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3D surface-based gray matter density analysis can predict conversion from mild cognitive impairment to Alzheimer’s dementia

Objective: To test the hypothesis that conversion of mild cognitive impairment (MCI) to Alzheimer disease (AD) is inversely correlated with gray matter density in entorhinal/parahippocampal, inferior cingulate, precuneal, inferior and lateral temporal cortices.

Background: MCI is an intermediate state between normal aging and dementia. While most MCI patients transition to AD at a rate of 10-15% per year, some develop non-AD dementia and some improve. Neocortical atrophy is known to occur as AD evolves and may herald the transition to AD.

Methods: We analyzed baseline magnetic resonance imaging (MRI) data (SPGR TR 28, TR 6, FOV 220 mm, 256x192, slice thickness 1.5 mm) of eight MCI subjects with three-year clinical and neuropsychological follow-up. Four subjects converted to AD during follow-up (MCI-c) and four remained stable (MCI-nc). The groups had similar age, education, racial and gender distribution and baseline Mini-Mental State Examination scores. All MRI scans were co-registered to the ICBM53 template, bias field inhomogeneity corrected and skullstripped. Following 3D hemispheric surface reconstruction, 35 sulci per hemisphere were traced. The individual cortical surfaces were parametrized, flattened and warped so that data from corresponding gyri could be explicitly matched before averaging across subjects. Segmented gray matter (GM) was mapped onto the corresponding parametric hemispheric model in exact spatial correspondence. An average group gray matter density map was created. Statistical maps of the linkage between structural differences and clinical outcome were created. Volumetric data for specific ROIs were extracted and subjected to statistical analyses.

Results: The volumetric data and the statistical maps showed significant correlations between atrophy and conversion status. On the left, the middle/inferior temporal (p<0.02) posterior cingulate (p<0.03), entorhinal/parahippocampal (p<0.03) and superior temporal cortices (p<0.05) were significantly more atrophic at baseline in converters vs. nonconverters. On the right, significant effects were observed for the fusiform (p=0.03), parahippocampal/entorhinal (p=0.04) and superior temporal gyri (p<0.04).

Discussion: The pattern of atrophy demonstrated both by the cortical maps and the ROI analysis was in line with our predictions. The parahippocampal/entorhinal, fusiform, posterior cingulate and lateral temporal cortices showed significantly more atrophy in MCI-c compared to MCI-nc. These results conform to the pattern of disease progression observed in post mortem studies. Our findings indicate that MCI-c can be adequately discriminated from MCI-nc based on cortical atrophy patterns and may prove valuable for patient counseling and therapeutic decision-making, as well as for planning and recruitment for therapeutic trials.
Hippocampal radial atrophy mapping can predict the outcome of mild cognitive impairment

Objective: To test the hypothesis that smaller hippocampi predict conversion to Alzheimer’s disease (AD), and large hippocampi predict cognitive stability or improvement in mild cognitive impairment (MCI).

Background: MCI is a transitional state between normal aging and dementia. While most patients transition to AD at a rate of 10-15 % per year, some develop non-AD dementia and some improve. The hippocampus is one of the first regions to show atrophy in AD. Although hippocampal volume can adequately discriminate AD from normal aging and MCI, it remains unclear whether it can predict clinical outcome of MCI.

Methods: 20 MCI subjects with three-year clinical and neuropsychological follow-up were analyzed. 6 subjects converted to AD during follow-up period (MCI-c), 7 remained cognitively stable (MCI-nc) and 7 improved (MCI-i). The groups had similar age, education, racial and gender distribution. MCI-c had lower baseline Mini-Mental State Examination score vs. MCI-nc but not vs. MCI-i. Baseline magnetic resonance imaging data (MRI) (SPGR TR 28, TR 6, FOV 220 mm, 256x192 matrix, slice thickness 1.5 mm) were co-registered to the ICBM53 template. Image inhomogeneities were corrected. The hippocampal traces included the hippocampus proper, dentate gyrus and subiculum. 3D parametric mesh modeling of the hippocampal contours normalized the spatial frequency of the digitized surface points within and across brain slices and ensured precise comparison at each surface point of the hippocampus. A medial core for each hippocampus was computed. Hippocampal radial distance measures (from the medial core to each point on the hippocampal surface) were recorded at each corresponding surface point. Individual distance maps were generated and then transformed into group average distance maps for statistical comparison. Volumetric data was extracted and subjected to statistical analysis.

Results: MCI-c had significantly smaller hippocampi compared to MCI-nc largely due to lateral hippocampal atrophy. (MCI-c vs. MCI-nc: left p=0.015; right p=0.028). Both MCI-c and MCI-nc had significantly smaller hippocampi compared to MCI-i due to preferential atrophy of the hippocampal tail. (MCI-c vs. MCI-i: left p = 0.008; right p = 0.003; MCI-nc vs. MCI-i: left p<0.03, right p=0.03)

Discussion: As expected MCI-c had significantly more hippocampal atrophy than MCI-nc, and both MCI-c and MCI-nc had significantly more atrophy relative to MCI-i. Atrophy of the lateral body of the hippocampus likely reflects CA1 involvement and is a poor prognostic sign for conversion to AD. Preservation of the tail of the hippocampus may be a good prognostic sign indicating high likelihood of cognitive improvement.