HIPPOCAMPAL NEUROGENESIS VISUALIZED BY DIFFUSION TENSOR IMAGING

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Introduction:

Neurogenesis may play a role as enhancing or repairing brain functionality during both normal and pathological conditions. If the process can be detected in vivo and noninvasively (Pereira, et al., 2007), it may serve as a valuable indication of brain functional status clinically. Neurogenesis involves constant addition of newly-generated neural cells to the existing neuroarchitecture. The morphogenesis associated with the process may be detected by diffusion tensor imaging (DTI), which is a sensitive MRI modality for detecting the diffusion properties of water molecules in brain tissues. To test this possibility, hippocampal neurogenesis under either normal or pathological circumstances was examined in the present work.

Materials and Methods:

Hippocampal neurogenesis was induced by subcutaneous injection of bFGF (fibroblast growth factor) given at the dose of 25ug/Kg in 4 week-old rats, or by middle carotid artery occlusion (MCAO) as a stroke model in 9 week-old rats. Both treatments were well known for their effects on the enhancement of hippocampal neurogenesis. Upon hippocampal neurogenesis, the rat was scanned for DTI. A spin echo imaging sequence was employed for acquiring the required series of axial diffusion-weighted images (DWIs) with b values of 0 and 1100 mm^2/s applied along six directions: [Gx, Gy, Gz] = [1,1,0], [1,0,1], [0,1,1], [–1,1,0], [0,–1,1], and [1,0,–1] with repetition time = 1.5 s, spin echo time = 31 ms, time between diffusion gradient pulses = 15 ms, duration time of diffusion gradient = 7.5 ms, slice thickness = 1 mm, field of view = 2.56 cm, data matrix = 128x128, and four averages. Following scanning, the rat was immediately perfused and the brain tissue was processed for staining against a cell proliferation marker, Ki67, for histological confirmation. The correlations between the DTI and Ki67 index were examined by Pearson's test.

Results and conclusions:

DTI results showed that water diffusion in the dentate gyrus appeared to be more anisotropic in response to bFGF-induced (Figure 1A, and 1B) or MCAO-induce neurogenesis (Figure 2A, and 2B). Moreover, metrics representing diffusion tensor shapes including CP and CS were significantly altered by neurogenesis in both conditions of treatments. Water diffusion of the dentate gyrus appeared as a more planar (indicated by the CP index) motion yet less spherical (indicated by the CS index) (Figure 1C, 1D, and 1E and Figure 2C, 2D, and 2E). No significant differences in the CL index were observed following either bFGF or MCAO. There was a statistically significant correlation between FA and Ki67 counts in both bFGF-induced (Figure 1F) and MCAO-induced neurogenesis (Figure 2F). The findings altogether indicate that hippocampal neurogenesis may be visualized noninvasively by DTI. The CP index is particularly sensitive at detecting the effects associated with neurogenesis. The results also demonstrate the sensitivity of DTI in detecting subtle neural activity such as neurogenesis.

Figure 1.

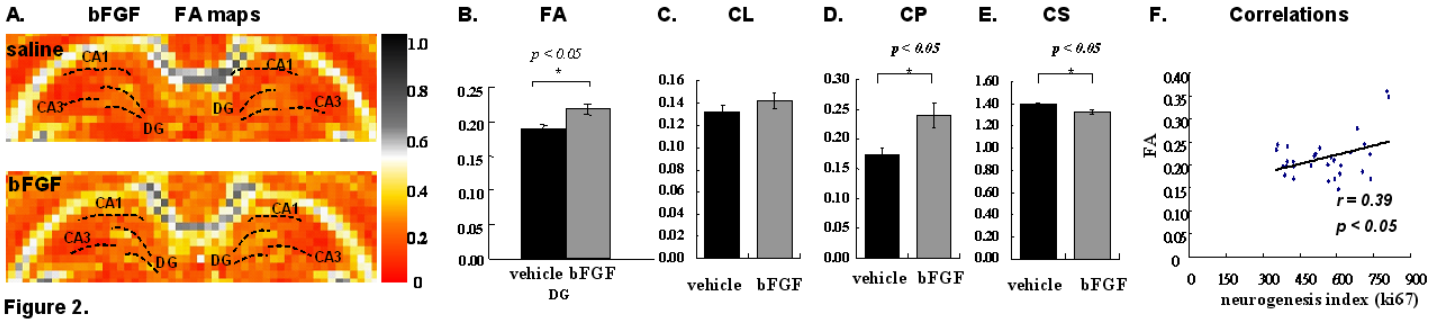
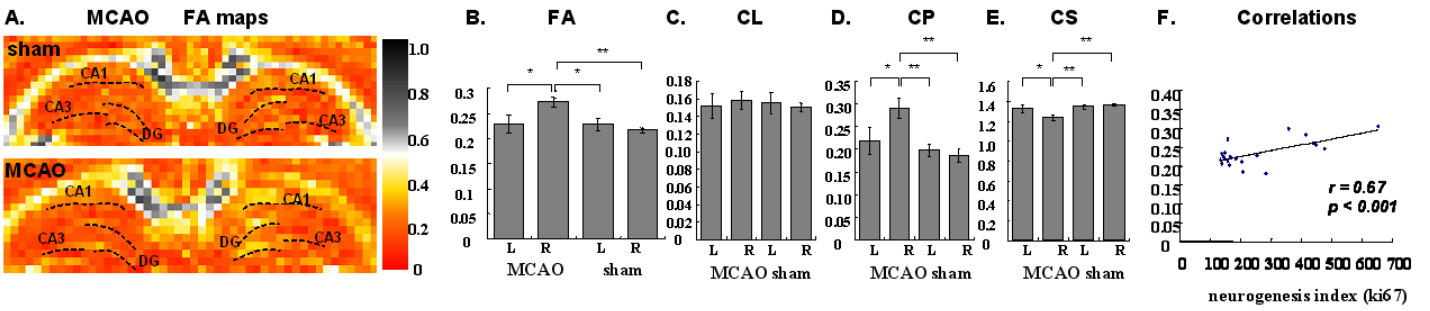


Figure 2.



References: Pereira et al., 2007. Proc Natl Acad Sci U S A. 104,5638-43.