Alterations of Regional Cerebral Perfusion and Water Diffusivity in Mild Cognitive Impairment Measured with MRI and SPECT

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Purpose

Mild cognitive impairment (MCI) appears to be a transitional state between normal aging and Alzheimer's disease (AD). The studies on the structural and functional physiology in AD brain are of particular interest. Prior qualitative and semi-quantitative SPECT studies report lower regional cerebral blood flow (rCBF) in certain brain areas in MCI than normal aging [1], and diffusion-weighted imaging (DWI) studies find an elevated water diffusivity in hippocampus in AD and MCI [2]. However, the partial volume effect relevant to the regional cerebral atrophy remains an issue when interpreting those findings. Therefore, we hypothesized that after correction for the atrophy effect, alterations of regional cerebral perfusion and water diffusivity would remain in MCI when compared to normal aging. Consequently, with an MRI-guided ROI-based quantitative analysis of DWI and SPECT images, this prospective study was to compare the regional cerebral perfusion and water diffusivity between MCI and normal controls.

Methods

Thirteen MCI subjects (MCI, age = 73.9 ± 6.3 years; 9 men, 4 women) and thirteen healthy age-matched controls (controls, age = 75.4 ± 3.6 years; 7 men, 6 women) were studied under the IRB approved protocol. The MRI and DWI studies were performed on a 1.5 Tesla Eclipse MRI scanner (Phillips Medical Systems, Inc.). A standardized imaging protocol was used. A T1-weighted three-dimensional volumetric spoiled gradient recalled echo (3D-SPGR) sequence was used to acquire the high-resolution anatomical images. Axial DWI images were obtained by single shot echo planar FSAT sequence. A baseline image with minimum diffusion weighting was acquired using a small *b* value (*b*= 0 s/mm^2). Diffusion-sensitized images were then obtained with the diffusion gradient in the readout direction (x), in the phase-encoding direction (y), and in the section-select direction (z), with *b* value of 1000 s/mm^2. 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.

With the methods described previously [3], on coronal T1WI images, the same experienced investigator, blind to all clinical information, used mouse-oriented method to manually trace the boundaries of hippocampus, amygdala, parahippocampal gyrus (PHG), corpus callosum, and cerebellum (intra-rater ICC > 0.95). The anterior (AC) and posterior cingulate gyrus (PC) was separately traced by a neuroradiologist who was blind to the clinical diagnosis. The boundaries of frontal, temporal, parietal, and occipital lobes were defined with the WFU PickAtlas program [4, 5]. The gray matter (GM)/white matter (WM) segmentation with skeleton-based region competition algorithm was then performed for the ROIs obtained from the AC, PC, frontal, temporal, parietal, and occipital lobes.

After Chang attenuation correction, the 3D-SPGR MRI images were co-registered to the SPECT images and co-registration transformation matrices were obtained. With these transformation matrices and an in-house ROIMAP program, we mapped each ROI onto SPECT images and calculated the regional cerebral perfusion activity. The regional cerebral perfusion ratio (CPR) relative to cerebellum was used for further statistical analysis. With this same concept, the ADC values for three orthogonal axes were calculated after each ROI was mapped onto the ADC maps, including ADC-x, ADC-y, and ADC-z. The ADC-trace and the mean ADC (ADC-mean = ADC-(x+y+z)/3) are used as values for diffusion status. General linear model (GLM) was applied to compare the difference in CPR and ADC between MCI and control groups.

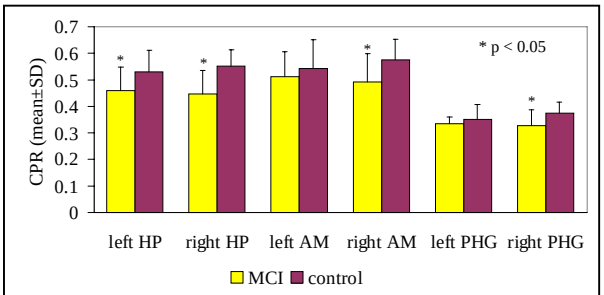

Figure 1. Significant hypoperfusion as measured with CPR is exhibited in bilateral hippocampus, right amygdala and PHG among MCI subjects when relative to normal controls. HP = hippocampus; AM = amygdala; PHG = parahippocampal gyrus.

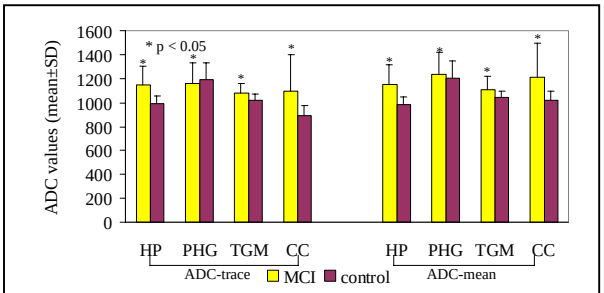

Figure 2. The water diffusivity as measured with ADC-trace and ADC-mean was significantly increased in hippocampus, PHG, temporal gray matter (GM) and corpus callosum in MCI when relative to normal controls. HP = hippocampus; PHG = parahippocampal gyrus; TGM = temporal gray matter; CC = corpus callosum.

Results

Age and gender distribution ($p > 0.05$) were comparable between MCI and control groups. Figure 1 indicates significant reduction of perfusion activity in bilateral hippocampus, right amygdala and PHG among MCI subjects when compared to controls ($p < 0.05$), suggesting potential hypoperfusion of medial temporal lobe in MCI. As shown in Figure 2, ADC-trace and ADC-mean were significant increased in hippocampus, PHG, temporal GM, and corpus callosum in MCI ($p < 0.05$), suggesting regional elevation of water diffusivity in MCI.

Discussion

In this study, we used MRI-guided quantification of perfusion activity obtained with SPECT and ADC values obtained with DWI techniques. This method allows defining ROI more precisely and taking the focal atrophy into consideration. With the co-registration matrix between MRI-SPECT images, two commonly used neuroimaging modalities are combined and allow the quantification of regional cerebral perfusion. We observed a reduction of perfusion activity in medial temporal lobe and an increase in the hippocampal diffusion in MCI relative to controls, indicating alterations in the functional physiology and microstructure of medial temporal lobe, especially of hippocampus in MCI. These provide more evidence that hippocampus is predominantly involved in neuro-degeneration during the development from normal aging to mild AD via MCI. Besides, increased water diffusivity was observed in PHG, temporal GM and corpus callosum, suggesting possible micro-structural alterations in these regions. Such alterations are possibly due to the neurodegenerative process occurred in these regions during the development of MCI. These findings indicate that after focal atrophy effect is corrected, the functional and microstructural alterations remain in MCI. The MRI-guided ROI-based analysis may facilitate the perfusion and diffusion studies on MCI and AD. The hippcampal perfusion and ADC may, therefore, serve as early markers to monitor the progression from MCI to mild AD.

References

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