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Magnetic Reasonance Imaging in Medical Imaging Disease Biomarkers

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DESCRIPTION

With the increase in life expectancy and the prevalence of age-related cognitive disorders, there has been a surge of interest in studying normal and pathological ageing in order to identify early predictors of degenerative disorders, differential diagnosis, and the efficacy of pharmacological and cognitive approaches in the treatment of these disorders. Indeed, given the significant financial and therapeutic burden of degenerative diseases on national healthcare systems, research aimed at improving early and differential diagnosis of these pathologies is required.Alzheimer's disease (AD) is the most common neurodegenerative disease, affecting millions of people around the world. The identification of sensitive and specific markers of very early Alzheimer's disease progression is intended to assist researchers and clinicians in developing new treatments and monitoring their effectiveness, as well as to reduce the time and cost of clinical trials. Individual diagnosis of Alzheimer's disease is currently based primarily on clinical examination and neuropsychological assessment, but definite diagnosis can only be performed through post-mortem analysis. The Alzheimer's Disease and Related Disorders Association and the National Institute of Neurologic and Communicative Disorders and Stroke developed clinical diagnostic criteria for AD in the 1980s using a binary approach to diagnosis. This approach requires a cognitive impairment for the diagnosis of Alzheimer's disease, with definite, probable, and possible categories. Following that, neuropathological data based on senile plaques and neurofibrillary tangles were introduced. The National Institute on Aging-Association Alzheimer's workgroup developed revised diagnostic criteria for AD in 2011. Additional supportive features can be obtained by neurogenetic testing, measurement of cerebrospinal fluid (CSF), amyloid and tau, and neuronal injury biomarkers as measured by neuroimaging studies, including Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) (MRI). PET and MR changes provide measurements of metabolism/amyloid markers and atrophic regions, respectively, to help identify Alzheimer's disease (AD) even before dementia appears. Because of the non-invasive nature of the MR modality, significant effort has been put into developing advanced MR image processing techniques in order to identify MR-related biomarkers that could be used to improve the accuracy of clinical diagnosis of AD. The majority of studies that focused on identifying MR image differences between patients with a clinical diagnosis of AD and healthy subjects used pre-defined regions of interest or mass univariate image analysis methods. However, neither method detects spatially distributed patterns of brain anatomy. To overcome these limitations, there has been a growing interest in the neuroimaging community in recent years in alternative approaches to neuroimaging data analysis that take into account multivariate pattern analysis, including machine-learning algorithms. Machine-learning techniques, due to their multivariate properties, can automatically extract multiple information from image sets without requiring a priori hypotheses of where this information may be coded in the images. Several studies have evaluated the diagnostic value of these techniques in the classification of Alzheimer's disease using cerebral MRI studies, with promising results also for the prediction of conversion in the early stages of the disease. Klöppel et al. (2008), for example, used machine learning classification and structural MR images to extract spatially-distributed multivariate diagnostic biomarkers. The authors were able to identify MR-related biomarkers useful for the differential diagnosis of Alzheimer's disease in terms of Fronto-Temporal Lobar Degeneration and normality. However, due to the difficulty of quantifying patterns of structural change during early stages of AD or clinically normal stages, early diagnosis of AD by structural MR imaging studies is currently an open challenge. Patients with prodromal Alzheimer's disease (AD) are frequently clinically classified as having Mild Cognitive Impairment (MCI), but not all MCI patients progress to AD. According to a meta-analysis of research and clinical reports, the rate of conversion of MCI to AD is around 5–10% per year (Mitchell and Shiri-. MCI criteria have been developed,

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and several forms have been described. In the clinical setting, detecting the transition from the asymptomatic phase to the symptomatic pre-dementia phase or from the symptomatic pre-dementia phase to dementia onset is a difficult task. This leads to diagnostic uncertainty in the early stages of disease. To achieve this goal, it appears critical to identify multivariate MR-related diagnostic biomarkers capable of accurately diagnosing MCI converters. As a result, by revealing which image features are the most informative in supporting an early diagnosis, different morphological characteristics between normal ageing and MCI can be identified. In this paper, we propose a machine learning method for extracting spatially distributed multivariate diagnostic biomarkers from structural MR brain images, which can then be used to make an early and accurate diagnosis of Alzheimer's disease. Our method, in particular, can identify MRI-related biomarkers of MCI subjects that will progress to AD, opening up new avenues for the early management of AD patients.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.