Age Related Cognitive Decline and Regional Brain Changes Studied by Diffusion MRI

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Background: Aging is a complex heterogeneous process accompanied by a cognitive decline. Although defined as a natural condition, many pathological neurodegenerative processes are involved in aging, manifested by reduced memory, executive function, motor abilities and processing speed, that may be associated with multi-regional neurodegenrative processes [1,2].
Diffusion-tensor imaging has been used over the last 10 years to quantify micro structural tissue changes in the brain, either by the apparent diffusion coefficient (ADC) or fractional anisotropy (FA) indices [3]. Several DTI studies focusing on normal aging and white matter found significant changes in fractional anisotropy (FA) in the corpus callosum, internal capsules and frontal, parietal and occipital white matter along with normal aging, despite a normal appearance on conventional MR images. In most studies the deterioration of regional white matter has a steeper decline in frontal areas than other regions [4,5]. In this study we investigated the relationship between age-related changes in brain structures and cognitive performance in multiple domains, under the hypothesis that age-related cognitive decline is a non-specific, multi-regional process.

Methods: DTI was performed on brains of 46 subjects, age 25-82y. Subjects had no history of neurological diseases. MR imaging was performed on a 3T (GE) MRI system. The DTI protocol consisted of 48 axial slices, with resolution of 2.5x2.5x2.5 mm^3, acquired for 19 gradient directions. The sequence was gated to the cardiac cycle with TR of 30 R-R intervals, and TE was 88ms. The duration of the entire MRI protocol was approximately 20 min.
The DTI images were corrected for motion using SPM (UCL, London, UK) software. DTI was analyzed and calculation of FA and ADC maps was performed as described previously [3]. The FA maps of each subject were normalized according to the standard Montreal Neurological Institute (MNI) stereotactic space and spatially smoothed, using the SPM software. Subjects also completed a battery of computerized tests (Mindstreams®, NeuroTrax Corp., NY[6]) assessing memory, executive function, motor abilities, visual-spatial, information processing speed, and verbal function, outside the scanner.
Test performance and age served as covariate correlation inputs for voxel based morphometry (VBM) of FA and DTI maps. Region of interest (ROI) analysis was guided by the VBM results and correlation coefficients were computed for age and test performance per ROI. The ROIs were: thalamus, , inferior frontal gyrus (IFG), corpus callosom, medial frontal gyrus (MFG), cingulum and others.

Results: In the VBM analysis, a significant correlation was found between DTI indices with age in multiple brain regions, with FA more specific to white matter ($p<0.005$, figure 1A) and ADC more specific to gray matter ($p<0.001$, figure 2A). In the ROI analysis, the correlation with age was relatively high in all regions; however, correlation between DTI indices and cognitive performance was test and ROI specific. For example, in the medial frontal gyrus (MFG), correlation between FA and performance in some cognitive tests (e.g. Information processing speed and stroop) were relatively high (r = -0.55, r = -0.5 respectively) but in other tasks (e.g. non verbal memory) the correlation was relatively low (r = 0.22) (figure 1B). In the inferior frontal gyrus (IFG) the correlation between ADC and cognitive performance in the verbal rhyming was high (r = -0.58) but was low in other tasks (e.g. Go No Go, r = 0.18) (figure2B).

Discussion and Conclusions: Cognitive tests have been developed in the last century to point to performance of specific brain regions. In the present study we found strong correlations between regional brain changes and cognitive performance. Those correlations are well in line with the expected localization of the cognitive tasks.
Brain changes related to age are multi-regional, involving gray and white matter, cortical and sub-cortical regions. ROI analysis revealed region-specific brain changes associated with performance in particular cognitive domains. Combining advanced MRI methodologies (e.g. DTI) with cognitive assessment enables a more focused observation of specific relationships between structural cognitive decline in the heterogeneous aging process. With VBM analysis of DTI images, as performed in the current study, we can relate regional changes, cognitive performance and aging.

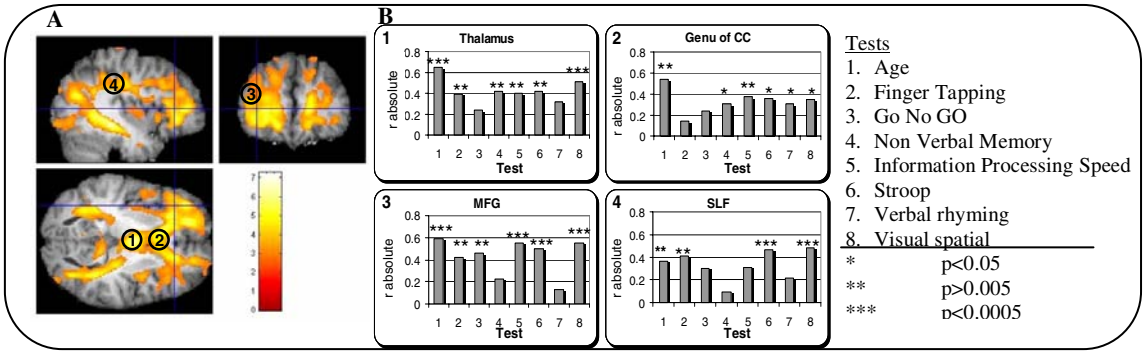

Figure 1. (A) The colored areas indicate significant negative correlation between FA and Age ($p<0.005$, $n=46$). (B) ROI analysis of the 4 regions indicated in (A). Correlation coefficient (absolute r) between cognitive performance and FA is depicted.

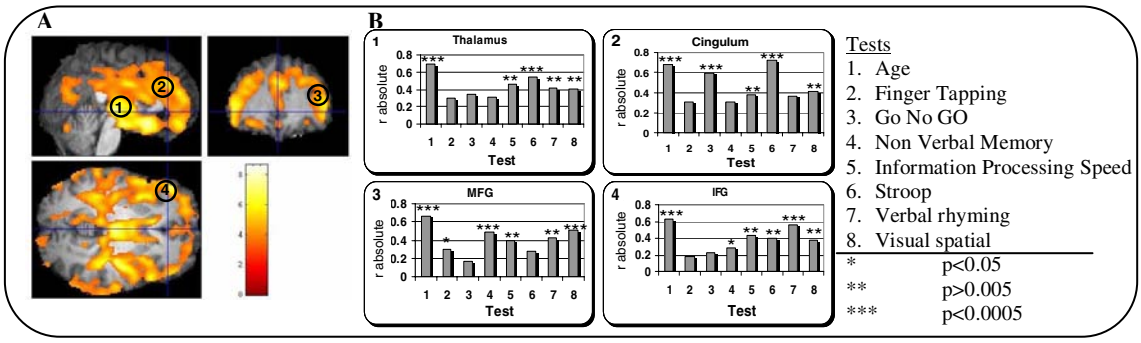

Figure 2. (A) The colored areas indicate significant positive correlation between ADC and Age ($p<0.001$, $n=46$). (B) ROI analysis of the 4 regions indicated in (A). Correlation coefficient (absolute r) between cognitive performance and ADC is depicted.

References:
1. Bartzokis G., Neurobiol Aging. 2004;25:5-18. ; 2. Peters A., J Neurocytol. Psychiatry Res. 2002;31:581-93.; 3. Basser PJ, Pierpaoli C. Magn Reson Med 1998;39(6):928-934. ; 4. Moseley M. NMR Biomed 2002;15(7-8):553-560.; 5. Sullivan EV, Pfefferbaum A. Eur J Radiol 2003;45(3):244-255. ; 6. Dwolatzky, T et al.. BMC Geriatrics. 2003; 3: