Multiparametric MR in Aging and Dementia

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Highlights

- Multiparametric MRI has played a major role in uncovering brain abnormalities associated with dementia, and is a great tool for elucidating brain changes in the pathological cascade leading to dementia, as well as for assessing treatment efficacy.
- MRI-based biomarkers hold promise, however their predictive ability is limited due to a number of reasons, including the fact that mixed pathologies are common and that different pathologies have overlapping clinical manifestation.
- Combining MRI and neuropathologic evaluation on the same older persons is crucial for the development of accurate MRI biomarkers of the neuropathologies leading to dementia.
- MRI will continue to contribute towards elucidating the role of structural, functional, biochemical and other brain characteristics in the mechanisms supporting cognitive health or leading to cognitive decline in old age.

Overview

Dementia has a significant effect on the quality of life of patients and caregivers, and places heavy demands on the health care system. Thus, prevention, early detection and treatment of the causes that lead to the various forms of dementia are critical public health challenges. MRI is a critical tool in the fight against dementia. In this talk, we will present the contributions of MRI in research of aging and dementia in reverse order in terms of the pathological cascade. We will also discuss potential future contributions that remain largely underexplored.

A number of MRI studies have demonstrated brain abnormalities associated with dementias such as Alzheimer's disease, vascular dementia, dementia with Lewy bodies, Parkinson's disease with dementia, frontotemporal dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, Huntington's disease, Wernicke-Korsakoff syndrome. Those studies have used MRI techniques such as structural T_1-weighted MRI, FLAIR, T_2 mapping, diffusion imaging, task-based and resting state functional MRI, arterial spin labeling, MR spectroscopy, and susceptibility-weighted imaging, to assess brain atrophy patterns, white matter lesions, infarcts, MR relaxation parameters, microstructure, structural and functional connectivity, function, perfusion, biochemical characteristics, and microbleeds. We will provide an overview of MRI investigations of the most common forms of dementia, and will demonstrate the importance of early detection.

Research on the development of MRI biomarkers for early detection of factors that lead to dementia is ongoing, mainly for Alzheimer's disease. We will present examples of these efforts. In Alzheimer's, PET and CSF-based biomarkers provide earlier warning than MRI-based biomarkers. However, the potential of multiparametric MRI and novel MR modalities has not

been thoroughly investigated, especially for age-related neuropathologies other than Alzheimer's for which no other biomarker is currently available.

The predictive ability of available MRI biomarkers is limited due to a number of reasons, including the fact that mixed pathologies are common and that different pathologies have overlapping clinical manifestation. Combining MRI and neuropathologic evaluation on the same older persons is crucial for the development of accurate MRI biomarkers of the neuropathologies leading to dementia. We will present MRI signatures of neuropathology produced in recent studies that linked MRI and neuropathologic evaluation, as well as the substantial complexities associated with such investigations. We will discuss solutions that may simplify and enhance efforts to understand the effects of pathology on brain MRI measures.

In the final part of this talk, we will focus on healthy aging. Understanding the complex role of brain characteristics in the mechanisms supporting cognitive health in old age is of critical importance. Towards this goal, multiparametric MRI is used in older adults without dementia to establish the array of brain characteristics integral to cognitive function in old age, and uncover how these brain characteristics are influenced by genetic, demographic, lifestyle and clinical factors, as well as interventions. Such investigations in older adults without dementia are fundamental to the development of strategies for the prevention of cognitive impairment. In this talk, we will present several of these efforts and discuss the role of cognitive reserve.

In conclusion, multiparametric MRI has an important role in research of brain characteristics in aging and dementia. The potential of MRI-based biomarkers of various age-related neuropathologies remains largely underexplored. As the number of investigations combining MRI and neuropathology evaluation increases, and as the number of older persons included in these investigations increases, the potential of MRI for predicting age-related neuropathology will unfold.