Double-Pulsed-Field-Gradient MRI at long mixing time of global hypoxia

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Introduction: Diffusion weighted MRI (DWI) and diffusion tensor imaging (DTI), have been extensively used to study different neuropathologies, brain connectivity and neuronal development [1]. However, the most frequently used parameters extracted from DWI and DTI i.e. the apparent diffusion coefficient (ADC), the fractional anisotropy (FA) and the mean diffusivity (MD), have limited sensitivity to structural changes and also have a limited specificity [1]. Therefore there is a constant need to develop new methods that have the potential of providing more specific indices. In recent years, methods which were all collectively termed as "beyond the tensor" methods, are gaining more importance [2]. Recently, the angular double-pulsed-field-gradient (d-PFG) MR technique, which was first proposed by Mitra [3], is attracting more attention in the context of neuroimaging [4-5]. It has been demonstrated that d-PFG MR, and more importantly d-PFG MRI methods enable obtaining microstructural information also in systems characterized by macroscopic isotropy, such as the grey matter of the CNS [6-7]. This implies that d-PFG MRI provides additional indices that may provide a means to follow, more specifically, microstructural changes and different neuropathologies. The apparent eccentricity, extracted from d-PFG MRI at long mixing times, seems to be such an index. However to better understand the dependency of these d-PFG MRI indices in different pathologies and fully exploit them in future work more information regarding these d-PFG indices is needed .

Objectives: To study the effect of global hypoxia (GH) on the indices extracted from angular d-PFG MRI, at a long mixing time, and to compare them with the changes observed in FA and MD obtained from DTI.

Methods: MRI experiments were conducted on a 7-T Biospec scanner equipped with a gradient system capable of producing pulsed field gradients of 400 mT/m. Four male rats were scanned before (for 150 minutes) and after sacrifice (for 220 minutes) which occurred by increasing the isoflurane doze (from 2% to 5%). Angular d-PGSE experiments were performed twice before the global hypoxia (GH) and twice after death while the DTI protocol was performed twice before and three times after death.

The field of view (FOV) of all MR images was 2.56 × 2.56 cm and was collected with a 128 × 128 matrix, resulting in an in-plane spatial resolution of 200 × 200 μm^2. Three axial slices were acquired with a slice thickness of 1.5 mm (3mm inter-slice gap).

The d-PGSE echo-planar MRI experiments were conducted in the xy plane with 9 φ values between 0° and 360° with the following parameters: $\delta_1 = \delta_2 = 3.5$ ms, $\Delta_1 = \Delta_2 = 17$ ms, $t_m = 5$ ms and $|G_1| = |G_2| = 320$ mT/m, resulting in a 2q-value of 954 cm^{-1}. A TR/TE of 3000/61 ms was used and the number of averages was 20.

The DTI experiments were collected with a spin-echo diffusion EPI sequence with 15 non-collinear directions and the following parameters: δ = 3.5 ms, Δ = 17 ms and $|G|$ = 320 mT/m, resulting in the b value of 1194 s/mm^2.The TR/TE were set to 3000/35 ms and 10 averages were collected. DTI images were analyzed using the ExploreDTI tool in Matlab®.

Results and Discussion: Figure 1 shows representative images of absolute apparent eccentricity (abs aE), fractional anisotropy (FA) and mean diffusivity (MD) maps extracted from angular d-PGSE MRI and DTI experiments performed on the same rat. Figure 1 shows that the MD decreases, as expected, after GH while the behavior of the FA and abs aE and is region and tissue dependent. To gain more detailed information we analyzed a few specific regions of interest (ROIs, see Figure 1 for ROIs definition).

Figure 2A and 2B show the plots of the normalized E(φ) signal in both ROIs before and after GH. In ROI 1 (Figure 2A), different oscillations of the normalized E(φ) signal are observed before and after death. A slight asymmetry in the graphs might be a result of a small tilt angle compared to the main axis of the compartment. The oscillations in the hippocampal ROI (ROI 2) are shown in the Figure 2B, however are similar before and after death.

Figure 2C and 2D present the time course of the absolute aE (abs aE), FA and MD values in the internal capsule (ROI 1, a yellow rectangle) and hippocampus (ROI 2, red ellipse), respectively, before and after global hypoxia. We observe a decrease in the MD in both ROIs following death as one can expect from cytotoxic edema. The FA values in both ROIs significantly increase after death. For the absolute aE, obtained from the d-PFG MRI, we observe a significant reduction in ROI 1, however the aE remains almost without change in the hippocampal region (ROI 2).

Conclusions: The results suggest that different microstructural information can be extracted from angular d-PGSE MRI as compared to DTI experiments.

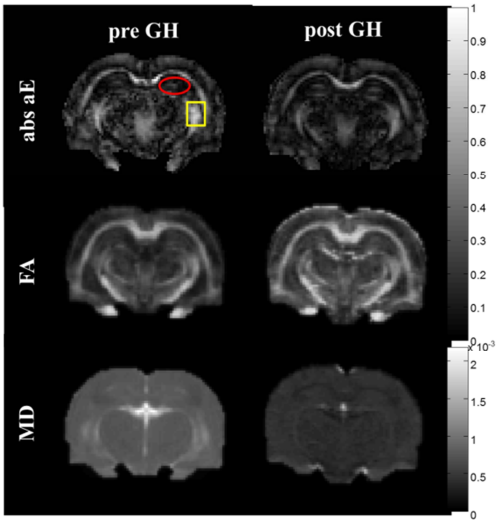

Figure 1: Apparent eccentricity (aE), fractional anisotropy (FA) and mean diffusivity (MD, [mm^2/s]) maps before and after GH (postmortem). The analysed ROIs are depicted on the abs aE image.

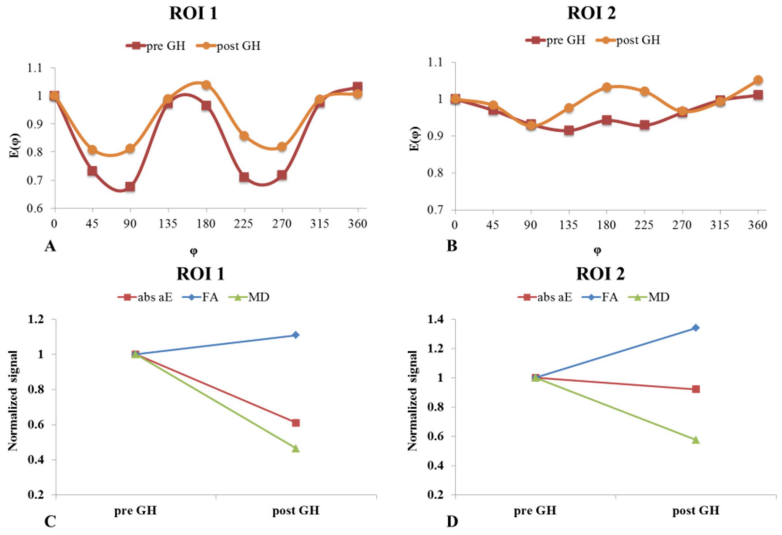

Figure 2: (A-B) The plots of the normalized E(φ) signal before and after GH and **(C-D)** the time course of absolute aE (abs aE), FA and MD values in two different ROIs before and after GH (postmortem).

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