Diffusion Tensor Imaging at 11Tesla in IFNγ Overexpressing Mice

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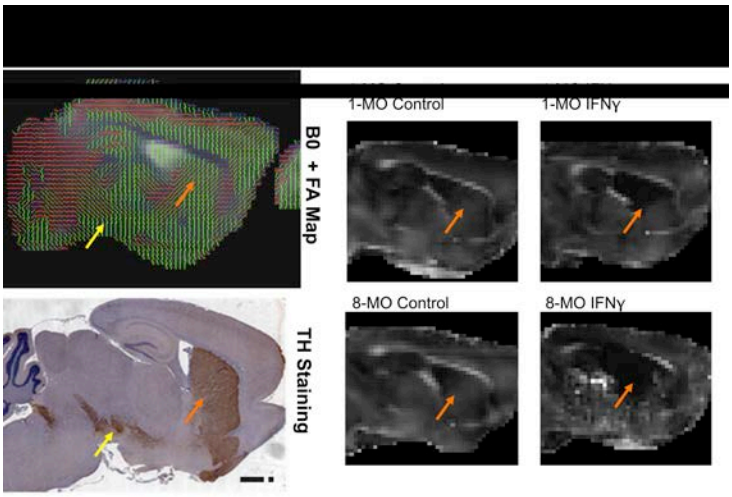
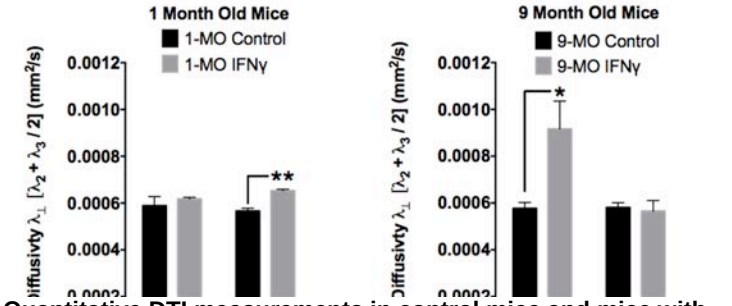
Introduction

We have found that recombinant adeno-associated virus mediated, choroid-targeted, expression of mouse interferon-g (IFN-g) induces robust, progressive, selective nigrostriatal degeneration, locomotor impairment and midbrain calcinosis [1], associated with symptoms characterized by progressive Parkinsonism. High field MR imaging methods to screen pathological changes in mice with genetic mutations provides a key step forward in understanding the gradual progression of neurodegenerative diseases.

Experimental

IFNg overexpressing mice and control background strains (6-7 months old; 23-24g) were anesthetized and maintained under 1.25-1.5% isoflurane and prepared for diffusion imaging at 11.1Tesla. Imaging was carried out using a transmit/receive surface coil. Images were collected using a diffusion weighted spin echo EPI sequence with 42 directions (Agilent Technologies) and the following parameters: field of view (FOV) 25mm^2, 6 slices, 0.75 mm slice thickness, TR=2seconds, TE=38ms, NEX = 4, amplitude 18.47G/cm, delta=6ms with 12ms separation between pulses, and maximum b-value = 900s/mm^2.





Quantitative DTI measurements in control mice and mice with neurodegeneration as a result of midbrain interferon gamma IFNγ overexpression.

Results and Discussion

Our preliminary findings appear to support significant changes in various diffusion-weighted parameters. We observed reduced FA in the corpus callosum of IFNg mice that seemed mostly associated with increased radial diffusivity (IFNg= 0.8mm^2, control= 0.58mm^2). Other ROI such as hypothalamus, septum and striatum showed greater FA index values in IFNg mice. The ongoing experiments will provide new findings on the role of IFNg on *in vivo* pathological markers relevant to midbrain specific neurodegeneration.

Conclusions

We demonstrate the feasibility of carrying out in vivo diffusion weighted imaging at 11Tesla. At 1 months of age, values for axial and radial (and mean diffusivity; not shown here) is higher in the midbrain IFN$_\Upsilon$ mice than in controls. At 8 months, there are clear and dramatic differences in various DTI parameters between control and IFN$_\Upsilon$ mice. These were observed in striatum, thalamus and white matter regions (splenium and genu).

Acknowledgements

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References

[1] Chakrabarty *et al.,* Nat Neurosci. 14(6): 694-6, 2011.
[2] Chakrabarty *et al.,* Society for Neuroscience Abstracts (2012).