Age Related Cognitive Decline and White Matter Changes Studied by Diffusion MRI

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Introduction: Normal aging is accompanied by pathological processes that affect cognitive abilities of the elderly population. Age related cognitive decline is manifested in reduced memory, attention, and response speed to challenging situations [1-2]. Recent publications have suggested that substantial damage to WM in the microstructure of myelin is strongly related to normal aging [1-2, 6-7]. Imaging studies have shown age related reduced functionality of the pre-frontal cortex (PFC) [3-5] as well as reduced WM volume in the frontal lobe. In addition, diffusion tensor imaging (DTI) studies found significant fractional anisotropy (FA) reduction as a function of age occurring in frontal regions [5].
High b-value diffusion weighted imaging (DWI) / q-space imaging (QSI) were found to be very sensitive to subtle white matter changes in several pathologies, such as multiple sclerosis and vascular dementia [9-11] suggesting higher specificity to intra-axonal water diffusion. In the present research, we hypothesized that myelin metabolism is an important factor in age related cognitive decline. To that end, the white matter of young and old subjects was investigated using QSI and DTI and correlated with their cognitive performance.

Methods: The study consisted of 11 subjects, age 60 and above, and 9 subjects, age 20-30. Subjects had no history of neurological diseases. MR imaging was performed on a 3T (GE) MRI system. The MRI protocol included DWI data set consisting 15 axial slices covering the frontal, temporal and occipital lobes with resolution of 3x3x5 mm^3. For each slice, 16 diffusion-weighted spin-echo EPI images were acquired, in which the diffusion gradients were incremented linearly from 0 to 4 G/cm to reach a maximal *b* value of 12,000 s/mm^2 (Δ/δ=57/51ms). This set of diffusion images was acquired at six gradient directions. To avoid intrinsic pulsative brain motion artifact the sequence was gated to the cardiac cycle with effective TR of 15 R-R intervals, and TE of 163ms. The DTI protocol consisted of 50 axial slices, with resolution of 2.5x2.5x2.5 mm^3, acquired for 19 gradient directions and b value of 1000 s/mm^2, the sequence was gated to the cardiac cycle with TR of 30 R-R intervals, and TE of 88ms.
The DTI and QSI images were corrected for motion using SPM (UCL, London, UK) software. DTI was analyzed and calculation of FA maps was performed as described previously [8]. Q-space images were calculated from the high *b* value DWI data as described previously [10-11] to extract the displacement maps. The FA and displacement maps of each subject were normalized according to a template brain and spatially smoothed, using the SPM software. Subjects also underwent a series of tests for cognitive evaluation outside the MRI scanner using Mindstreams® computerized cognitive tests (NeuroTrax Corp., NY[15]), including short and long term memory, stroop interference, go-no-go and verbal rhyming and naming.

Results: The results showed an age related significant increase in q-space displacement in frontal white matter and in the genu of the corpus callosum (CC) as well as a significant age related reduction in FA ($p<0.01$), (Fig 1).
Among the old age group, we used the stroop interference cognitive task to define two subgroups based on the duration of their response time. We found that elderly subjects who had longer response times are characterized also by higher displacement and lower FA in the genu of CC (Fig 2) and in the superior longitudinal fasciculus (SLF) (n=6, $p<0.05$, not shown).

Discussion and Conclusions: The results demonstrate that structural pathophysiological alternations in white matter can be related to age and cognitive performance using DTI and QSI, which are not detected by conventional MRI. QSI seem to reveal larger areas of white matter changes than DTI (see Fig. 1). This is true also for the analysis performed on the two elderly sub-groups defined by the cognitive evaluation. The groups differentiated in terms of the displacement and FA values in the genu of the corpus callosum indicating that the flow of information between the two hemispheres is damaged. In addition, the fact that these two groups differ also in region of the SLF (especially in its temporal end) suggest that the age related cognitive decline might not be due to frontal changes solely.

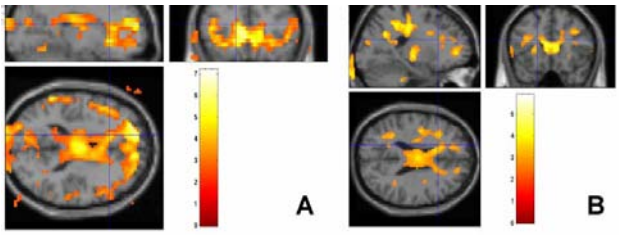

Fig 1. Differences between the old (n=11) and young (n=9) groups. (A) displacement (B) FA, $p<0.01$.

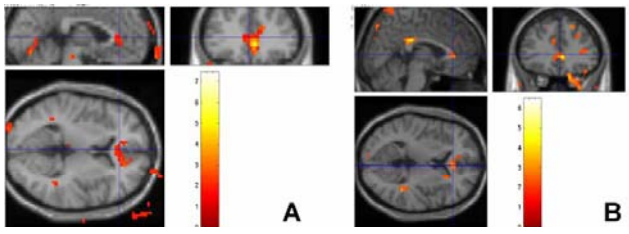

Fig 2. Differences between subjects with slow and fast response time within the elderly group. (A) displacement, (B) FA, $p<0.05$.

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