Diffusion tensor imaging and cortical thickness mapping of mild cognitive impairment

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Introduction Mild cognitive impairment (MCI) is typically diagnosed using neuropsychiatric criteria. Neuroimaging approaches that are sensitive enough to distinguish MCI from healthy aging are desirable and remain to be developed. It has been reported that MCI exhibits early effects in the cerebral white matter (WM) [1] besides the changes in cortical regions. DTI has been used for studying WM changes in MCI. However, the diagnostic utility of DTI as compared to structural brain analysis such as cortical thickness indices has not been determined. Objective of this study was to examine whether measuring changes in both WM and GM can improve the distinction of MCI from healthy aging. Fractional anisotropy (FA), apparent diffusion coefficient (ADC) and averaged cortical thickness in temporal lobes were measured. We tested whether DTI or cortical thickness or both can be used to distinguish MCI from healthy aging.

Methods and Subjects Elderly subjects with normal cognition (n=10; 3 men, 7 female; age 70.1±7.7 years), MCI (n=16; 9 men, 7 female; age 71.4±7.7 years) were included in this study. DTI and 3D T1W MPGR images were recorded at 3T. For T1W imaging, TR/TE/angle = 25ms/2ms/30°, FOV = 224 mm, matrix = 256^2 and slice thickness=1 or 2 mm were used. For DTI, diffusion weighted single-shot spin echo-planar imaging (DW SSEPI) sequence was used with 16 diffusion sensitized gradient directions. Images were recorded with the isotropic pixel in the axial direction with 60 slices using 2 mm thickness without gap to cover the entire brain. The imaging parameters typically are: FOV= 224 mm, matrix of 112^2 (reconstructed to 224^2), TR =8.5 sec; DTI and anatomic 3D T1 images were collected in the same plane. For DTI data post-processing, images were processed and analyzed using PRIDE (Philips Medical System) or FSL (FMRIB, Oxford, UK). Regions of interest (ROI) analysis were used. Selected ROIs are shown in **Fig 1**. Whole brain voxel-by-voxel comparison was also performed using SPM2 software, which all b_0 images were spatially normalized to a standard template, then all FA maps were normalized and smoothed. Two sample t-test of SPM2, absolute threshold of FA>0.2, Statistical significance was set at p<0.005, extent threshold was set at 10 voxels. Cortical thickness averages were obtained from 3D T1W MPGR images using FreeSurfer software tools. A two-sample T-test was used to determine significant different between the two groups. The powers of DTI and cortical thickness measures to correctly classify MCI and control were estimated based on nonparametric statistics receiver operator characteristics (ROC) with sensitivity and specificity of the classifications were expressed as area under the curve. A lever of significance of *P<0.05* was considered statistically significant.

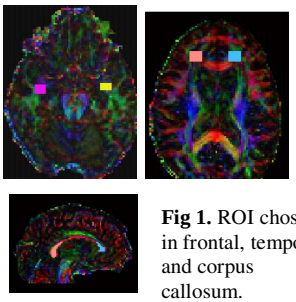


Fig 1. ROI chosed in frontal, temporal and corpus callosum.

