DTI Detection of Microstructural Changes Induced by Sleep Deprivation

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Introduction

Sleep has an important role in learning and memory (1). It has been reported that insufficient sleep could lead to neurocognitive deficits in humans (2). Rapid eye movement (REM) sleep is believed to be critical for memory consolidation (3). REM sleep deprivation (SD) has been widely employed to investigate the mechanisms underlying sleep and learning, however, mostly restricted to behavioral or histological studies (4). DTI is emerging as a powerful tool for probing neural plasticity. Its noninvasive nature allows the exploration of plasticity network between various brain regions simultaneously and longitudinally. This study aims to assess the microstructural plasticity using DTI, which may provide insights into the plasticity network changes that accompanies SD in vivo.

Methods

MRI Protocols: Nine male Sprague-Dawley rats (~8 weeks old) were scanned twice using a 7T Bruker scanner before and after SD treatment. Animals were kept warm under circulating water at 37°C with respiratory monitoring. Diffusion-weighted images were acquired using a SE 4-shot EPI sequence with 30 diffusion gradient directions. Five additional images with b-value=0 (B_0 images) were also acquired. The imaging parameters were: TR/TE=3000/31.62ms, δ/Δ=5/17ms, NEX=4, FOV=3.2x3.2cm^2, acq matrix=128x128 (zero-filled to 256×256), slice thickness=1mm (0.2mm gap), b-value=1000s/mm^2. ***Sleep deprivation*** (5): A 72-hour REM-SD was employed using the multiple small platform technique. Five platforms with each 6cm diameter were placed in the middle of a water tank. Platforms were spaced 9cm apart so that rats could easily move between them but could not lie across any two. The water reached up to ~2 cm below the surface of the platform. Food and water were available *ad libitum*. All treatments lasted 72 hr under a 12 hr day/night cycle. Video monitoring was performed throughout REM-SD and was used for later behavioral validation. ***Data Analysis:*** Each rat brain volume was normalized to a custom mean B_0 template generated from all animals. Voxel-wise paired t-test was performed between pre- and post-SD DTI index maps, the resulting significant voxels were projected onto each individual animal's DTI index maps at each time point for quantitation comparisons. The normalization and statistical procedures were performed using SPM5.

Results

FIG.1 illustrates the significant voxels with decreased axial diffusivity between pre- and post-SD in the voxel-wise paired t-test analysis, where altogether 203 voxels were bilaterally identified in various locations in hippocampus in three continuous slices, and 236 voxels were bilaterally identified in cortex. FIG.2 shows the pre- and post-SD DTI index measurements from the resulting voxels pointed in FIG.1 for hippocampus and cortex. In hippocampus, a consistently significant decrease was observed in all diffusivity measurements, whereas FA exhibited little change. In cortex, axial diffusivity decreased more than radial diffusivity, significant decrease was found in axial, mean diffusivity and FA.

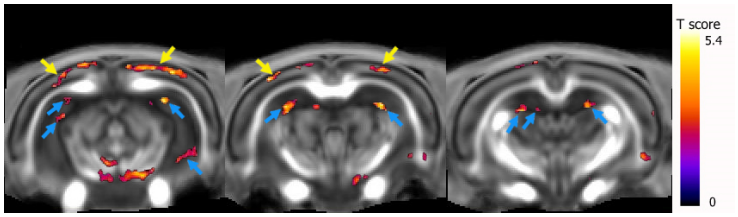

FIG.1 Voxels showing significant axial diffusivity decrease between pre- and post-SD with threshold p<0.05. Statistical map was overlaid on the average FA map from all animals (n=9). Significant voxels were extracted for DTI indices quantitation in hippocampus (blue arrows, 203 voxels) and cortex (yellow arrows, 236 voxels). Color bar indicates T score of the statistical map.

Discussions and Conclusions

The main finding in this study is the significant diffusivity decrease identified in the hippocampus and cortex using voxel-wise paired t-test. The significant voxels observed in hippocampus were located in multiple slices in separated clusters. They were possibly located within specific layers, such as dentate gyrus and CA1, which are believed to be sensitive to SD (5). Our high resolution manganese enhanced MRI study results also indicated that neuronal activity in specific layers of hippocampus such as dentate gyrus was exceptionally susceptible to SD (data submitted in another abstract). Previous studies reported that REM-SD dramatically impaired hippocampal-dependent learning, which is demonstrated by neuron loss as well as synaptic remodeling in cortex and specific layers of hippocampus (5-7). As little is known about how these cellular factors affect DTI indices particularly in gray matter regions, evidences from probing axonal plasticity and neurite density in rat hippocampus using DTI and DWI (8, 9) have provided some insights into the structural basis underlying the DTI measurements. On the other hand, it is possible that the physiological consequences of severe sleep loss, such as increased metabolic rate, weight loss and hypothermia (10) may also affect the DTI measurements. However, the REM-SD protocol employed in this study was mild compared to the chronic total SD model where severe physiological alterations were observed (10). Although the exact biological processes underlying the DTI changes post SD remain to be elucidated, this study demonstrated that DTI is a sensitive and non-invasive in vivo tool that can provide insights into the microstructural plasticity in specific regions during REM-SD.

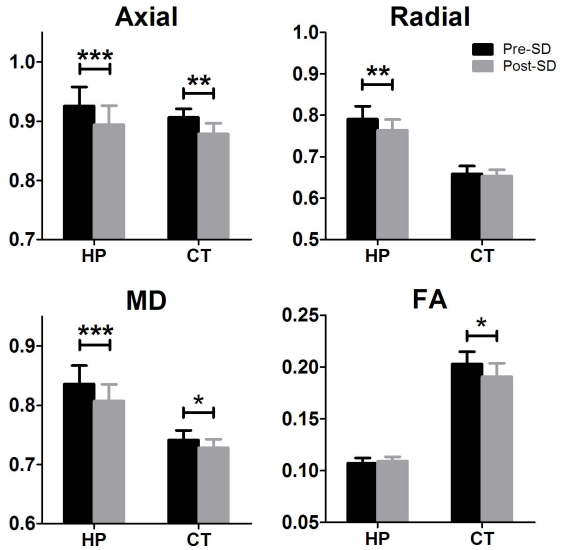

FIG.2 DTI index quantitation and comparisons between pre- and post-SD in the voxels indicated in FIG.1 (n=9). Two-tailed paired t-test was performed. * p<0.05, ** p<0.005,

References

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