Localization of Cognitive Function in Rats with Magnetic Resonance Imaging

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Introduction

The brain localization of cognitive functions is limited to invasive lesion or electrophysiological studies. Non-invasive imaging techniques such as functional magnetic resonance imaging (MRI) are less informative in rodents due to the use of anesthetics.

Anatomy and function of the brain are linked – the cyto-architectonic mapping of the brain resembles its functional mapping, i.e. the morphological composition of a tissue is correlated with its function and vise versa. To that end quantitative measures of brain tissue morphology can be used to study anatomy-behavior correlation and provide, indirectly functionally related information. Diffusion MR.

Methods

A group of 29 wistar male rats were scanned in a 7T MRI system (Bruker, Germany) at age of 9 months. Sixteen rats of this group were scanned also at the age of 3 months. At age of 12 month all rats underwent a learning and memory performance test (Morris water maze). In the test the rats need to find the location of a hidden platform in a pool. The test is repeated 4 times a day for 6 days. The MRI protocol included a diffusion tensor imaging (DTI) protocol acquired with a 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 DTI analysis 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 and normalized with a template rat atlas. Following these steps simple regression (correlation) tests between the FA and ADC indices and the rats latency (time to reach to the platform in second) was performed. The registration, normalization and statistical analysis were performed with SPM2 (FIL, UCL, London, UK).

Results and discussion

The behavioral results show the learning processes that rats underwent as the latency time reduces from day to day (Figure 1). It is well known that different areas of the limbic system (e.g hippocampus, amygdale, olfactory) are involved in this process. Correlation analysis between the DTI indices with the water maze performance results (the latency) during the behavioral test (at days 1,5 and 6) shows significant correlation at 4 main locations: the amygdala, the pirifrom cortex (part of the olfactory system), the hippocampus and the septum (Figure 2). The ADC in the area of the amygdala complex positively correlated with the first day performance. This can be explained by response of anxiety to the pool. The ADC in the area of the piriform cortex which related to the olfactory system positively correlated with the 5th day performance and may indicate the use of smell in relation to memory. The hippocampus and septum are known to be involved in learning and memory and the ADC and FA in these areas were correlated to the latency in the 5th and 6th day respectively. These results imply that the cellular morphology of the limbic system correlates with learning and memory abilities of the rat.

A surprising result was the correlation analysis of between the DTI parameters measured at the age of 3 months with the performance in the learning and memory task (that was performed 9 months later). It was found the morphology of hippocampus as characterized by the FA and ADC indices correlates with latency at day 5 of the water maze (Figure 3). This result implies that already at the developmental stage the formation of the hippocampus is related to memory abilities at older age.

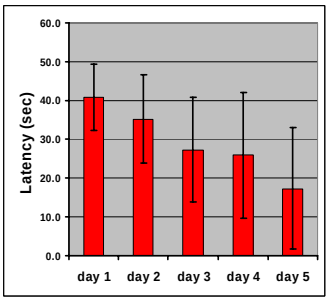

Figure 1: The latency in a Morris water maze test as a function of trial day. Note the decrease in latency time during the test days.

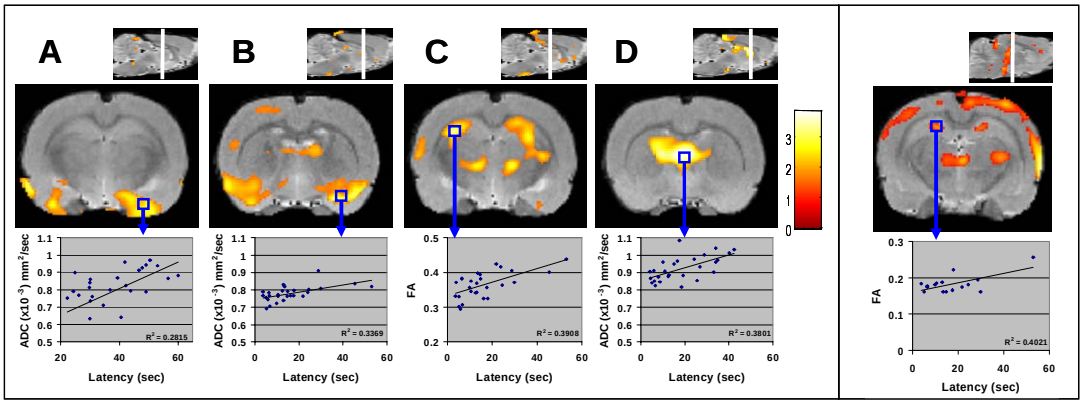

Figure 2: Correlation between DTI indices (at 9 months) with the leaning and memory performance:
A. Positive correlation between the latency in the 1st day with the ADC - located in the amygdala complex.
B. Positive correlation between the latency in the 5th day with the ADC - located in the piriform cortex.
C. Positive correlation between the latency in the 5th day with the FA - located in the hippocampus.
D. Positive correlation between the latency in the 6th day with the ADC – located in the septum.

Figure 3: Positive correlation between the performance results in the 5th day of the water maze with the FA (at 3 months).

Conclusions:

Correlation between diffusion MRI indices and behavioral performance allows localization of cognitive performance. Although this procedure is a not a direct functional measure, this study validates its accuracy as this regions that were found to be correlated (areas of the limbic system) are known to play a crucial role in learning and memory tasks.