Probing Neural Structure Using Diffusion Spectrum Imaging and Temporal Diffusion Spectroscopy

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Introduction

Diffusion MRI is a technique for studying various aspects of microscopic tissue composition and organization in the central nervous system (CNS). The diffusion time is a key parameter to determine restricted diffusion in microstructures and hence the sensitivity of diffusion MRI to different spatial dimensions. However, it is not straightforward to implement pulsed gradient spin echo (PGSE) diffusion experiments with short diffusion times that are needed to highlight structures at microscopic scales. One alternative is to use oscillating gradient spin echo (OGSE) or the so-called temporal diffusion spectroscopy, which allows short diffusion time better than PGSE sequence, to provide a unique way to measure water diffusion [1-3].

Diffusion spectrum imaging (DSI) is one of the diffusion MRI techniques that can map complex fiber architecture in the brain [4]. We sought to apply OGSE DSI to identify minuscule neuroarchitecture in the brain. By applying oscillating diffusion-sensitive magnetic gradients to tag translational motion of water molecules, 3D probability density function (PDF) of molecular displacement can be reconstructed from the measured OGSE DSI data. For comparison, diffusion tensor images (DTI) of the rat brain were acquired using the OGSE and PGSE sequences. We demonstrate DSI maps with oscillating gradient revealed novel tissue contrast in the rat hippocampus.

Materials and Methods

This study was approved by the local Institutional Animal Care and Use Committee. Male Wistar rats (300-350g) were used for ex vivo MRI. The rat brains were fixed by transcardiac perfusion of 4% paraformaldehyde (PFA) in phosphate buffered saline (PBS) and immersed in 4% PFA in PBS for 24h at 4^{o}C. Imaging was performed on a Varian 9.4T scanner equipped with a gradient system of maximum gradient strength = 40 G/cm and rise time of 135μs. A 25-mm inner diameter volume coil was used for radio frequency transmission and reception. Images of OGSE DSI were acquired with an oscillating gradient spin echo sequence with frequence = 34.3 Hz, in-plane resolution of 200 μm, slice thickness of 1 mm, TR/TE = 2200/70 ms. The diffusion-encoding scheme constituted 123 diffusion-encoding directions with effective b values changing from 0 to 25,975 s/mm^2. The effective diffusion time was calculated to be 10.93 ms. For PGSE DTI, diffsuion attenuated images with Δ / δ = 12.72/3 ms, 30 diffusion-encoding directions, and b value of 1,200 s/mm^2 were acquired with the same resolution and TR/TE = 2200/23 ms in 2.4 h. The total scan time was about 13 h.

For data analysis, zero filling interpolation was applied in inplane dimensions and Gaussian smoothing (FWHM = 2 pixels) was used. OGSE DSI and OGSE DTI were reconstructed from DSI dataset, and PGSE DTI was calculated from DTI dataset. To quantify the diffusion anisotropy of probability density function, generalized fractional anisotropy (GFA), isoradius indices were used for DSI [5] and fractional anisotropy (FA), apparent diffusion coefficient (ADC) indices were used for DTI.

Results and Discussions

Apparently the largest fiber bundles like corpus callosum, internal capsule -- except fimbria -- were not seen in DSI with oscillating gradient (Fig. 1a-c) while all were visible in both OGSE DTI (Fig. 1d-f) and PGSE DTI (Fig. 1g-i). This may be due to difference in fiber size/density or the way GFA was calculated. The structures in hippocampus were particularly enhanced in oscillating gradient DSI (Fig. 2a) or DTI (Fig. 2b). The ADC of hippocampus in OGSE DTI (4.66 x 10^{-4} mm^2/s) (Fig. 1f) was higher than it in PGSE DTI (1.49 x 10^{-4} mm^2/s) (Fig. 1i). It suggested larger dimension than OGSE diffusion distance, while high anisotropy could still be seen by OGSE DSI (Fig. 1a) that may be related to fiber organization of different cellular layers.

