Abnormal white matter integrity of striato-thalamic structures in children with Tourette Syndrome.

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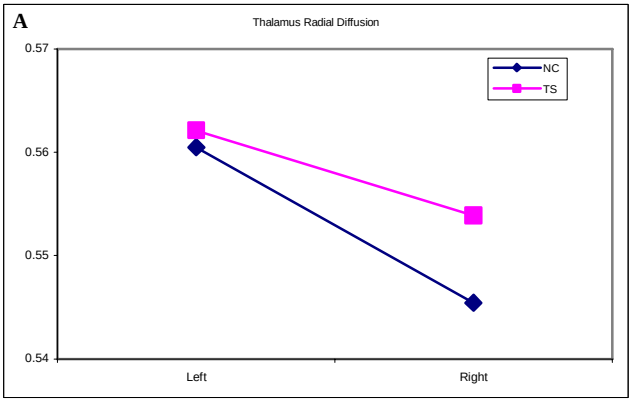
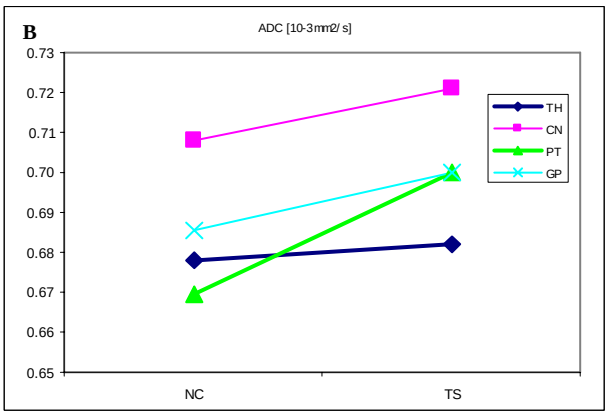
Introduction: Current theories of TS assume that tics are associated with an imbalance or disturbance of the FST circuit [1-4]. This notion is supported by neuroimaging studies, which have found structural and functional abnormality in basal ganglia and thalamus of TS subjects [5,6]. However, there has been relatively little direct investigation of white matter integrity of this circuit in TS. Using DTI, we investigated the structural integrity of basal ganglia and thalamic components of the FST white matter circuit in children with TS as compared to age-matched healthy controls. Additionally, we examined the association of white matter integrity of basal ganglia and thalamus to tic severity (tics) and comorbid OCD symptoms. We hypothesized that TS may be associated with specific white matter abnormalities in the lentiform nuclei, thalamus, and caudate nucleus, and that individuals with TS will show decreased FA and increased ADC in fiber bundles of FST projections as compared to healthy controls.

Material and Methods: Twenty-three children with TS, mean age = 11.75 ± 3.25 years, (19 females, 4 males) and 35 age matched typically developing children (NC), mean age = 13.1 ± 3.17 years, (17 males, 18 females) underwent DTI with 6 diffusion sensitization gradients in addition to standard T1W, T2W and FLAIR sequences. For DTI indices, manual structural delineation was achieved by 2 observers to measure parallel (λ_1), averaged perpendicular (λ_{23}) diffusions, apparent diffusion coefficient (ADC) and fractional anisotropy (FA) of each structure in both hemispheres, using DTIstudio software (H. Jiang and S. Mori; Johns Hopkins University; http://cmrm.med.jhmi.edu). Between group differences were tested via separate 2 (group) x 2 (side) x 4 (structure) mixed-model ANCOVAs. Assessment of tics involved administration of the Tic Symptom Self-Report measure (TSSR) [7], where the total motor and vocal scores are combined into an overall tic severity score which was used as the index of tic severity for the present study. Obsessive-compulsive symptoms were assessed via a semi-structured interview described by the Children's Yale-Brown Obsessive Compulsive Scale [7] that assesses the severity of obsessions and compulsions.

Results: The TS group showed a significant increase in λ_1 *(p=0.003)* and *ADC (p=0.027)* in the bilateral putamen (figure 1B) and an increase in λ_{23} in the right thalamus *(p=0.008)* as compared to controls (Figure 1A). The TS group also showed a reversed asymmetry in FA *(p=0.03)* in the thalamus as compared to controls (Figure 1C). We observed a significant positive correlation between λ_{23} in the right thalamus with tic severity *(p=0.03),* and a significant negative correlation between FA of the right globus-pallidus and tic severity *(p=0.019).*





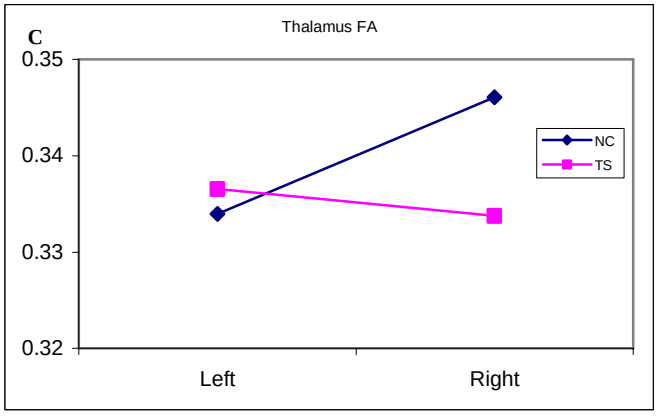


Figure 1: Plots illustrating (A) increased λ_{23} in the right thalamus; (B) significant bilateral increase in ADC in the putamen of TS patients; and (C) reversed asymmetry of thalamic FA of TS patients vs normal control (NC). NC = healthy control group, TH = Thalamus, CN = Caudate nucleus, PT = Putamen, GP = globus pallidus

Conclusion: Our findings represent the first direct evidence for abnormal white matter integrity within the FST circuit. Furthermore, abnormality in the FST was correlated with tic severity. Future studies will focus on tractography of the various segments of the FST pathway.

Reference: [1], Gerard and Peterson. J Psychosomatic Res 55 (2003) 13– 22; [2] Groenewegen HJ, Neural Plast. 2003;10(1-2):107-20., 2003, [3] Singer and Minzer, Brain Dev. 2003 Dec;25 Suppl 1:S70-84; [4] Berardelli A, et al., J Neurol. 2003 Jul;250(7):781; [5] Peterson BS and Leckmann JF; Biol Psychiatry. 1998 Dec 15;44(12):1337-48; [6] Leckman et al., Life Sci. 1988;43(24):2015-23. [7] Scahill L et al., J Am Acad Child Adolesc Psychiatry. 1997 Jun;36(6):844-52.

Acknowledgment: We would like to thank Rosalie and Bruce Rosen for their generous support of this research.