Reduced temporal gray matter volume in MCI as detected by voxel based morphometry.

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Introduction

Mild cognitive impairment (MCI) is a condition characterized by cognitive decline, the severity of which does not reach the criteria for dementia, but is distinguishable from normal aging.[1-3] Since the MCI population is at higher risk for the development of Alzheimer's disease (AD)[3], MCI has become a target of intervention[1]. MCI patients have been investigated using MRI[4], PET[5], SPECT[6], fMRI[7], MRS[8, 9] and DTI[10] to study function, metabolism, composition, and volume of the involved brain regions. Brain volumetry using MRI has proven its importance in the field of neuropsychiatric disorders.[4] A recent approach to assessing volume throughout the entire brain, without the constraint of a priori identification of regions of interest, is voxel-based morphometry (VBM)[11]. The goal of our study was to apply VBM in a well-characterized group of MCI patients to evaluate a) reduction in gray matter (GM) volume and b) relationship between brain volume and performance on neuropsychological tests.

Methods

High resolution 3D T_1-weighted MRI (coronal SPGR, 1.5 mm slice thickness, TR/TI/TE=11.1/300/2.1 ms, 1 average, 256 x 256 matrix, 240 mm FOV) was performed at 1.5 T in 10 patients with clinical diagnosis of MCI (average age 73.5±5.5 years, 5 M) and 20 healthy elderly volunteers (75.5±4.6 years, 10 M). Subjects included in the study were screened for systemic diseases; subjects in the control group were also free of psychological and neurological diseases. All subjects took a battery of neuropsychological tests, including the Mini-Mental State Examination (MMSE), Hopkins Verbal Learning Test–Revised (HVLT-R) and Hopkins Board Test (HBT). Comparison of individual test scores between the control and MCI groups was performed using multiple regression analysis with gender and age as independent variables. The optimized VBM procedure involved a voxel-wise statistical comparison of gray matter volume after tissue class segmentation, spatial normalization into a standard stereotactic space, volume modulation, and smoothing with an 8mm Gaussian kernel.[11,12] Statistical parametric maps were obtained, showing regions where GM volume differed significantly ($p<0.05$) between groups. The main VBM analysis was performed between control and MCI groups and included gender and MMSE scores as independent variables. To evaluate the relationship between regional tissue volume and neuropsychological test scores, multiple regression analyses were performed for each test score, controlling for age.

Results

Scores on all neuropsychological tests were significantly reduced in the MCI group (all $p<0.05$). The main VBM analysis revealed significant reduction of modulated GM tissue volume predominantly in the left mesial superior temporal gyrus (Brodman Area (BA) 38, two clusters, cluster size (CS) = 519/641, Z=4.15/3.8), inferior temporal gyrus (BA 20, CS = 172, Z=3.57) and medial frontal gyrus (BA 6, CS = 51, Z=3.35), as well as the right uncus (BA 38, CS = 43, Z=3.43) and lingual gyrus (BA=17/18, three clusters, CS = 110/154/104, Z=3.33/3.27/3.26) (Figure 1) for the MCI group (all $p<0.001$, uncorrected). VBM regression analysis for neuropsychological test scores showed significant clusters in the left inferior frontal gyrus for the HBT (trials to criterion) (Brodman Area (BA) 45, cluster size (CS)=623, Z=3.86), in the left inferior temporal gyrus for the HVLT-R (sum of learning trials) (CS=648, Z=3.69), in the right superior temporal gyrus (BA 38, CS 62, Z=3.5) and the right superior frontal gyrus (BA 10, CS 12, Z=3.26) for the HVLT-R (recognition discrimination).

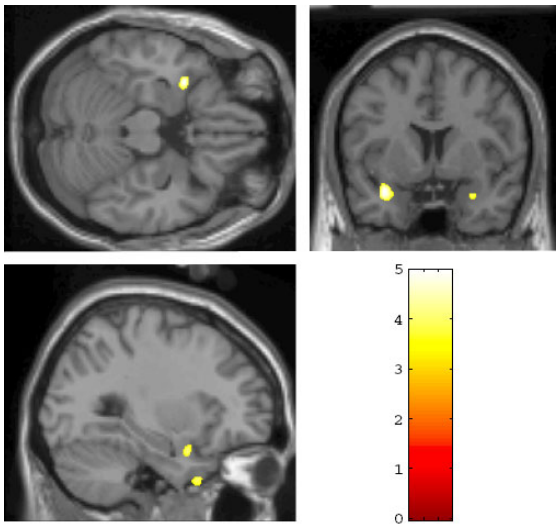

Figure 1: Areas of significant GM reduction in the MCI group overlaid on standard single subject T_1-weighted MR image template. The color scale depicts the T value.

Discussion

We applied VBM, an objective technique for evaluation of density and volume changes in brain parenchyma, to examine patterns of GM volume differences in a well-characterized group of healthy controls and patients with MCI. A previous VBM study of MCI and AD revealed reduced gray matter volumes in the medial temporal lobe, thalamus and insula.[13] Our results confirm the finding in the temporal lobe[13] and are in agreement with lateralized left hemisphere atrophy.[14, 15] The analyses, indicating an association of regional volume differences with performance on neuropsychological tests, also suggest involvement of the temporal neocortex, consistent with previous VBM data.[16] In conclusion, our results showed a potential of VBM to investigate changes in GM volume in MCI and might prove useful in future, preferably longitudinal, studies with a larger number of subjects.

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