DTI characteristics of amnestic and non-amnestic mild cognitive impairment

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Background and Objective: Mild Cognitive Impairment (MCI) is an important construct in the field of aging and dementia, denoting a transitional stage between normality and dementia.The broad clinical definition of mild cognitive impairment (MCI) includes amnestic MCI (aMCI) with impairment in memory domain and non-amnestic MCI (naMCI) with impairment(s) in cognitive domains other than memory such as attention/executive functioning, language, and visuospatial processing. While people with the aMCI subtype most commonly eventually progress to Alzheimer's disease (AD), the natural history, imaging characteristics and the pathological underpinnings of naMCI are less clear. Longitudinal studies however, suggest that patients with naMCI also have a higher rate of progressing to dementia than the cognitively normal individuals. Non-invasive imaging markers for underlying pathologies in MCI may be useful in identifying patients who may benefit from disease specific treatments at the prodromal stage of dementia. Our objective was to determine the characteristic DTI profiles of the MCI subtypes.

Methods: We studied clinically diagnosed age, gender and education matched patients with aMCI (n=28), naMCI (n=28), and cognitively normal (CN) (n=28) at 3Tesla using an 8-channel phased array head coil (GE,Milwaukee, WI). MCI subjects were further matched on the severity of cognitive impairment using Clinical Dementia Rating Sum of Boxes scores. 3D Magnetization Prepared Rapid Acquisition Gradient-Echo (MPRAGE) TR/TE/TI = 7/3/900 ms; flip angle 8 degrees; in plane resolution of 1.0 mm and a slice thickness of 1.2 mm was performed for anatomical segmentation and labeling. EPI FLAIR DTI (TR/TI/TE=8800/2200/60 msec) was performed with 21 diffusion sensitive gradient directions (b=1000 ms/mm^2), an in plane resolution of 3.0 mm and a slice thickness of 3.3 mm. We measured the apparent diffusion coefficient (ADC) from segmented cortical gray matter in regions derived from the automated anatomic labeling atlas. Each of the diffusion weighted image volumes from 21 directions were affine registered to non diffusion weighted b0 volume to correct for eddy current and motion artifacts. ADC and fractional anisotropy (FA) maps were computed using DTIstudio. Each subject's MPRAGE was segmented into gray matter, white matter, and CSF with SPM5 unified segmentation. The gray matter mask was then multiplied with registered customized AAL atlas. MPRAGE and GM atlas were warped to subject's b0 using SPM High Dimensional Warping. Mean ADC values from the gray matter atlas regions were computed. Color FA maps generated in DTIStudio were used for measuring tract-based FA and ADC by manual placement of tract-based regions of interest.

Results: Patients with aMCI had elevated ADC in the hippocampus ($p<0.05$ t-tests), and decreased posterior cingulum tract FA ($p<0.01$ t-tests) compared to CN subjects. Patients with naMCI had decreased posterior cingulum tract FA ($p<0.01$ t-tests), but normal hippocampal ADC compared to CN subjects. In regions that are not typically involved with the neurodegenerative dementia pathologies such as the precentral and postcentral gyrus (ie. internal control values), the ADC values were not different among the clinical groups **(Table).**

Conclusion: The hippocampus is involved in memory function and the neurodegenerative pathology of AD involves the hippocampus early during the pathological progression. The magnitude of diffusivity measured with ADC increases, and the directionality of diffusivity measured with FA decreases with neurodegeneration. For this reason, elevated hippocampal ADC most likely represent a high frequency of early AD pathology in aMCI patients. Conversly, finding normal hippocampal ADC on avearge in the naMCI subtype suggest that the underlying pathological substrates may include pathologies other than AD in some proportion of naMCI patients. Decreased FA in the posterior cingulum tract of both aMCI and naMCI patients indicate that the pathological involvement of cingulum tract is common to both aMCI and naMCI subtypes. Clinical follow-up will determine DTI findings that may be useful in identifying MCI patients who will progress to specific dementia syndromes in the future.

Table: Atlas-based cortical gray matter ADCs and posterior cingulum ADC and FA in clinical groups

ROI values on DTI (mean ± SD)	Cognitively normal	Non-amnestic MCI	Amnestic MCI
N	28	28	28
Amygdala ADC (mm^2/sec*10^{-6})	795 ± 35	810 ± 31	820 ± 30
Hippocampus ADC (mm^2/sec*10^{-6})	813 ± 30	822 ± 21	834 ± 28*****
Temporal lobe ADC (mm^2/sec*10^{-6})	775 ± 17	781 ± 19	779 ± 19
Postcental gyrus ADC (mm^2/sec*10^{-6})	768 ± 32	775 ± 27	769 ± 29
Precentral gyrus ADC (mm^2/sec*10^{-6})	762 ± 43	769 ± 33	758 ± 20
Post. cingulum ADC (mm^2/sec*10^{-6})	724 ± 38	735 ± 47	740 ± 51
Post. cingulum FA	0.60 ± 0.06	0.55 ± 0.07******	0.54 ± 0.07**

*ADC is higher than CN ($p\leq 0.01$);** FA is lower than CN ($p<0.05$)

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