Brain Localization of Cognitive Domains with 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, language, motor and processing speed, that may be associated with multi-regional structural brain changes[1,2].

Diffusion-tensor imaging (DTI) measures the displacement of water molecules *in vivo* non-invasively[4]. This technique has demonstrated that aging is associated with an increase in the apparent diffusion coefficient (ADC) and decrease in fractional anisotropy (FA), more significantly in the frontal lobe[5].

In this study we performed factor analysis of 55 cognitive scores, isolating three cognitive domains: non-verbal memory, verbal function and information processing speed. We used DTI to quantify regional brain changes due to age-related cognitive decline in the three cognitive domains. Each domain was used as a covariate correlation input to voxel-based analysis (VBA) of ADC. In order to exclude the effect of aging, we performed partial correlation between the ADC and each of the cognitive domains controlling for age.

Methods: Subjects were 53 healthy volunteers, 25-82 y, all right handed. 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 ADC maps was performed as described previously [4]. ADC map 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., NJ[6]) that evaluate performance across an array of cognitive domains (memory, executive function, visual spatial perception, verbal function, attention, information processing speed, and motor skills) and provide precise measurements of accuracy and reaction time. Factor analysis of 55 cognitive scores was performed and three cognitive domains were extracted - memory, verbal function and processing speed. Memory domain is an average of five scores of accuracy in immediate and delayed non verbal memory task, verbal function is an average of four accuracy scores in verbal memory task and in verbal rhyming task, and information processing speed domain is an average of three measures of reaction time and two standard deviation of reaction time in a calculation task.

VBA analysis: partial correlation was performed excluding the age effect between ADC and the three cognitive domains controlling for age, using an in-house program employing Matlab's function *partialcorr*. SPM software was used for visualization of the correlated brain regions.

Results: The brain localization of the three cognitive domains is different based on the DTI partial correlation analysis. Negative partial correlation between the accuracy in the memory domain and ADC is found mainly in temporal and frontal gray and white matter, including the parahippocampus, orbitofrontal, inferior frontal gyrus, middle frontal gyrus, anterior cingulate, braca's area, and insula (red, figure 1). Negative partial correlation between the accuracy in the verbal domain and ADC is found mainly in white matter, in frontal white matter, in the superior longitudinal fasciculus (SLF) and in the cingulum (blue, figure 1). Positive partial correlation between the reaction time in the information processing speed domain is mainly in the white matter, in the posterior parts of the SLF, cingulum, posterior corona radiate and postcentral gyrus (GM) (green, figure 1).

Discussion and Conclusions: The main finding of this study is that regional measurements of ADC correlate with age-related cognitive decline. The partial correlation of each of the cognitive domains with ADC revealed a region-specific pattern of changes. The regions exhibiting substantial correlation in our study are known to play an important part in the corresponding functional domain. For example, the ADC in the hippocampal complex, orbitofrontal cortex, and broca's area were significantly correlated with the memory domain. These regions are known to play an important role in memory performance; The ADC in the SLF and in the cingulate was significantly correlated with the verbal domain. The SLF is known to connect the language areas (Wernicke's and broca's area). The ADC in the posterior corona radiata and parietal white matter were significantly correlated with the information processing domain. The corona radiata is related to motor function, and can be related to response speed. Parietal regions are known to be involved in performance of calculation tasks. The observed changes in ADC correlated with loss of cognitive function seem to reflect neurodegenerative processes. Gray matter changes probably involve cell and tissue loss, while white matter changes probably involve myelin deterioration and axonal loss. Correlating cognitive performance and quantitative measures of brain morphology can be used for indirect functional localization of cognitive domain and in future should be correlated with more direct functional measures such as fMRI and PET.

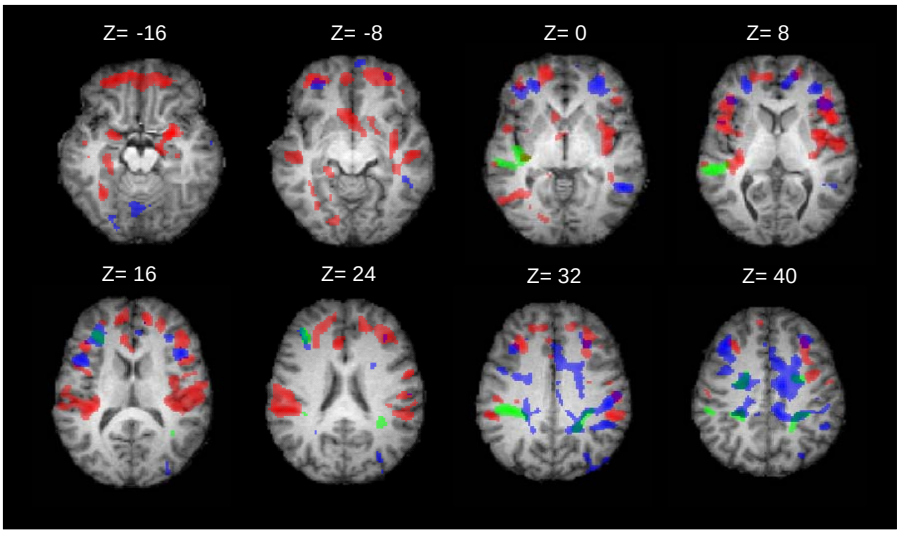

Figure 1. VBA partial correlation between ADC and cognitive domains: Red blobs: negative correlation with memory domain; blue blobs: negative correlation with accuracy in verbal domain; green blobs: positive correlation with reaction time in the information processing speed domain.

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; 3:4.