1H MRS IN MILDE COGNITIVE IMPAIRMENT
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Development of new therapies for Alzheimer’s disease (AD) and other neurodegenerative conditions has become of increasing societal importance given our aging population and increasing longevity, combined with the fact that this disease typically begins late in life. Early diagnosis and treatment of AD is crucial to sustaining the quality of life of many elderly individuals and their families. While there are no proven treatments that can reverse AD pathology, treatments that can arrest or slow down disease progression generate the prospect for preventive interventions. There is considerable interest in early diagnosis by identifying individuals with cognitive difficulties who eventually progress to dementia, from those who are aging with normal cognitive function.

The syndrome of amnestic mild cognitive impairment (MCI) was established in order to identify such individuals who have prodromal AD. MCI is characterized by a cognitive complaint, cognitive function not normal for age, a decline in cognition, essentially normal functional activities, and not demented 1. Non-invasive neuroimaging techniques such as 1H magnetic resonance spectroscopy (1H MRS) may have an important role in the clinical evaluation of dementia for early diagnosis, differential diagnosis, and monitoring of disease activity starting from the MCI stage 2. The neuronal metabolite NAA is consistently found to be lower and the glial metabolite mI is found to be higher in the 1H MR spectra of patients with MCI and AD than cognitively normal elderly 3-12 and with increasing AD pathology at autopsy 13. There are conflicting reports on the membrane integrity marker choline (Cho) levels. Some studies identified elevated Cho levels 7, 10, 14 in people with AD, and some did not 11, 15-17. Whereas one study found elevated Cr levels in AD 18, many have shown this metabolite peak to be stable in AD compared to age matched controls 11, 16, 17, 19-22. For this reason, Cr peak is generally used as an internal reference to adjust for atrophy and acquisition related variability. There is a longitudinal decline in NAA/Cr levels in MCI 23, and NAA/Cr levels at baseline predict the time to progression to dementia in people with MCI 24.

Recently, the concept of MCI has been broadened to the transitional state between normal aging and a variety of different dementias 25. This broad clinical definition of MCI includes amnestic MCI (aMCI) with impairment in the memory domain, and non-amnestic MCI (naMCI) with a impairment in cognitive domains other than memory such as attention/executive functioning, language, and visuospatial processing 26. People with the aMCI subtype have a higher risk of progressing to Alzheimer’s disease (AD) compared to their cognitively normal peers. Other common pathologies encountered in aMCI include cerebrovascular disease, and Lewy body pathology 34,35. The natural history and the pathological underpinnings of naMCI are less clear 27-33. There are distinct differences in 1H MRS findings between aMCI and naMCI subtypes. 1H MRS findings in patients with aMCI are characterized by an AD-like pattern of elevated mI/Cr in the posterior cingulate gyrus suggesting a high frequency of AD pathology in aMCI. Patients

who are naMCI on the other hand, do not have the $^1$H MRS features of AD, therefore underlying pathological substrates may include pathologies other than AD in some naMCI patients. 

People with MCI may progress to a variety of dementias that require different therapeutic strategies. Furthermore, all people with MCI do not develop dementia at a similar rate. This heterogeneity of MCI warrants development of non-invasive biomarkers such as $^1$H MRS metabolite measurements that can predict the rate of future progression to different dementias for potential disease specific preventive interventions.

References

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