Regional Cerebral Hypoperfusion of Medial Temporal Lobe in Mild Cognitive Impairment

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Synopsis

Progressive atrophy in medial temporal lobe (MTL) is prominent in the progression of Alzheimer's disease. We hypothesized the presence of cerebral hypoperfusion in MTL among MCI individuals in addition to the volume loss. With the hybridization of MRI and SPECT, the volumes and regional cerebral perfusion activity (CPR) of MTL structures in 8 MCI individuals and 12 healthy older adults were measured. The regional CPRs of MTL structures relative to cerebellum were significantly lower in MCI than control group. These results imply that regional hypoperfusion of MTL might contribute to the cerebrovascular dysfunction of MCI and AD.

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Progressive atrophy in medial temporal lobe (MTL) is prominent in the progression of Alzheimer's disease (AD). We hypothesized the presence of cerebral hypoperfusion in MTL among MCI individuals in addition to the volume loss. With the hybridization of MRI and SPECT, the volumes and regional cerebral perfusion activity (CPR) of bilateral MTL structures in 8 MCI individuals and 12 healthy older adults were measured. The regional CPRs of MTL structures relative to cerebellum were significantly lower in MCI than control group. These results imply that regional hypoperfusion of MTL might contribute to the cerebrovascular dysfunction during the progression of MCI and AD.

Purpose

Structural MRI analyses consistently find that atrophy in medial temporal lobe (MTL) is prominent in Alzheimer's disease (AD) and mild cognitive impairment (MCI) compared to healthy elderly. We asked the question whether there is a significant reduction of cerebral perfusion in MTL among individuals of cognitive impairment, because the rCBF in certain brain areas, e.g., parahippocampal gyrus, frontal lobe, and parietal lobe, has been qualitatively reported lower than that of the normal elderly. SPECT has been established to be a reliable method to localize the change of regional blood flow (rCBF) in the brain areas, while suffering a low spatial resolution. We assumed that a hybridization of high resolution MRI and SPECT would be better to quantify the regional cerebral perfusion status. With this hybridization method, the main purpose of our current pilot study was to compare the regional cerebral perfusion activity of MTL in MCI and normal aging.

Methods

Eight MCI subjects and 12 healthy elderly were recruited from the demented cohort and the successful aging program in the Alzheimer's Disease Research Center (ADRC). All participants completed the MRI scanning and SPECT examination at UC Irvine Medical Center. All the MRI images were obtained with a FAST sequence performed on a Picker 1.5 Tesla Eclipse scanner. The acquisition parameters were TE=4ms, TR=11ms, flip angle=20°, FOV=22, matrix=256x256, slice thickness=1.5mm with no gap. All subjects received a ^{99m}Tc-ECD SPECT scan. A bolus of 25 mCi ^{99m}Tc-ECD was injected intravenously. Imaging was commenced at least 60 minutes after injection. A SPECT scanner (ADAC Vertex dual-head scanner) was used to acquire the projection data. Image reconstruction was performed by filtered back projection using a Butterworth filter. The spatial resolution of SPECT images was 128x128.

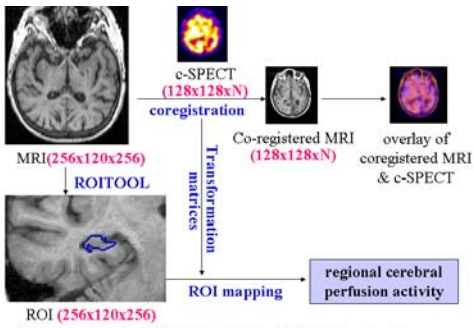

Fig.1. Flow chart of hybridizing MRI and SPECT to calculate regional cerebral perfusion activity (ROI demo: right hippocampus)

On coronal planes, we used mouse-oriented method to manually trace the boundaries of the intracranial volume and MTL memory structures, including hippocampus, amygdala (AM), and parahippocampal gyrus (PHG). Then, we used an in-house MatLab-based program (ROITOOL) to calculate the volume of these structures and saved all ROIs matrices. The volumetric measurement and ROI matrix of cerebellum were also obtained. All MTL structures and cerebellar volumes were normalized with the individual intracranial volume and the volumetric ratios were used for further analysis.

We used the Chang attenuation correction (attenuation coefficient: 0.15/cm) to reconstruct all SPECT images. We coregistered high-resolution anatomical MRI images to the corrected SPECT images (c-SPECT) using SPM and obtained coregistration transformation matrices. Then, with these transformation matrices, each ROI acquired with ROITOOL was mapped onto c-SPECT images and the regional cerebral perfusion activity of each brain region was calculated (*see* Fig. 1). The cerebral perfusion ratio (CPR) of each structure relative to cerebellum was used for further analysis.

Results

As shown in Fig. 2, there was a tendency that the volumetric ratios of each lateral MTL structures were lower in MCI group than those in normal controls (*see* Fig. 2). These results suggested a significant MTL atrophy in MCI. The volumetric ratio of cerebellum was similar in MCI group and normal controls, supporting that cerebellum might be preserved during the development of MCI. We also observed the lower cerebral perfusion ratios (CPR) of each lateral MTL structures in MCI group than those in control group (*see* Fig. 3). This finding suggested a possible hypoperfusion in medial temporal lobe in cognitive impairment.

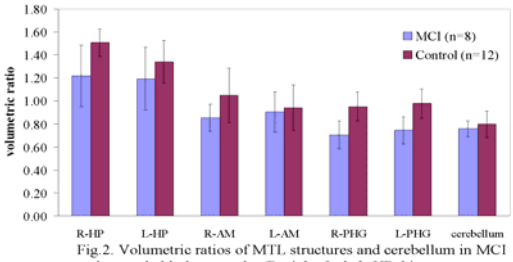

Fig.2. Volumetric ratios of MTL structures and cerebellum in MCI and normal elderly controls. (R: right; L: left. HP: hippocampus; AM: amygdala; PHG: parahippocampal gyrus.)

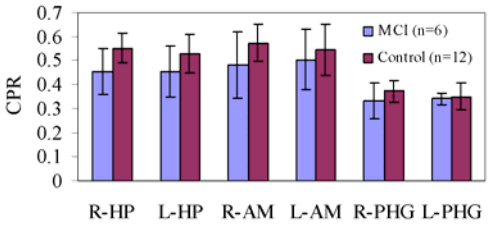

Fig.3. Regional cerebral perfusion ratio of MTL regions relative to cerebellum in MCI and normal elderly controls. (R: right; L: left. HP: hippocampus; AM: amygdala; PHG: parahippocampal gyrus.)

Discussion

Our study observed prominent MTL atrophy in MCI patients when compared to normal older adults. This is consistent with the previous reports. The major objective of our study was to investigate the regional cerebral perfusion activity in MTL. As cerebellum is rarely reported to be affected by the progression of AD and MCI, we used the perfusion ratio (CPR) relative to the cerebellum as an indicator of cerebral perfusion activity. The findings that regional CPR of bilateral hippocampus, amygdala and PHG were lower among MCI subjects indicate the hypoperfusion in MTL. This further provides some evidence that hypoperfusion in MTL might contribute to the development of cognitive impairment. Therefore, we propose a further longitudinal study to investigate the perfusion status in MTL during the progression from MCI to AD, which might facilitate explorations on the cerebrovascular risks in the development of AD.

References

Huang C, et al. NeuroImage 2003; 19:1137-1144.
Kogure D, et al. J Nucl Med 2000; 41: 1155-1162.
Visser PJ, et al. J Neurol 1999; 246(6):477-85.

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