Diffusion MRI of Short-Term Spatial Memory Related Brain Plasticity

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Introduction

Neuroimaging studies of brain plasticity reveal significant volumetric changes via voxel-based morphometry of T1 weighted scans [1]. The micro-structure correlates of these changes are not well understood. Diffusion tensor imaging (DTI) became one of the most popular imaging techniques in neuroimaging and is regarded as a micro-structural probe [2]. Recently, tract-based spatial statistics (TBSS) analysis of DTI scans before and after motor coordination training (juggling) revealed regional fractional anisotropy (FA) increase in parietal pathways [3]. In that study, FA changes were reported following few weeks of training.

Long-term experience necessitates structural plasticity which, in the adult brain, is characterized by changes in the shape and number of the synapses (synaptogenesis) as well as other process (neurogenesis, gliogenesis and white matter plasticity). An open question is what happens at shorter term learning and memory processes. Studies performed on rodents revealed that short term micro-structural changes in the hippocampus and other limbic and motor system related regions can be observed with diffusion MRI [4].

In this work, we study the diffusion MRI changes in a short term spatial memory task in humans. For that purpose, subjects underwent two DTI session separated by 2 hour car-racing game. Significant changes both in FA and apparent diffusion coefficient (ADC) were observed mainly in the medial temporal lobe.

Method

36 subjects were divided into a learning group (LG, n = 18), control group 1 (CG1, n = 9) and control group 2 (CG2, n = 9). All subjects underwent two series of DTI scans two hours apart, separated by either a spatial learning task (LG), non-spatial learning task (CG1) or passive waiting (CG2). The DTI protocol included a series of diffusion weighted images with b value of 1,000 s/mm2 sampled at 19 directions with additional image with b=0 s/mm2. The image resolution was 1.57x1.57x2.10 mm^3.

The learning task included 16 laps of the car game track (Electronic Arts©), divided into 4 sessions. Their objective was to learn the track and achieve better lap times. To enhance memorization, at the end of each session subjects were given snapshots of locations in the track which they had to arrange in the correct order. The CN1 group participated in the same task, except the track was different in each trial. Therefore, apparently no spatial learning was induced. The CN2 group did not perform any task between the scans.

DTI analysis included extraction of ADC and FA maps using an in-house software. All maps were normalized to the MNI coordinate system based on the FA maps. All registration and normalization routine were done in SPM2. For each subject, the pre- and post-learning task images were normalized to a mean image of these two scans (following normalization to template). This procedure reduced the normalization bias artifact. We performed statistical voxel-based analysis of the DTI maps, by using a mixed-design ANOVA of 3 (experimental group) X 2 (scan time) with repeated measures on the second factor.

Results

The ANOVA test revealed a regional significant interaction between experimental group and scan time for each of the DTI indices. For the ADC ANOVA (Figure 1), at statistical threshold of $p<0.01$, only left hippocampus showed significant effect ($p=0.0052$ at the most significant voxel). For the FA ANOVA (Figure 2), at statistical threshold of $p<0.01$, the right amygdala, bi-lateral entorhinal cortex and left insula showed significant effect ($p=0.0023$, 0.0010, 0.0015 respectively).

Post-hoc analysis revealed that the main contributor to the ADC interaction is reduction in ADC in the LG group with no effect in the control groups. In the most significant voxel in the hippocampus, the ADC decreased by 2.5 ± 0.6 %. This decrease was a result of 2.1% decrease in parallel diffusivity and 2.8% decrease in radial diffusivity. Post-hoc analysis on the FA interaction revealed that the main contributor for this observation was FA increase in the LG group with no effect in the control groups. In the most significant voxels in the right amygdala, bi-lateral entorhinal cortex and left insula, the FA increase was 6.4 ± 1.6 %, 3.0 ± 1.8 % and 4.8 ± 1.7 %, respectively. In the amygdala, this FA increase was a result of radial diffusivity decrease of 0.7% and axial diffusivity increase of 0.8%. In the entorhinal cortex, larger decrease in radial than axial diffusivity caused the FA increase (1.6% and 0.7%, respectively). In the Insula, the FA decrease was a result of radial diffusivity decrease of 1.6%, while axial diffusivity barely changed (0.2%).

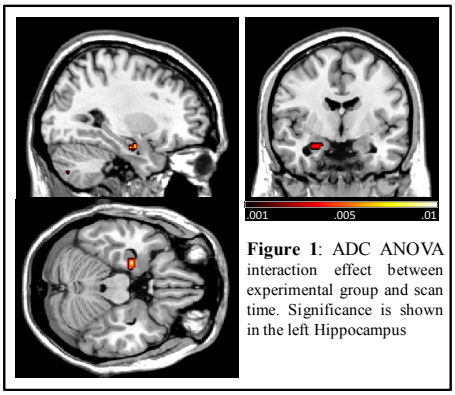

Figure 1: ADC ANOVA interaction effect between experimental group and scan time. Significance is shown in the left Hippocampus

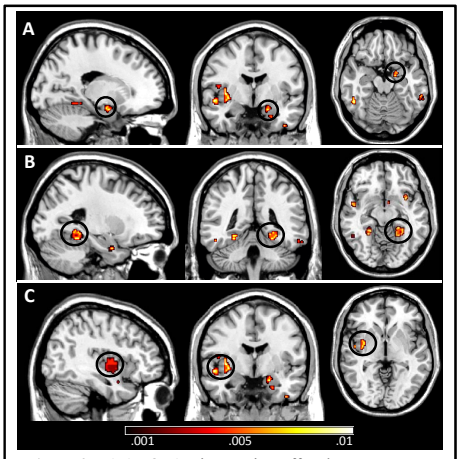

Figure 2: FA ANOVA - interaction effect between experimental group and scan time. Significance is shown in the right amygdala (A), bi-lateral entorhinal cortex (B) and left insula (C).

Discussion & Conclusions

The main result of this work is that DTI can follow on micro-structural tissue changes, induced by cognitive experience, already 2 hours following the training episode. The obtained areas: hippocampus, amygdala, insula and entorhinal cortex are well described in the literature in relation to immediate learning and memory. The lateralization of obtained results (e.g. left hippocampus) might be related to the nature of the cognitive task (i.e. spatial, procedural and episodic memory).

The cellular and micro-structural correlates of diffusion imaging are not well understood, and this study brings up even more questions. It appears that the diffusion MRI signals are extremely sensitive to the fine micro-structure of the tissue, not only in white matter but also in gray matter. Further studies should be directed at studying the exact relation between tissue morphology and DTI indices. Nevertheless, with the ability to follow tissue plasticity with MRI, and at such short time scales, new insights on the process structural brain plasticity could be gained.

References

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