Neuroimaging in Healthy and Pathological Aging

With the aging of the population, there is increased interest in understanding changes in the brain that occur in healthy and pathological aging. Researchers at the MMIL are actively investigating age-related changes in brain structure and function to determine the factors associated with successful cognitive aging, and to develop biomarkers for earlier detection and tracking of pathological changes.

Studies of healthy aging have examined atrophy rates in cross-sectional and longitudinal analyses to determine the pattern and degree of regional atrophy that occurs in healthy aging, and to relate measures of regional brain atrophy to changes in cognitive function. Studies have also examined changes in white matter integrity, as inferred from measures of fractional anisotropy (FA) in diffusion tensor data, to examine the influence of age-related changes in white matter on cognitive function in healthy older adults. Age-related differences in spatiotemporal activity patterns obtained from magnetoencephalographic recordings of brain activity during the performance of working memory tasks are being compared with measures of regional atrophy and FA, to further understanding of how changes in brain grey and white matter with age influence functional activity and cognitive performance.

Studies of pathological aging have focused to a large extent on Alzheimer’s disease, the most common cause of dementia in the elderly. Researchers at the MMIL have described a pattern of regional atrophy characteristic of mild AD and predictive of clinical decline in patients with mild cognitive impairment. They have documented regional differences in rate of atrophy according to disease severity, and have related atrophy measures to changes in cognitive and functional abilities. Researchers have also compared quantitative MRI measures to other biomarkers of AD, including reduced glucose metabolism as measured by FDG-PET, or abnormal levels of cerebrospinal fluid (CSF) amyloid beta and tau proteins, finding that quantitative structural MRI measures are just as sensitive, if not more so, than these more invasive measures as predicting the development of Alzheimer’s disease.

These results have important implications for clinical trial design and individual patient prognosis: Research at the MMIL has demonstrated that constraining enrollment in a clinical trial to individuals with amnestic MCI who show, on a screening MRI, evidence of a pattern of regional atrophy characteristic of AD, would allow reductions in sample sizes of 40 to 60%, dependent on outcome measure. Research at the MMIL has also shown that measures of volumetric change in the entorhinal cortex, using longitudinal MRI methods developed with the MMIL, would improve power to detect a disease-modifying effect of a new AD treatment relative to the clinical or cognitive tests currently used as outcome measures in clinical trials. Results have also shown that measures from a single, baseline MRI, as well as measures of change from serial MRI scans can be used for individual patient prognosis.
Related References:


