A Permutation Test Statistical Analysis of Learning Induced DTI Changes

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Introduction

Diffusion MRI is widely used in recent years to investigate the relation between brain structure and cognitive abilities, by scanning subjects before and after a learning task[1-3]. Different methodologies (e.g. voxel-based analysis or TBSS) are applied in such studies; all require some kind of spatial normalization procedure and a statistical comparison in the group level to reveal an averaged effect of 2-3%. In a previous work, Jones (2003)[4] used a bootstrap method to estimate the uncertainty within a diffusion tensor imaging (DTI) data. Here, we propose a similar approach in order to execute a permutation test for performing statistical comparison between 2 DTI scans in the single subject level. The main principle is to examine in which voxels the change in DTI parameters is bigger than the inherent noise.

Methods

5 subjects were scanned before and immediately after participating in a spatial navigation task, based on a computer car racing game (see sagi et al., 2012[1]). Previous work showed that such practice induces structural brain changes in the hippocampus, parahippocampal gyrus and insular cortex, expressed by a reduction in mean diffusivity (MD). The DTI protocol included diffusion weighted images with b value of 1,000 s/mm^2 at 57 directions and 3 b=0 image with isotropic resolution of 2.1 mm^3. Such dataset was acquired for each subject before and after the task, from which MD maps were calculated. Our test statistic was the MD difference between the first and the second scan, which under the null hypothesis equals to zero. To obtain the distribution of the MD difference under the null hypothesis we rearranged the data in 1000 permutations, in which diffusion weighted images from the first and second scan were randomly shuffled. Then, MD maps were calculated for the reshuffled dataset and the difference was calculated. For each voxel we calculated the proportion of sampled permutations in which the MD difference was greater or equal to the real MD difference. We rejected the null hypothesis in voxels where this proportion was less than 5%.

Results

We found significant clusters of MD reductions in the anatomical regions of interest in all of the subjects: 2 subjects showed significant reduction in MD in the anterior part of the left hippocampus and another subject showed MD decrease in its middle part. MD reduction in the posterior hippocampus was found in the other 2 subjects (see Fig. 1). MD reduction in the parahippocampal gyrus was found in all of the subjects, 3 of them in both hemispheres (see Fig. 2). In addition, all subjects showed MD reduction in the insular cortex bilaterally (Fig. 3).

Discussion

We demonstrated here that statistical voxel based analysis in DTI is feasible on the single subject level, using the fact that DTI requires the acquisition of a large dataset with inherent noise. On the single subject level, where each voxel is represented by one number for the pre and post scans - separation of the effect from noise is impossible. Using the permutation approach described here, we are able to put apart the noise and biological effect, per each voxel, for each subject in it native space. Such a methodology spares the need to perform spatial normalization and acquire large cohorts. In addition, it enables us to detect differences between the subjects and to detect regions that had changed in some subjects but not in the others.

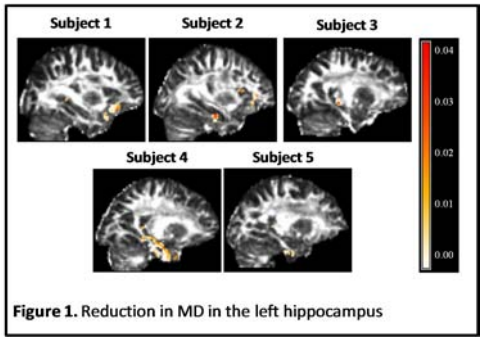

Figure 1. Reduction in MD in the left hippocampus

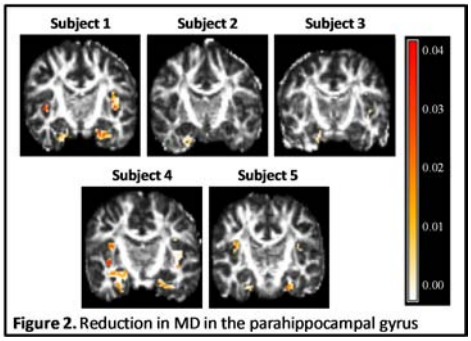

Figure 2. Reduction in MD in the parahippocampal gyrus

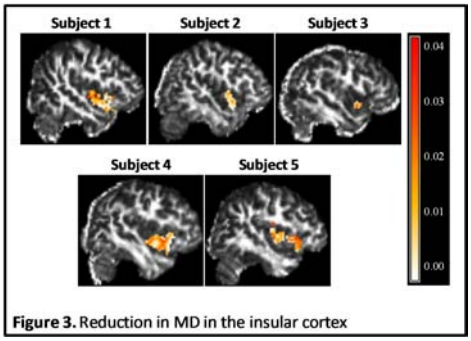

Figure 3. Reduction in MD in the insular cortex

References: (1) Sagi, Y. et al. *Neuron* 73, 1195–203 (2012). (2) Scholz, J.et al. Training induces changes in white-matter architecture. *Nat Neurosci*, *12*, 1370–1 (2009). (3) Blumenfeld Katzir, T. et al. Diffusion MRI of structural brain plasticity induced by a learning and memory task. *PLoS One 6*, e20678 (2011). (4) Jones, D. K. Determining and visualizing uncertainty in estimates of fiber orientation from diffusion tensor MRI. *Magn Reson Med 49*, 7–12 (2003).