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Publication Date

2004-07-01

DOI

10.1016/s0197-4580(04)80956-4

Peer reviewed

P2-210 REGIONAL MR BRAIN VOLUMES IN THE PREDICTION OF COGNITIVE DECLINE IN AD

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Background: The characteristic pattern of cognitive deterioration in Alzheimer's disease (AD) is a decline in episodic memory followed by a progressive worsening of other cognitive abilities including executive, language and visuomotor skills. Consistent and predictable neuropathological changes have also been observed in AD. In its earliest stages, AD neuropathology originates in the mesial temporal areas including the hippocampus and entorhinal cortices followed by a spreading to cortical association areas (Braak & Braak, 1998). **Objective:** In an effort to predict annual rate of cognitive decline, we examined regional structural magnetic resonance (MR) brain volumes in mild-to-moderate AD. Given the pattern of progressive cortical atrophy, we expected cortical brain changes in mild-to-moderate AD patients to be more highly correlated with language and visuomotor abilities than with memory abilities, given its primacy and prominence in the earliest stages of the disease. **Methods**: Thirty-one patients with mild-to-moderate AD were administered a measure of general cognitive abilities, Dementia Rating Scale (DRS, Mattis, 1973) both at the time of receiving a structural MR scan and approximately one year later. One-year change in general cognitive abilities was calculated by subtracting the baseline DRS total score from the DRS total the following year. Multiple regression and simple correlations were calculated between brain volumes of 8 cortical regions (i.e., left and right frontal, temporal, parietal and occipital areas). **Results:** The mean DRS decline was 8.29 points (SD = 12.37). A correlation matrix indicated that left and right occipital gray ($r = 0.39$; $p = 0.02$, $r = 0.35$; $p = 0.03$, respectively) and left parietal gray volumes ($r = 0.37$; $p = 0.02$) had the strongest linear relation with a one-year decline in cognitive functioning. Multiple regression analysis revealed that only the left occipital cortical area was retained in the final model ($R^2 = 0.15$; $p = 0.03$). **Conclusion:** Cognitive decline in this sample of mild-to-moderate AD patients was best predicted by atrophy in regions other than the temporal lobes, consistent with the known pattern of neuropathologic spreading in this stage of AD. Support: NIH/NIA P50AG05131, AG12674, & AG04085, DVA Medical Research Service

P2-211 NEURAL CORRELATES OF IMPAIRED SEMANTIC MEMORY IN ALZHEIMER'S DISEASE

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Background: Our model of semantic memory includes feature knowledge for categories, and processes such as categorization that use this knowledge to make semantic decisions. AD patients have impaired semantic memory that may involve degraded semantic feature knowledge and impaired categorization processes. **Objective:** Determine the basis for impaired semantic memory in AD. **Methods:** 123 mild-to-moderate AD patients performed a semantic category membership judgment task. Feature representations were assessed by examining judgments for natural vs manufactured stimuli. Semantic processes were examined by assessing judgments of foils: Errors discriminating between category members and related non-members (e.g. for the category VEGETABLE, a related foil is "apple") suggest a deficit using rule-based processes to distinguish between partially-overlapping stimuli; Errors discriminating between category members and unrelated non-members (e.g. for the category VEGETABLE, an unrelated foil is "chair") suggest a deficit with similarity-based processes used to distinguish between non-overlapping stimuli. Regression analyses related semantic performance to cortical volume in a subgroup of 12 AD patients using voxel-based morphometry analyses of spatially normalized and segmented structural MRI images obtained at 1.5T (voxels $0.9 \times 0.9 \times 1.3$ mm). **Results:** AD patients had significantly impaired overall category membership judgments. Individual patient analyses revealed a significant impairment in 24% of AD patients, according to z-scores relative to 25 matched controls. Judgments of the natural category were significantly less accurate than the manufactured category. Error analyses revealed a deficit in the rule-based categorization process needed to discriminate between category exemplars and partially-overlapping foils that are not category members. This categorization impairment was more evident in the natural than the manufactured category. MRI correlations associated overall semantic judgment performance with dorsolateral prefrontal and inferior temporal cortex of the left hemisphere in AD. This overlapped with the MRI correlations for the rule-based categorization processing impairment, but not with correlations for the degraded natural category of knowledge. **Conclusions:** Category-specific semantic deficits in AD may be due in part to impaired categorization processes. Consistent with fMRI activation studies in healthy adults and AD patients, MRI correlations relate impaired semantic categorization to disease in a left hemisphere network involving multimodal frontal and temporal association cortex.

P2-212 AGE-RELATED CORTICAL GREY MATTER REDUCTIONS IN NONDEMENTED DOWN'S SYNDROME ADULTS DETERMINED BY MAGNETIC RESONANCE IMAGING WITH VOXEL-BASED MORPHOMETRY

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Background: Aging in Down's syndrome (DS) is accompanied by amyloid and neurofibrillary pathology whose distribution replicates pathological features of Alzheimer's disease (AD). Based on these findings, DS has been proposed as a model to study the predementia stages of AD. **Objective:** To investigate age effects on regional cortical grey matter in predementia stages of DS. **Methods:** We applied the automated and objective technique of voxel-based morphometry, implemented in SPM 99 (Wellcome Department of Imaging Neuroscience, London, UK), to the analysis of structural MRI from 27 nondemented DS adults (mean age 41.1 years, 15 women). **Results:** Regional grey matter volume was decreased with advancing age in bilateral parietal cortex (mainly the precuneus and inferior parietal lobule), bilateral frontal cortex with left side predominance (mainly middle frontal gyrus), left occipital cortex (mainly lingual cortex), right precentral and left postcentral gyrus, left transverse temporal gyrus, and right parahippocampal gyrus. The reductions were unrelated to gender, intracranial volume or general cognitive function. Grey matter volume was relatively preserved in subcortical nuclei, periventricular regions, the basal surface of the brain (bilateral orbitofrontal and anterior temporal), and the anterior cingulate gyrus. **Conclusions:** Our findings suggest grey matter reductions in allocortex and association neocortex in the predementia stage of DS. The most likely substrate of these changes is alterations or loss of allocortical and neocortical neurons due to AD type pathology.