Association of Regional Atrophy, MRI-Guided SPECT Perfusion, and Memory Performance in Patients with Mild Cognitive Impairment Compared to Healthy Elderly Controls

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Purpose

Mild cognitive impairment (MCI) appears to be a transitional state between normal aging and Alzheimer's disease (AD). Further understanding of the disease progression (conversion) from MCI to AD may allow MCI patients to choose optimal early interventions. If the risk of conversion is high, aggressive pharmacological treatment to slow down disease progression is needed; on the other hand, if the risk is low, non-pharmacological interventions (such as diet, exercise, etc.) may be chosen. Hippocampal atrophy and hypoperfusion in the medial temporal lobe are commonly found in MCI, which has been shown to be associated with AD conversion [1, 2]. Although imaging has been an important part in the management of dementia, most studies were interpreted by radiologists, and as such its value in overall diagnosis and management care can not be established. In this study we present a comprehensive image analysis approach to analyze regional atrophy, as well as MRI-guided regional perfusion. Manual drawing (for specific structures), as well as automated segmentation and atlas-based ROI mapping (for gray matter and white matter in different brain lobes) were performed to measure regional volume, then these ROI's were mapped on to SPECT images to measure regional perfusion within each ROI. They were compared between MCI and healthy elderly controls; furthermore compared to memory performance scores in neuropsychological test.

Methods

Thirteen MCI subjects (MCI, 74 ± 6 years; 9 M, 4F) and twelve healthy age-matched controls (75 ± 4 years; 6 M, 6F) were studied. A coronal view T1-weighted 3D-SPGR sequence was used to acquire anatomical images using a 1.5 T Philips Eclipse scanner. The resolution was 0.86 x0.86 mm in-plane, and 1.5 mm thickness. All subjects also received a technetium-99m-ethyl cysteinate dimer (^{99m}Tc-ECD) SPECT scan (ADAC Vertex dual-head scanner) after a bolus intravenous injection of 740 MBq ^{99m}Tc-ECD. The ROI of specific structures in medial temporal lobe (hippocampus, amygdala, parahippocampal gyrus) were measured by manual drawing. The 3-D images were segmented using a skeleton-based region-competition algorithm developed in our lab to generate gray matter and white matter maps (Fig.1) [3]. Then an atlas-based mapping technique (WFU PickAtlas) was applied to obtain frontal, temporal (Fig.2), parietal, and occipital lobes. The lobal ROI multiplied with the gray matter and white matter maps yielded the GM and WM ROI within each lobe.

The 3D-SPGR MRI images were co-registered to the attenuation-corrected SPECT images and co-registration transformation matrices were obtained. With these transformation matrices, all ROI's obtained on MRI were mapped onto SPECT images to calculate the regional cerebral perfusion. A composite medial temporal lobe perfusion was calculated as volume weighted average of perfusion measured from right and left hippocampus, amygdala, parahippocampal gyrus. The memory scores obtained in 5-min and 30-min delayed recall of CERAD word list, and Wechsler logic memory-1 and 2 were used in the correlation analysis. Each score was normalized with respect to its mean, and a composite memory score was calculated as the sum of these 4 normalized scores.

