Diffusion Tensor Imaging of Memory Decline

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Background: Memory is a specific notable cognitive function that declines significantly during aging[1]. The brain localization of memory known from lesion studies[2] includes the hippocampus, cerebellum, medial temporal lobe, motor areas and language areas[3].
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 used DTI to quantify regional brain changes due to age-related memory decline. Memory performance was used as a covariate correlation input to DTI indices using voxel-based analysis (VBA). In order to exclude the effect of aging, we performed partial correlation between the DTI indices and memory performance controlling for age.

Methods: Subjects were 51 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 FA and ADC maps was performed as described previously [4]. ADC and 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., NJ[6]) assessing cognitive performance in multiple domains, outside the scanner. The memory domain tests included non-verbal and verbal memory.
VBA analysis: conventional correlation was performed using the SPM simple regression routine with memory performance as covariate. The age effect was excluded by performing partial correlation between the imaging parameters and memory performance controlling for age, using an in-house program employing Matlab's function *partialcorr*.

Results: ***Simple correlation with memory performance:*** The localization of ADC-memory negatively correlated regions (fig.1A) overlapped between the verbal (red) and non-verbal (blue) tasks and included large sections of the temporal lobe and frontal lobe. A notable correlation was found within the ventricular space, probably indicating strong correlation between atrophy and memory performance. This strong correlation might be a biased result of the memory-age correlation due to age related atrophy. This observation was even more impressive on the FA-memory correlation maps (fig.1A), where both tasks showed strong positive correlation throughout the entire ventricular space. To exclude the age effect on the memory-imaging correlation we performed partial correlation analysis.
Partial correlation with memory performance: The negative partial correlation between ADC and non-verbal memory (blue, Fig. 1B) was found in the inferior frontal gyrus (IFG; Broca's area), bi-lateral hippocampus, nucleus accumbans and caudate, insular gray matter, superior temporal gyrus (STG; Wernicke's area), and medial frontal gyrus ($p<0.005$, Fig. 1B). The most significant correlation was found for Broca's area in the right hemisphere ($r = -0.6$, $p<0.0001$; Fig. 2A). FA was found to have only negligible positive correlation with non-verbal memory accuracy in small regions of the lateral ventricles, especially in their posterior part.
The partial correlation between ADC and verbal memory (red, Fig. 1B) was found in the left hippocampus and Wernicke's area, with the latter showing the strongest correlation ($r = -0.39$, $p=0.005$; Figs 2B). FA was positively correlated with verbal memory performance only in the superior longitudinal fascicules and some adjacent gray matter areas (Fig. 1B).
The extent of correlated regions is more localized in the partial correlation test (Fig. 2) compared to the simple correlation (Fig. 1). In addition the overlap in the localization of verbal and non-verbal correlation with ADC was much smaller than in the simple correlation.

Discussion and Conclusions: The main finding of this study is that regional measurements of DTI based indices correlate with age-related memory decline. The partial correlation of memory performance with DTI parameters revealed a region-specific pattern of changes mostly in the gray matter. The regions exhibiting substantial correlation in our study are known to play an important part in memory performance. The observed changes in DTI indices correlated with loss of cognitive function reflect neurodegenerative processes – most likely cell and tissue loss – in those regions that are related to memory decline.
Thus, **diffusion MRI, especially the ADC, can be used as a regional quantitative marker for memory decline.**

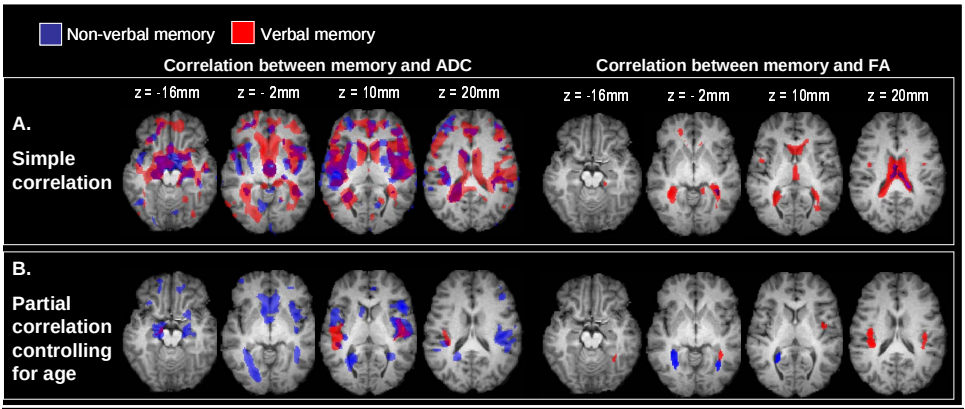

Figure 1. VBA correlation between DTI indices and memory performance:
(A) Negative correlation between ADC (left column, $p<0.005$) and positive correlation between FA (right column, $p<0.01$) and the verbal (red) and non-verbal (blue) memory accuracy.
(B) Negative partial correlation between ADC (left column, $p<0.005$) and positive partial correlation between FA (right column, $p<0.01$) and the verbal (red) and non-verbal (blue) memory accuracy, adjusted

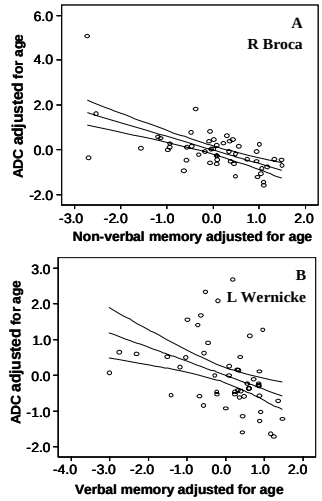

Figure 2. Partial correlation between ADC and memory performance for the peak voxel:
(A) non-verbal memory controlling for age (r=-0.6,$p<0.0001$,n=51) (B) Verbal memory controlling for age (r=-0.39,p=0.005, n=51).

References: 1. Larrabee GJ, Crook TH, 3rd (1994), Int Psychogeriatr 6:95-104; 2. Ojemann G, Mateer C (1979), Science 205:1401-1403; 3. Thompson RF, Kim JJ (1996), Proc Natl Acad Sci U S A 93:13438-13444. 4. Basser PJ, Pierpaoli C (1998), Magn Reson Med 39:928-934; 5. Sullivan EV, Pfefferbaum A. (2003) Eur J Radiol 45(3):244-255. 6. Dwolatzky, T et al.. BMC Geriatrics. 2003; 3:4.