



## Free-water improves detection of changes in the substantia nigra in Parkinsonism: A multi-site study

Ofori, E. (Univ. of Florida, Applied Physiology); Krismer, F. (Penn State Univ., Neurosurgery); Burciu, R.G. (Univ. of Florida, Applied Physiology); Pasternak, O. (Harvard Univ. Psychiatry); McCracken, J.L. (Univ. of Florida, Applied Physiology); Lewis, M.D., Du, G., McFarland, N.R., Okun, M.S. (Univ. of Florida, Neurology); Poewe, W., Mueller, C., Gizewski, E.R., Schocke, M., Kremser, C. (Medical Univ. Innsbruck; Neuroradiology); Li, H. (Medical Col. South Carolina, Public Health); Huang, X. (Penn State Univ. Neurology); Seppi, K. (Medical Univ. Innsbruck, Neurology); Vaillancourt, D.E. (Univ. of Florida, Applied Physiology)

### Introduction

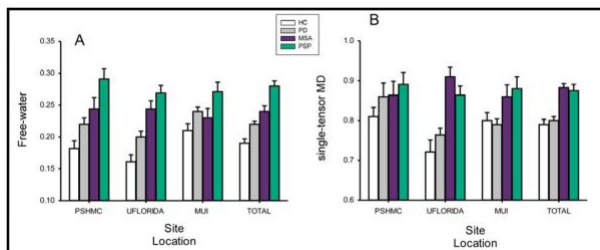
Imaging markers that are sensitive to parkinsonism across multiple sites are critically needed for clinical trials. Loss of dopaminergic neurons in the substantia nigra is common to several forms of parkinsonism, including Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP) [1-3]. The goal of the current study was to study changes in the substantia nigra using single- and bi-tensor models of diffusion magnetic resonance imaging in PD, MSA, and PSP. We tested the following two hypotheses: 1) free-water in the substantia nigra will be elevated in the substantia nigra of Parkinsonism across sites, and 2) free-water in the posterior substantia nigra estimated with a bi-tensor model correlates with clinical symptoms across sites.

### Experimental

The study cohort (N=425) included 107 healthy controls, 184 PD, 63 MSA, and 71 PSP patients from 3 movement disorder centers. Bi-tensor free-water, free-water corrected fractional anisotropy, free-water corrected mean diffusivity, single-tensor fractional anisotropy and single-tensor mean diffusivity were computed for anterior and posterior substantia nigra. Correlations were computed between diffusion MRI measures and clinical measures.

### Results and Discussion

In the posterior substantia nigra, free-water was greater for PSP than MSA, PD, and controls. PD and MSA both had greater free-water than controls. Free-water corrected fractional anisotropy values were greater for PSP when compared to controls and PD. PSP and MSA single-tensor mean diffusivity values were greater than controls and single-tensor fractional anisotropy values were lower for PSP than healthy controls. The parkinsonism effect size for free-water in the posterior substantia nigra was 0.145 and for single-tensor mean diffusivity was 0.072. The direction of correlations between single-tensor mean diffusivity and free-water values and clinical scores were similar at each site.



**Fig.1** Free-water and single-tensor mean diffusivity across sites. The bar graphs indicate the levels of free-water and single-tensor mean diffusivity for healthy controls, Parkinson's disease (PD), multiple systems atrophy (MSA), and progressive supranuclear palsy (PSP) subjects across all sites and within each site.

### Conclusions

Free-water values in the posterior substantia nigra provide consistent pattern of findings across PD, MSA and PSP in a large cohort across three sites. Free-water in the posterior substantia nigra relates to clinical measures of motor and cognitive symptoms in a large cohort of parkinsonism.

### Acknowledgements

A portion of this work was performed at the National High Magnetic Field Laboratory, which is supported by National Science Foundation Cooperative Agreement No. DMR-1157490 and the State of Florida. This study was funded by the National Institutes of Health (RO1 NS52318, ROI NS75012, T32 NS082169).

### References

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