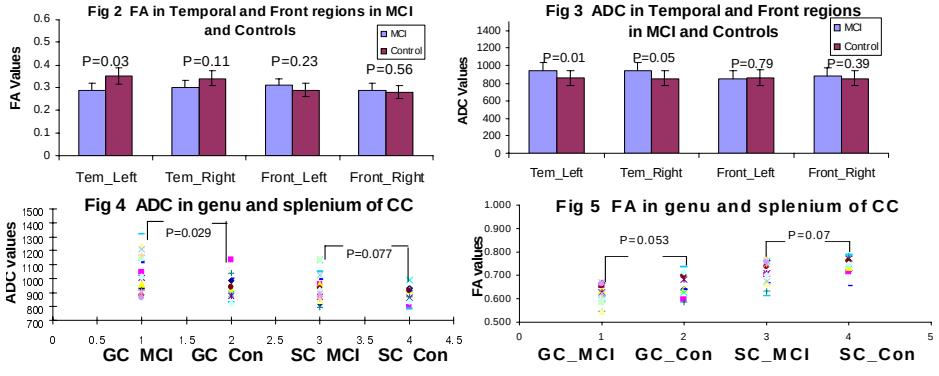
Results No statistical significant differences in age, gender, and educational levels were found between the two groups. Compared to normal controls, patients with MCI demonstrated decreased FA (*P* = 0.03) and increased ADC values (*P* = 0.01) in the left temporal region and a trend of higher ADC values (*P=0.05*) in the right temporal region but no significant difference (*P=0.11*) in FA measurements (**Fig 2, 3**). Changes in FA and ADC were found more noticeable in the genu than in the splenium (**Fig 4, 5**). Interestingly, MCI showed slightly higher FA and lower ADC changes in frontal WM in both hemispheres than those of controls, however, such changes were not reach statistical significances (**Fig 2, 3**). Cortical thickness analysis showed the decreased cortical thickness in several regions of GM in the left hemisphere (shown in **Table 1**), while no significant differences in the temporal areas of the right hemisphere were observed. No statistical significant changes were found in the frontal areas. Cortical thickness average in several GW regions showed cortical atrophy in temporal, entorhinal, fusiform and parahipocampal areas. ROC analysis applied in the left temporal region demonstrated that the approach of using combined FA values and cortical thickness analysis yield the high sensitivity and specificity in differentiating MCI and control (**Fig 6**).

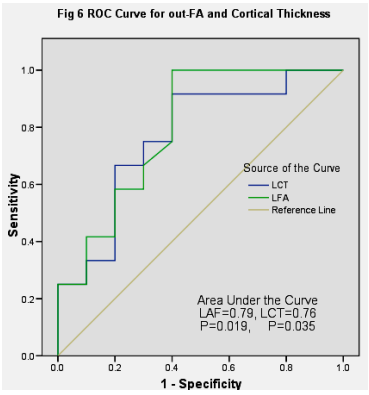
Table 1. Cortical thickness in several GM in MCI and controls

	Mean±SD	Mean±SD	P value
L_T	2.34±0.50	2.90±0.53	0.0011*
L_ph	2.02±0.41	2.73±0.87	0.0362*
L_en	2.28±0.71	2.97±0.87	0.0400*
L_fu	2.16±0.33	2.93±0.62	0.0038*
L_is	2.06±0.49	1.37±0.82	0.0345*
L_pc	2.07±0.68	2.80±0.76	0.0303*

L:left,R:right; T:temporal, ph:parahippocampal, en:entorhinal, fu:fusiform, is:isthmuscingulate, pc:postcentral, ***: P<0.05**

Discussion We found that the decreased FA and increased ADC values in temporal lobe WM is associated with MCI, and this effect is more pronounced in the left hemisphere. The difference in FA changes between left and right hemisphere in MCI has not been reported, although a few studies have demonstrated that cognitive performances in the left hemisphere correlates significantly with changes of anisotropy and diffusivity of selected WM regions [2]. It has been suggested that axonal loss or demyelination appears earlier in temporal lobe WM than other regions and in the left hemisphere than the right hemisphere in MCI. Our observations were consistent with previous reports. Our data showed that decreased FA and increased ADC values were more apparent in the genu of CC than in the splenium, which is inconsistent with other studies [3]. We also found that front WM and GW were not significantly different in MCI versus controls, in agreement with the hypothesis that the change of front region is more correlated with normal aging. Disease progression varies substantially among individuals with neurodegeneration and neurofibrillary pathology typically starts in the transentorhinal cortex and quickly spreads to the entorhinal cortex and the hippocampus. Patients with MCI have the pathological hallmarks of AD-neocortical senile plaques, NFT, atrophy, and neuronal loss in layer II of the entorhinal cortex. We utilized cortical thickness measurement not only separate MCI fro normal elderly controls, but also avoid time consuming for manual measurement. Therefore, taking into account of both FA measurement from DTI and structural cortical thickness mapping in left temporal lobe WM and GM improved ability to distinguish MCI from healthy aging controls.





References [1] Stahl et al, *Radiology* 2007,243:483-492. [2] Huang & Auchus, *Ann N Y Acad Sci* 2007,1097:259-264. [3] Zhang et al, *Neurology* 2007, 68:13-19.