Evidences of Learning and Memory Related Brain Plasticity from Diffusion Tensor Imaging in the Rat

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Introduction

Brain Plasticity is one of the enigmas of brain physiology – the ability of the brain re-organize following the demand for specific cognitive function. It is well accepted that neurogenesis and synaptogenesis, the two processes that accompanies brain plasticity are immutable following brain development but retain active in hippocampus. This is not surprising as the hippocampus is the funnel of new memories to brain and as such must be susceptible to plastic changes in-order to absorb new information.
Functional MRI has been used to study brain plasticity as it can follow brain activity changes through the hemodynamic response over time. This was used to assess brain activity pattern changes following stroke, longitudinally in multiple sclerosis or following cognitive experience of learning of some kind. However, up to date MRI could not indicate on the anatomical changes induced by plasticity. In this study we examined rats before and after a learning and memory task using diffusion tensor imaging (DTI) and compared the task induces brain changes using a voxel-wise analysis of the DTI indices (apparent diffusion coefficient, ADC and fractional anisotropy, FA).

Methods

Six-teen Wistar male rats were scanned twice in a 7T MRI system (Bruker, Germany) at age of 12 months. The time interval between the two MRI scans was 1 week in which the rats underwent a learning and memory performance test (Morris water maze). In the test the rats need to learn the location of a hidden platform in a pool in a period of 6 days. The MRI protocol included a DTI acquisition with cardiac gated diffusion-weighted spin-echo echo-planar-imaging (EPI) pulse sequence with the following parameters: TR/TE = 4000/25ms, Δ/δ=10/4.5ms, 4 EPI segments and 16 non-collinear gradient directions with b of 1000s/mm^2. Geometrical parameters were: 12 slices of 1.2 mm thickness and in-plane resolution of 0.2x0.2mm^2.
Image analysis included diffusion tensor imaging analysis of the DWI-EPIs to produce for each rat FA and ADC maps. For statistical comparison between rats we used a voxel-wise approach where each rat brain volume was co-registered normalized with template rat atlas. Following these steps simple ANOVA tests between the two groups was performed. The registration, normalization and statistical analysis were performed with SPM2 (FIL, UCL, London, UK).

Results and discussion

Statistical parametric maps of voxel based ANOVA test between the FA maps before and after the water maze shows significant signal changes localized at 3 locations: the posterior part of the corpus callosum (connecting V1 areas), the hippocampus and septum (Figures 1 and 2). The time interval between the two MRI scans was 14 days. The hippocampus and septum are known to be involved in memory and it is well accepted that neurogenesis/synaptogenesis in those regions can occur in relation to learning and memory experience. The posterior part of the corpus callosum which is not a learning & memory region also showed significant FA increase. This may relate to the fact that the memory task the rats were exposed to is of visual-spatial orientation. It is speculated that the fiber system connecting these regions (posterior part of corpus callosum) also underwent morphological changes. This might shed a new light on the plasticity phenomenon that may happen also in white matter and within very short periods of time.
The main observation that FA index increases in specific regions following learning and memory experience most probably indicating increase in tissue organization and density. In addition, the ADC in these regions decreased a phenomenon that is known to happen after stroke. In relation to learning & memory experience this may reflect increase in tissue density.

Conclusions

We show here for the first time that morphological tissue changes induced by short term learning and memory plasticity can be characterized with diffusion MRI. We studied here 12 months old rats, it can be speculated that the plasticity process and its morphological appearance will be more significant at younger age and much larger differences may be found there.

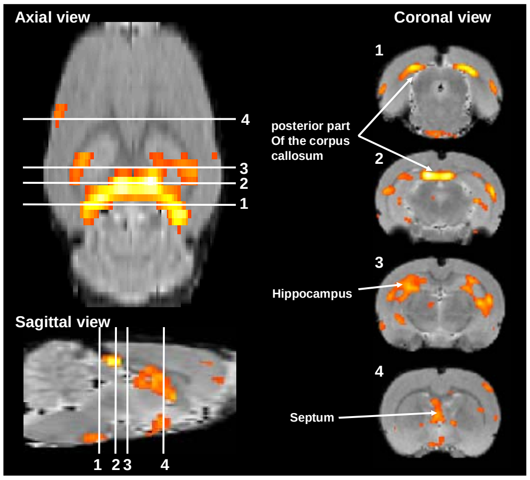

Figure 1: Statistical parametric maps of a voxel-based ANOVA test of FA maps before and after water maze learning test. Significant FA increase was obtained in the posterior part of the corpus callosum, hippocampus and septum.

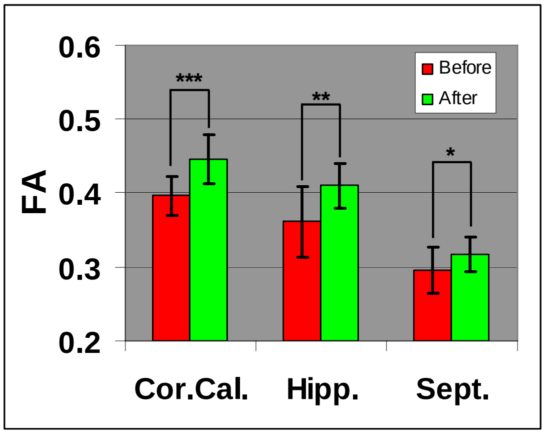

Figure 2: Changes in FA in the regions indicated in Figure 1 before and after the water maze. * p<0.05, ** p<0.005, *** p<0.0005.