Neurodevelopmental studies in C57B/L6 mice assessed by in vivo DTI

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INTRODUCTION

DTI is a noninvasive imaging technique which offers a unique window into neurodevelopment studies in transgenics or mutants. Understanding early brain development in mice is very important since several models are used to mimic a multitude of neurological disorders which manifest through development. Prior *in vitro* mouse brain DTI studies at high magnetic fields [1-3] that have revealed tissue anisotropy variations (e.g., Bcl-x knock-out or myelin-deficient shiverer mutant) were mainly conducted in fixed brain with DTI signal acquisitions requiring several hours to a day. The purpose of this work is to assess the feasibility of *in vivo* DTI with high angular resolution at high magnetic field and quantify the overall growth and maturation of microstructures in normal mouse brain from P15 to P45.

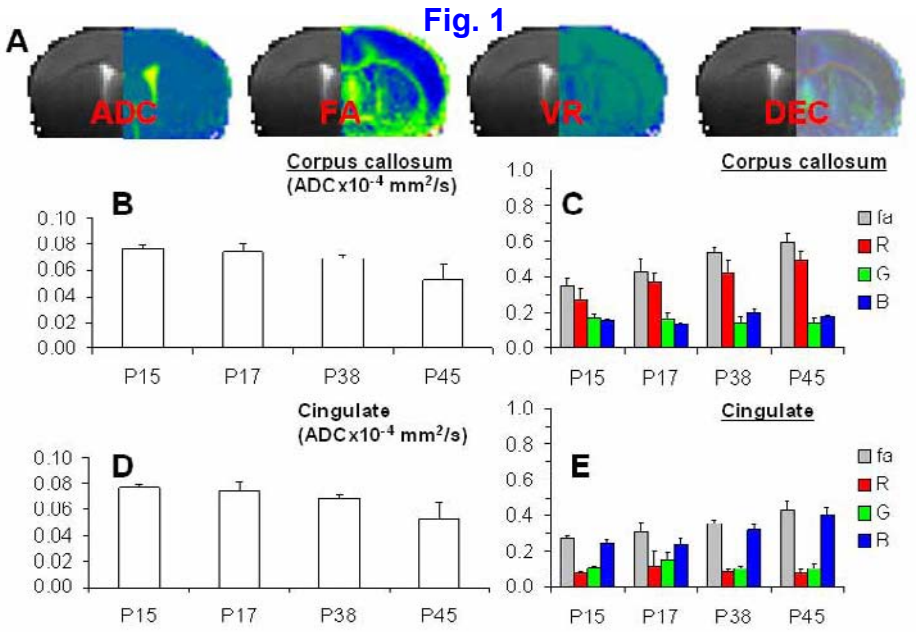
MATERIALS and METHODS

Normal C57B/L6 mice, from P15 to P45, were anesthetized with urethane (1 g/kg) and MRI experiments were performed on a 9.4T Bruker horizontal-bore system with custom-made surface coils. The animals were kept warm by a hot water blanket and whenever possible, blood samples were removed at the end of the experiment to verify physiology. DTI experiments were performed using a modified Stejskal-Tanner spin-echo diffusion-weighted sequence = 5 ms; Δ = 8 ms; TR/TE = 1000/18; NEX = 2; matrix = 128×128; FOV = 20×20 mm; slice thickness = 0.25 mm. Diffusion weighting (b ≈ 1000 s/mm^2) in 15 different directions were acquired with one reference image (b ≈ 0 s/mm^2). Maps of mean diffusivity (ADC), fractional anisotropy (FA), and volume ratio (VR) were calculated, and from which the primary eigenvectors were used to calculate diffusion encoded color (DEC) maps [4]. These data were used to generate trajectory maps in dominant coordinates: medial-lateral, dorsal-ventral, and anterior-posterior. Four regions were examined: cingulate, corpus callosum, forelimb cortex, and whisker barrel field.

RESULTS and DISCUSSION

The brain regions quantified by the current *in vivo* DTI studies through development (P15 to P45) showed some morphological changes (Fig. 1A). In the corpus callosum, the ADC decreased slightly with age (0.08×10^{-4} to 0.06×10^{-4} mm^2/s; Fig. 1B), the FA gradually increased with age (0.34± 0.04 to 0.59±0.04; Fig. 1C) which implied maturation of medial-lateral fibers (R^2=0.989) with marginal or no significant changes in anterior-posterior or dorsal-ventral fibers. The high FA value in corpus callosum in early age may be attributed to tightly packed axons that allow water diffusion primarily along the fiber direction as well as the myelination of axons. In the cingulate, the ADC values decreased slightly with age ($0.07.10^{-4}$ to $0.05.\ 10^{-4}$ mm^2/s; Fig. 1D), the FA increased with age (0.26±0.04 to 0.42±0.04; Fig. 1E), which implied maturation of anterior-posterior fibers (R^2=0.795) with marginal or no significant changes in medial-lateral or dorsal-ventral fibers. The high FA value in the cingulated may be attributed to glial morphological changes. In the forelimb and whisker barrel areas, no significant differences observed over development (data not shown). Since we used mice starting at P15 and these two regions change rapidly during the first postnatal week and stabilize afterwards, localized changes in these somatosensory areas may have to be studied at earlier stages in development (i.e., before P10).

Fig. 1



CONCLUSION

Our results shows that in *vivo* high angular resolution DTI at high magnetic field (>9.4T) allowed detection and quantification of brain structures through normal development in C57B/L6 mice. Differences in DTI parameters (e.g., FA, ADC) were observed mainly in white matter pathways, but other regions also showed some potential morphological changes.

REFERENCES

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