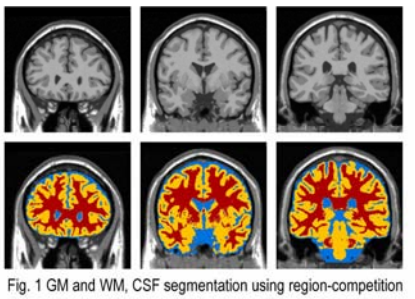

Fig. 1 GM and WM, CSF segmentation using region-competition

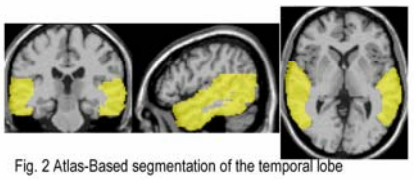

Fig. 2 Atlas-Based segmentation of the temporal lobe

Results

Since many parameters were analyzed, group difference of each parameter between MCI and controls was first evaluated for parametric reduction. All lobal ROI's (GM and WM of frontal, temporal, parietal, and occipital), volume or perfusion, did not reveal significant group differences. On the other hand the right side medial temporal structures, showed significant atrophy and hypoperfusion in MCI compared to controls (univariate and multivariate p values summarized in Table 1). It appears that atrophy and hypoperfusion was more pronounced in the right side. 12 of 13 MCI subjects were right-handed, which may spare the left side of the brain. The correlation between normalized MTL volume (sum of all 6 structures), MTL perfusion, and the composite memory score are shown in Fig.3, all showing significant correlations. MCI subjects had lower volume in the MTL, lower perfusion, and both volume and perfusion were correlated with the memory performance score. A combined multivariate analysis was performed using the 6 volume and 6 perfusion measurements, where the most significant variables are right parahippocampal volume, left parahippocampal volume, right hippocampal perfusion, right hippocampal volume, right amygdala volume, right parahippocampal perfusion, and right amygdala perfusion. A multivariate analysis using these 7 variables yielded $p = 0.005$ differentiating between MCI and controls.

Table 1: p values of volume and perfusion between MCI and NC

	Percent Volume	Perfusion
Hippocampus-R	0.011	0.004
Hippocampus-L	0.25	0.044
Amygdala-R	0.015	0.023
Amygdala-L	0.26	0.28
Parahippocampus-R	<0.0001	0.019
Parahippocampus-L	0.008	0.32
Multivariate	0.009	0.08

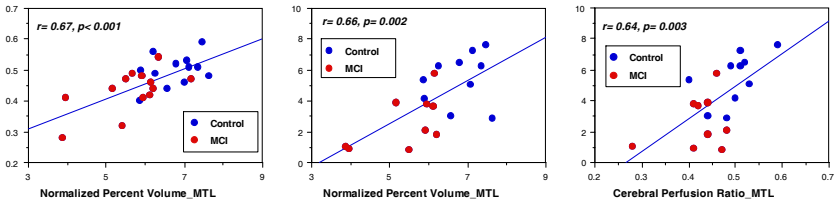

Fig.3 The correlation between the medial temporal lobe volume, perfusion, and the composite memory score

Discussion

In this study we applied both manual drawing and atlas-based mapping to comprehensively analyze regional atrophy from the whole brain. This approach can be used to precisely analyze medial temporal lobe structures (which usually had a vague boundary), as well as allow an efficient and automated analysis of different brain lobes. The segmentation can separate gray matter and white matter, allowing differential analysis which may provide imaging measures to correlate with neuropathological changes occurring in neurons in GM vs. fiber tracks in WM. These precisely defined ROI's based on high-resolution MRI were then mapped onto the SPECT images. The SPECT images had a lower spatial resolution (i.e. larger voxel size). Inevitably the edge voxel may contain atrophic tissues (partial volume effect); therefore the perfusion measurement is confounded by atrophy to some extent. In our analysis we excluded any voxel containing less than 30% of intact tissue to minimize the contamination. We also correlated each volume with perfusion, and did not yield a significant correlation, therefore suggesting that although the overall MTL volume was correlated with MTL perfusion, they were not dependent variables. The atlas-based automated analysis may be developed into a computer-based diagnosis (CAD) system, to integrate all anatomic imaging and functional imaging measures for quantitative evaluation. This may be used to establish the value of imaging for prediction of the risk of MCI-AD conversion, objective evaluation of brain changes over time, or for monitoring impact of drug interventions on the brain.

References: [1] Jack et al. Neurology 1999;52(7):1397-403. [2] El Fakhri et al. Arch Neurol. 2003; 60:1066-1072. [3] Chu et al. 13th ISMRM, Miami, 2005 #1271.