# Transverse relaxation rime abnormalities of the basal ganglia in Tourette syndrome

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*Introduction:* Tourette syndrome (TS) is a neuropsychiatric disorder characterized by the childhood onset of vocal and motor tics that fluctuate in severity and frequency. Though the specific physiological abnormalities underlying the disorder are unknown, research studies have implicated abnormalities of cortico-striato-thalamo-cortical (CSTC) circuits, which connect the basal ganglia and related thalamic and cortical structures (1). While several neuroimaging studies have reported abnormalities of components of CSTC circuits in TS (2), the underlying tissue abnormalities remain unknown. One method to examine tissue abnormalities *in vivo* is quantitative transverse relaxation time (T2) imaging. T2 is influenced by the molecular environment and tissue properties, particularly tissue water content, with increased T2 usually reflecting increased tissue water. The only published study using T2 imaging to investigate TS reported abnormal T2 asymmetry of the caudate nucleus and frontal white matter in adults with TS (3). The purpose of this study was to quantitatively evaluate T2 relaxation times of CSTC components in a group of children and adolescents with TS.

*Methods:* Twenty-two males with TS between the ages of 6 and 16 (mean: 10.8±2.4 years) and 23 male controls between ages 6 and 16 years (mean: 11.0±2.8 years) participated in this study. The diagnosis was made according to DSM-IV-TR criteria using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS). Control subjects were drawn from the local community and were assessed using the K-SADS to rule out psychiatric illnesses. The groups did not differ significantly in age, sex, race, or handedness, although patients did have lower full-scale IQ's ($p$=0.02). Six patients were medication-naive at the time of their scan, while four others had discontinued their medication prior to the scan. The remaining patients were being treated with stimulants (n=3), dopamine antagonists (n=6), and antidepressants (n=2). Thirteen patients required sedation with either oral midazolam (n=4) or chloral hydrate (n=9) in order to complete their scan.

Magnetic resonance imaging data were acquired on a 3T magnetic resonance scanner with a quadrature head coil. T2 data was acquired using a Gradient Echo Sampling of the Free Induction Decay and Echo (GESFIDE) sequence (TR=2800ms; matrix size=192x256; FOV=220mm; slice thickness=4mm with 1.5mm gaps for 22 slices; resolution=1.15x0.86x4mm; total scan time=9min). Five gradient echoes were acquired prior to the 180º radio frequency (rf) pulse, with a first-echo time of 9 msec and an inter-echo spacing of 8.70 msec. Six gradient echoes were acquired after the 180º rf pulse, each spaced by 8.78 msec. The k-space data was then reconstructed into R2* and R2- maps by performing a voxel-by-voxel least-squares fit of the natural logarithm of the signal amplitude versus echo time. R2 maps (1/T2 maps) were calculated from R2 = (R2* + R2-)/2.

Using SPM2, each subject's T2 weighted image was spatially normalized to the adult T2 template (icmb-152, Montreal Neurological Institute) using a 12 parameter affine registration, followed by an iterative non-linear global registration to account for inter-subject low frequency shape differences. The calculated transformation parameters were then applied to the subject's respective R2 map, yielding a volume of R2 values approximating Talairach space. Masks for each region of interest (caudate nucleus, putamen, globus pallidus, substantia nigra, subthalamic nucleus, and thalamus) in standard space were generated using the pickatlas toolbox for Matlab (Wake Forest University). Mean T2 values for each region of interest were then calculated by multiplying the normalized R2 maps by these binary masks.

Group differences in T2 of CSTC circuit structures were investigated using a Repeated-Measures Analysis of Covariance (ANCOVA). In the analysis, T2 was the dependent variable, diagnosis (TS or control) was the between-subjects factor, and structure (caudate nucleus, putamen, globus pallidus, substantia nigra, subthalamic nucleus, and thalamus) and side (left and right) were the within-subjects factors. Significant main effects of diagnosis or higher order interactions involving diagnosis ($p$<.05), were examined for each structure and side individually with Analyses of Covariance (ANCOVAs) to identify the region(s) that contributed to the significant main effect or interaction. Although age did not differ significantly between the groups, the age range in this study was wide. Given the changes in T2 described in childhood, we covaried the statistical analysis of T2 for age to reduce error variance and increase statistical power.

*Results:* Table 1 presents the mean T2 in each region assessed. Repeated measures ANCOVA revealed a significant main effect of diagnosis ($p$=0.04). There were no significant interactions involving diagnosis. Post-hoc analyses revealed that patients had an overall increase in caudate T2 ($p$<0.001) as well as an increase in both left ($p$<0.001)and right ($p$=0.01) caudate T2. No other significant group differences were found.

Table 1. Mean transverse relaxation times of the basal ganglia in milliseconds

| Region (white matter) | TS | Control |
|---|---|---|
| Left caudate | 73.5(4.8) | 70.3(3.9) |
| Right caudate | 77.1(5.9) | 74.8(6.5) |
| Left globus pallidus | 56.4(2.3) | 55.8(3.6) |
| Right glovus pallidus | 56.6(2.7) | 55.4(3.4) |
| Left substantia nigra | 65.5(3.3) | 65.7(3.2) |
| Right substantia nigra | 66.3(3.9) | 66.4(3.5) |
| Left putamen | 63.8(2.1) | 63.1(3.3) |
| Right putamen | 61.0(2.5) | 60.2(3.3) |
| Left thalamus | 67.1(2.9) | 66.5(3.0) |
| Right thalamus | 68.2(2.8) | 67.2(2.8) |
| Left subthalamic nucleus | 61.6(2.2) | 61.4(2.4) |
| Right subthalamic nucleus | 63.7(2.3) | 62.5(2.8) |

All data presented as mean (SD).

*Discussion:* Patients with TS in this study had an increase in T2 of the caudate nucleus, with both the left and right sides having increased T2 compared with controls. The interpretation of the results of this study is limited by a small sample size, the absence of female subjects, the use of medication and sedation in some patients and the use of an adult template for the spatial normalization of images. The finding of an increase in T2 of the caudate nucleus, suggesting increased tissue water in the caudate, complements and extends the results of other studies suggesting abnormalities of the caudate nucleus in TS (1,4,5). Future studies designed to more explicitly localize the abnormalities within the caudate will further our understanding of the neurobiological abnormalities involved in TS.

**References:**

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