High resolution OGSE DTI of ex vivo mouse brain to investigate the frequency-dependence of the apparent diffusion tensor in cerebellar white matter

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Introduction: In the past few years oscillating gradient spin-echo diffusion-tensor imaging (OGSE DTI) has been applied to measure changes to the apparent diffusion tensor (ADT) of brain tissue as a function of the frequency of the motion-probing gradients (MPGs) [1-4]. Most of these studies have been performed on ex vivo brain tissue (mouse [1], monkey [3] and human[4]) with just the one study of in vivo rat brain [2]. The study of ex vivo mouse brain was the first to demonstrate that increasing the MPG frequency strongly enhanced the mean diffusivity (MD) in the cerebellar granule cell layer (CBGr) of the cerebellum. There was also a much weaker increase for the cerebellar molecular layer (CBML). However, no data was presented for the cerebellar white matter (CBWM), which is odd because investigating the diffusion characteristics of white matter is one of the most prominent activities of diffusion-weighted MRI. The present study was performed to address this omission and report the first quantitative OGSE DTI measurements for mouse CBWM.

Methods: Three C57BL/6 mice (8 week old males, 25 gm) were euthanised and the brain was fixed by transcardiac perfusion with 4% paraformaldehyde in phosphate-buffered saline. The brain was then removed from the skull and stored in the fixation solution at 4°C for 3 months. In preparation for MR imaging, the brain was placed in a 5 ml syringe with fresh fixation solution. MRI data were acquired on a 7 T, 20 cm bore magnet equipped with a standard gradient system (Bruker BGA12S2, G_{max} = 450 mT/m) and interfaced to an Avance III imaging system (Bruker-Biospin, Germany). A high-sensitivity 2-channel RF surface coil (Cryoprobe^{TM}, Bruker-Biospin) was used for both transmit and receive. Sample position and RF pulse power were adjusted to maximise the signal from the cerebellum. OGSE DTI was performed with a protocol similar to that described in [2]. Two 0.4 mm thick sagittal slices centred at 0.4 and 1 mm away from the midplane of the brain were selected for imaging. The parameters for the oscillating MPGs were: MPG duration = 30 ms, b = 500 s/mm^2 and MPG frequencies of f = 33.3, 66.6, 100 and 133.3 Hz for 36 evenly distributed MPG directions. Other imaging parameters were TE = 80 ms, TR = 1000 ms, matrix size = 512 × 256, FOV = 25.6 mm × 12.8 mm. OGSE DTI scanning time was near to 13.5 hours. Offline reconstruction and analysis of the data was performed with the same procedures and purpose-written Matlab code as used in [2]. No spatial or temporal smoothing was applied at any stage during the analysis.

Results: Figure 1 presents typical OGSE DTI maps of the mean diffusivity (MD) as a function of MPG frequency. Pixelwise linear fits ($MD = \alpha_{MD} f + \beta_{MD}$) to the data were performed to create high quality α_{MD} maps that highlight those regions where the strongest changes to the MD occur. As expected, the tissue with the strongest positive change probably corresponds to the CBGr. It is also clear from inspection that the changes to the CBWM MD are much less abrupt. Although the images are not shown here, a similar analysis was performed to estimate the rate of change of the fractional anisotropy (FA) with MPG frequency (α_{FA}). Guided by the patterns apparent on the T2w images and the α_{MD} maps, CBWM, CBGr and CBML ROIs were drawn either side of the primary fissure. The values of α_{MD} within the CBML and CBGr ROIs are reasonably consistent with those reported in [1], but the significantly negative value for the CBWM is surprising (Table 1). For the CBGr α_{FA} was significantly less than zero, but the FAs of the CBML and CBWM were not substantially altered.

Parameter	ROI	Present study	[1]
α_{MD} (μm^2)	CBML	0.47 ± 0.05	0.56
	CBGr	2.92 ± 0.06	3.60
	CBWM	-0.65 ± 0.14	
α_{FA} (kHz^{-1})	CBML	0.19 ± 0.15	-0.3
	CBGr	-1.26 ± 0.13	-0.6
	CBWM	0.37 ± 0.20	

Table 1. $\boldsymbol{\alpha_{MD}}$ and α_{FA} for each ROI compared to values estimated from Fig. 3 and Table 2 of

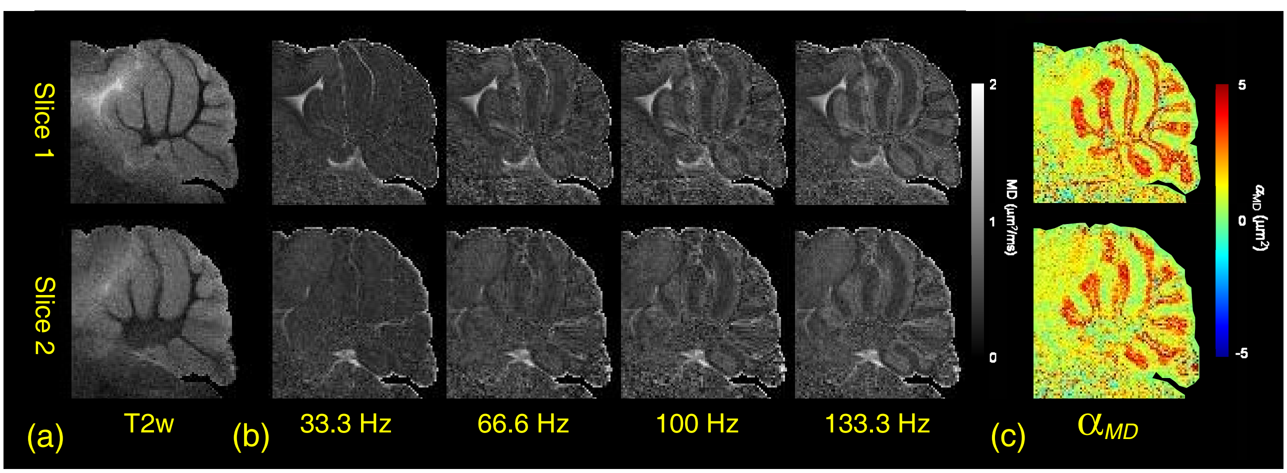

Fig 1: (a) T2-weighted images. **(b)** MD at each MPG frequency calculated from the OGSE DTI data. **(c)** α_{MD} estimated from a linear fit to the MD wrt MPG frequency.

Discussion: The cryogenically-cooled coil used for the present experiments improved the signal-to-noise sufficiently so that it was possible to image at a higher spatial resolution (0.05×0.05×0.4 mm^3) than that achieved in [1] (0.078×0.078×1 mm^3). Also, instead of a single, relatively thick midsaggital slice, the present experiments imaged two much thinner slices laterally displaced 0.4 and 1 mm away from the midsaggital plane. While the contrast in the first slice is similar to that in the midsaggital plane, the second slice contains a relatively broad white-matter-rich region around the medial cerebellar nucleus. The changes to the MD of white matter are much less abrupt than those in the surrounding granule cell layer.

References: [1] Aggarwal et al, MRM 67:98-109 (2012); [2] Kershaw et al, NeuroImage 70:10-20 (2013); [3] Lundell et al, Proc ISMRM, 2073 (2013); [4] Aggarwal et al, Proc ISMRM, 838 (2013).