The Relationship Between Cortical Thickness and Verbal Memory

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Background: Alzheimer's Disease (AD) is a neurodegenerative disorder that results in profound memory loss and dementia. MCI (mild cognitive impairment) is the intermediate stage between normal aging and dementia. Amnestic MCI patients suffer from memory impairment while still remaining functional in other aspects of their lives. Historically physicians have relied on neuropsychological tests of cognitive function to determine a subjects diagnosis as AD, MCI or Normal. Currently there is a movement to find imaging biomarkers for AD diagnosis.

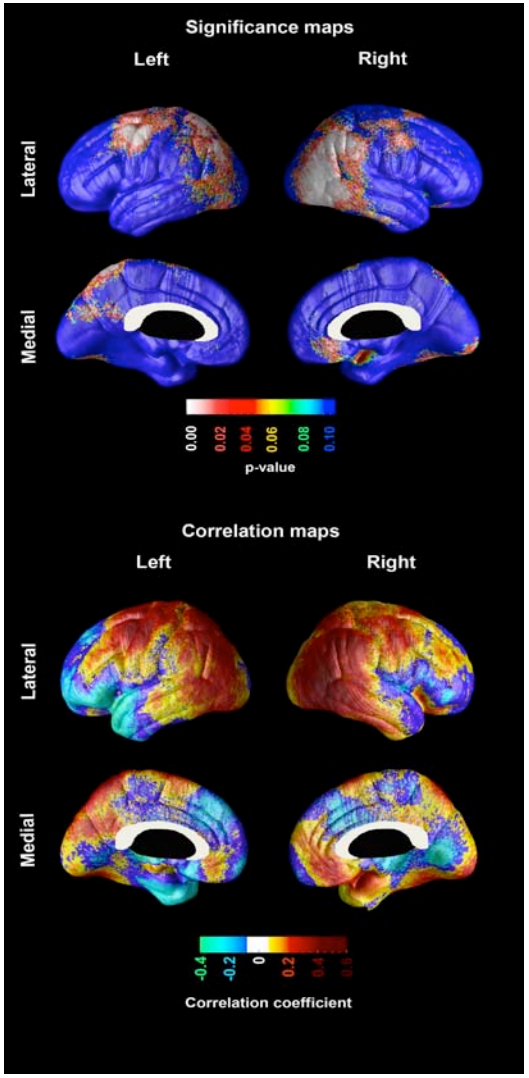
Objective: The goal was to investigate the association between the Delayed Word Recall section of the ADAS Cognitive Behavior Test (ADAS-COG) and cortical atrophy in order to determine if poor performance on delayed word recall neuropsychological tests is associated with cortical thinning. Additionally, if the association exists we wished to determine in what regions of the brain it occurs. This is designed to confirm cortical atrophy as a biomarker for AD.

Methods: We analyzed the structural magnetic resonance imaging (MRI) data of 10 Normal (NC), 22 Mild Cognitive Impairment (MCI), and 11 probable Alzheimer's Disease (AD) subjects from the ADNI study who were administered the ADAS-COG within one month of the MRI. All subjects were scanned with a standardized high-resolution MRI protocol on scanners developed by one of three manufacturers (General Electric Healthcare, Siemens Medical Solutions, and Philips Medical Systems) using a sagittal 3D T1-weighted sequence (with optimized echo, repetition, and inversion time for best signal to noise. Demographic Data is displayed in **Table 1**. A computational anatomy-based cortical thickness technique was performed on structural MRI scans. For this process the MRI images were aligned to ICBM space. Following 3D hemispheric reconstruction 38 sulci per hemisphere were traced and averaged across all subjects. The cortical surfaces were parameterised, flattened and warped, allowing for explicit matching of cortical topography prior to averaging across subjects. Cortical thickness defined as the 3D distance from the gray/white matter to the gray matter/cerebrospinal fluid interface was computed at each hemispheric surface point and mapped onto the corresponding hemispheric model in exact spatial correspondence. The overall significance of the statistical maps was assessed using permutation methods with a threshold $p<0.01$. We prepared correlation maps to demonstrate the association between cortical atrophy and Delayed Word Recall test performance and therefore verbal memory.

Table 1. Demographic information

Variable (SD)	NC (N=10)	MCI (N=22)	AD (N=11)
Age, yr	76.5 (7.7)	73.2 (9.5)	73.6 (8.3)
Gender (M:F)	6:4	14:8	7:4
Education, yr	15.5 (2.7)	16.2(2.3)	14.4 (2.4)

Figure 1. 3D cortical significance and percent difference maps



Results: As predicted there was an association between cortical thickness and performance on verbal memory tests (left $p_{corrected}=0.053$, right $p_{corrected}=0.035$; **Figure 1)** in the temporo-occipital (BA 6, 4) of the left hemisphere; and the lateral parietal (BA 39, 40), occipital (BA 19, 18), and temporal lobes (BA 22, 37) of the right hemisphere.

Conclusions: These results demonstrate that verbal memory performance is strongly associated with cortical thickness, which has previously been shown to be a predictor for AD. Our findings nicely align with the observations of others, who have reported activation in a fronto-parieto-occipital network during immediate and delayed recall tasks. Computational anatomy techniques have been increasingly utilized in human brain studies. Our cortical thickness technique is a promising in vivo biomarker tool that may prove useful for early diagnosis.

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