Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure 1. Thalamus definition. Thalamus definition from a single brain is shown in green in axial, sagittal, and coronal views.
eFigure 2. Age effects. Because of demographic variability between groups, and because morphometric differences in Tourette syndrome (TS) have frequently been found to vary with age, we compared surface morphology across diagnostic groups in children and adults in separate post hoc analyses. Here, right and left hemithalami are shown in rotating views of anterior (A), lateral (L), posterior (P), and medial (M) aspects. Dorsal and ventral views are also shown. Abbreviations are the same as Figure 1. Images to the left of the vertical line show color-coded maps of effect size (ie, mean differences across groups in distance from the surface of the template surface, left 2 columns) and variance (right 2 columns) illustrated at each point on the surface of the template thalamus. The statistical model included age and sex as covariates. Panel A illustrates the entire sample, and panels B and C show children (age ≤ 17 years) and adults (age > 17 years), respectively.

The color bars at the bottom provide the color-coded scaling for effect size (left) and variance (right). The regional patterning of group differences is generally similar across children and adults with TS, particularly in regions where groups differ significantly in surface morphological features (Figure 1). Images to the right of the vertical line display the atlas warped to the template brain. Cytoarchitectonic boundaries are depicted, and each of the 11 defined nuclei is uniquely colored. In panel D, scatter diagrams plot age for each subject against the sex-adjusted distance measures originating from a single surface point. The figure includes scatterplots from 2 surface points, 1 from the right lateral thalamus and 1 from the left lateral thalamus. The selected points are marked by a white circle depicted in the corresponding $P$ value map from Figure 1. The parallel regression lines in each scatterplot are representative of all significant main effects of diagnostic group at the thalamic surface and demonstrate that group differences are similar across the entire age range of study participants. Taken together, all panels of eFigure2 illustrate that lateral and posterolateral thalamic surfaces show comparable enlargement across subgroups of children and adults with TS. NC indicates normal control.
eFigure 2B Diagnosis Main Effect in Youth under 18 years

Effect Size  Variance

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Atlas

Right

- AN
- Ce
- LD
- LGN
- VN
- VA
- MD
- LP
- Pu
- MD
- LD
- LP
- AN
- MD
- VP
- MGN

Left

- AN
- Ce
- LD
- LGN
- VN
- VA
- MD
- LP
- Pu
- MD
- LD
- LP
- AN
- MD
- VP
- MGN
eFigure 2C Diagnosis Main Effect in Adults

Effect Size

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Variance

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Atlas

- AN
- Ce
- LD
- LGN
- MGN
- MD
- LP
- VA
- Pu
- A
- Ce
- VA
- L
- LD
- VP
- P
- M
- MD
- LD
- VP
- MGN
- Pu
eFigure 2D

P-Value

Right Lateral Thalamus

Distance, mm

Age, yrs

NC

TS

Left Lateral Thalamus

Distance, mm

Age, yrs

NC

TS
**eFigure 3.** Effect of comorbid symptom severity in the TS group. The topographic color map demonstrates $P$ values signifying the effect of current comorbid inattention (panel A) and current comorbid hyperactivity (panel B) in the TS group. Panel C demonstrates the effect of current symptom severity as measured by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The statistical model covaries for age and sex. Maps are corrected for multiple comparisons using FDR. Color bar, orientation, and abbreviations are as described in Figure 1. Comorbid attention-deficit/hyperactivity disorder symptoms (panels A-B) in large panel demonstrate deformation of the anterior and medial surfaces of the thalamus, and do not overlap with the effects of TS seen in the lateral thalamus. Similarly, comorbid obsessive-compulsive disorder symptoms (panel C) show varied effects over mainly anterior and medial thalamic surfaces.
eFigure 3

Effect of Symptom Severity

A. Inattention

B. Hyperactivity

C. Y-BOCS

Anterior

Lateral

Posterior

Medial

Dorsal

Ventral

P-Value
**eFigure 4.** Main effect of diagnosis in subsamples of pure TS and medication-free participants. The topographic color maps demonstrate $P$ values signifying the main effect of diagnosis in a subsample of comorbidity-free participants (pure TS; panel A) or a subsample of medication-free participants (panel B). The statistical model covaries for age and sex. Maps are corrected for multiple comparisons using false discovery rate (FDR). Color bar, orientation, and abbreviations are as described in Figure 1. Except for anterior surfaces overlying the anterior nucleus, the similarity between these maps and those from the full sample (Figure 1) support the assertion that surface alteration in lateral thalamus is due to the presence of TS pathophysiology and not to the effects of comorbidity or medication.
**eFigure 4 Diagnosis Main Effect**

**A. Pure TS**

- **Anterior**
  - Right: M
  - Left: P

- **Lateral**
  - Right: A
  - Left: L

- **Posterior**
  - Right: L
  - Left: P

- **Medial**
  - Right: P
  - Left: P

**B. Med-free**

- **Anterior**
  - Right: M
  - Left: M

- **Lateral**
  - Right: M
  - Left: M

- **Posterior**
  - Right: M
  - Left: M

- **Medial**
  - Right: M
  - Left: M

**Atlas**

- **Right**
  - AN
  - Ce
  - LGN
  - MD
  - LP
  - VA
  - VL
  - VP

- **Left**
  - AN
  - Ce
  - LGN
  - MD
  - LP
  - VA
  - VL
  - VP

**P-Value**

- Color scale: Red > Orange > Yellow > Green > Cyan > Blue > Purple

- P-values range from 0 to <0.0001.
**eFigure 5.** Main effect of medication use. The topographic color maps demonstrate $P$ values signifying the main effect of medication in the TS group. The statistical model covaries for age and sex. Maps are corrected for multiple comparisons using FDR. Color bar, orientation, and abbreviations are as described in Figure 1. Panel A shows that selected serotonin reuptake inhibitor (SSRI) use is associated with inward deformation over anterior and posterior surfaces of the thalamus. Panel B demonstrates that use of $\alpha$-agonists results in outward deformation over the ventral thalamic surface. The outward deformation seen in the left pulvinar does not overlap with that of the main effect of diagnosis. Panel C indicates that use of typical neuroleptics is associated with both inward and outward deformations of the thalamus.
### eTable 1

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The table indicates areas of robust deformation in reference to the nuclear areas defined by the atlas. Plus signs indicate outward deformation, and minus signs indicate inward deformation. Results from the right thalamus are shown to the left of the slash sign; results from the left thalamus are shown to the right of the slash sign. Pure TS refers to analysis of the subgroup of TS participants who were not taking medication at the time of the scan. TS – no meds refers to analysis of the subgroup of TS participants who were not taking medication at the time of the scan.

The 11 nuclei defined in the atlas include the following: AN – anterior nucleus, Ce – central nuclei including central medial, central lateral, centre median and parafascicular, LD – lateral dorsal nucleus, LP – lateral posterior nucleus, LGN – lateral geniculate nucleus (not shown), MD – medial dorsal nucleus, MGN – medial geniculate nucleus (not shown), Pu – pulvinar, VA – ventral anterior nucleus, VL – ventral lateral nucleus, VP – ventral posterior nuclei.