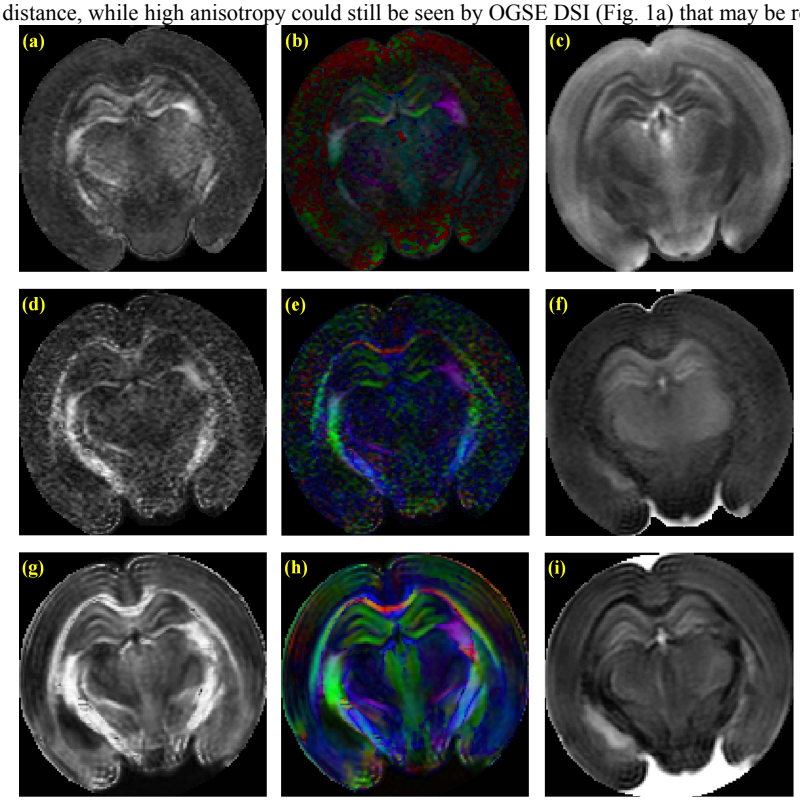

Fig. 1 (a) GFA, (b) color GFA, and (c) isoradius of OGSE DSI. (d) FA, (e) color FA, and (f) ADC of OGSE DTI. (g) FA, (h) color FA, and (i) ADC of PGSE DTI.

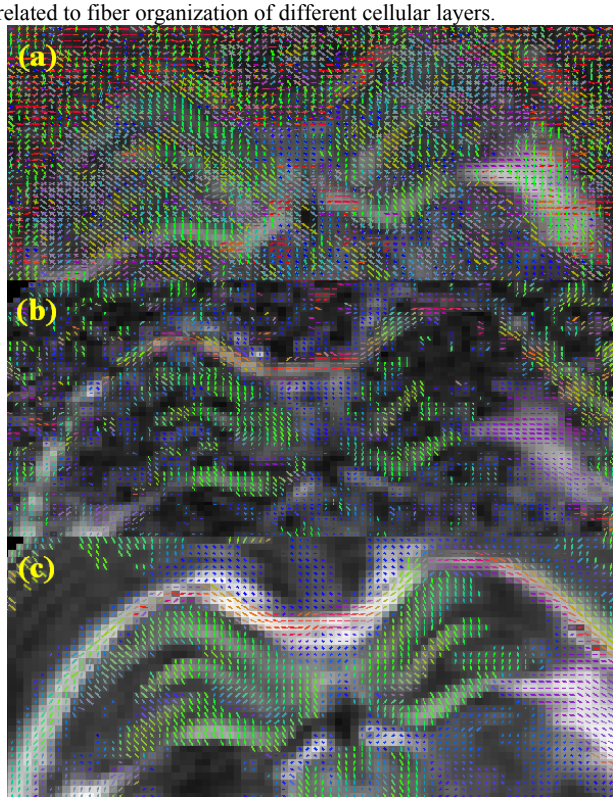

Fig. 2 (a) Max three vectors of OGSE DSI superimpose with GFA. (b) 1st eigen vector of OGSE DTI superimpose with FA. (c) 1st eigen vector of PGSE DTI superimpose with FA.

Conclusions

We have demonstrated that DSI with oscillating gradient revealed novel tissue contrast in the rat hippocampus. Combining both diffusion spectrum imaging and temporal diffusion spectroscopy techniques allows investigation of derangement involving both cellular and fibrous structures of the hippocampus. This may help to differentiate minor changes in neural plasticity and neurodegeneration.

References

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