warranted. Overall, the results of this report support MRI-based measures of neurodegeneration as effective biomarkers for AD, even in early clinical and preclinical disease stages. Future therapeutic trials may consider utilizing these measures to evaluate potential treatment efficacy and mechanism of action, as well as for sample enrichment with patients most likely to rapidly progress towards AD.

Description:

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