

A voxel-based morphometry study of Tourette syndrome

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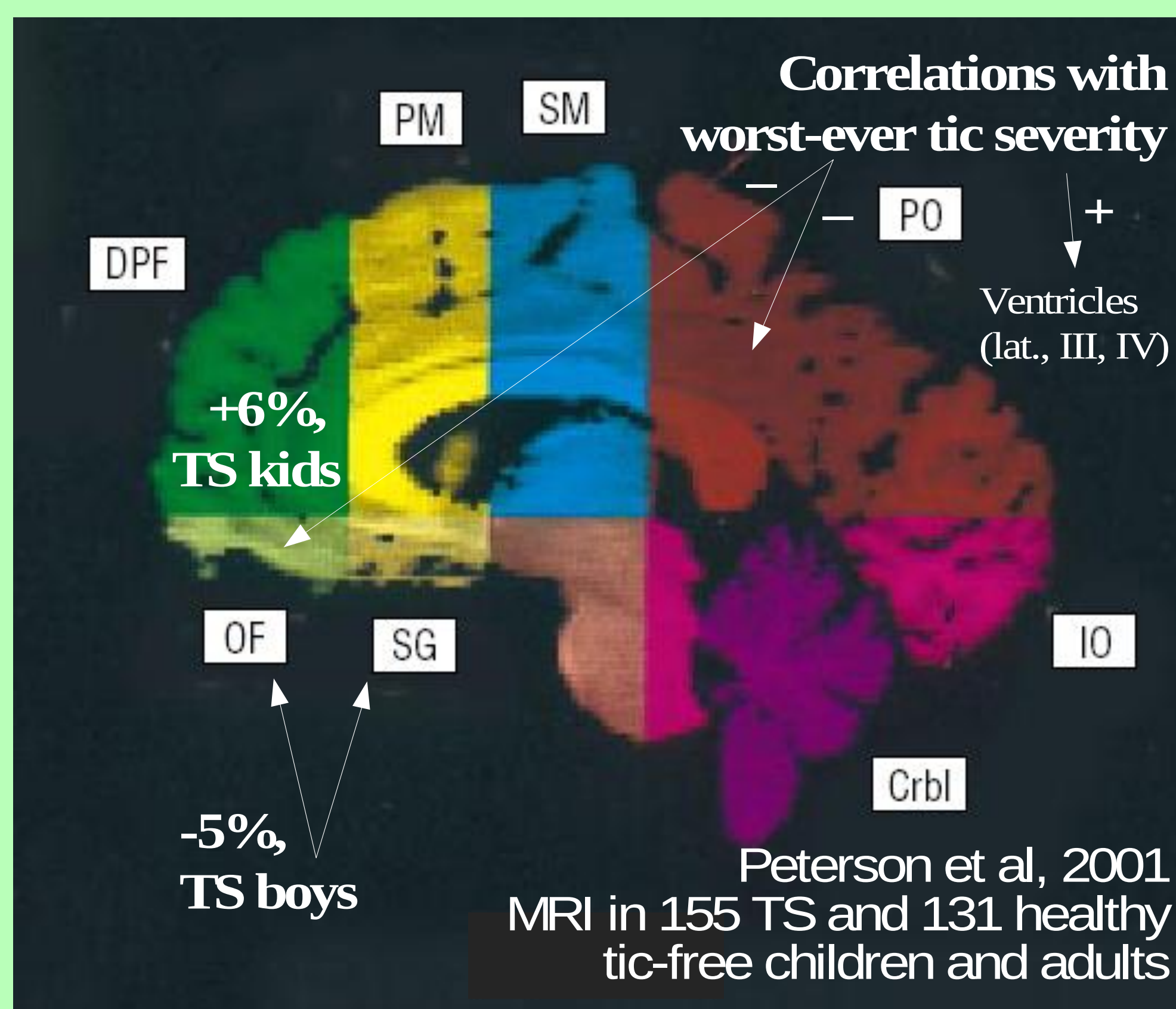
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Introduction

- There is evidence that brain structure is abnormal in Tourette syndrome (TS)
- The largest study to date compared 155 TS and 131 healthy children and adults and found significant regional differences in the volume of prospectively defined brain regions, especially in children.



- However, to our knowledge there has been no published report examining TS brain structure throughout the brain. Prior studies may have missed focal abnormalities that do not happen to correspond to the pre-defined regions.
- We used T1-weighted MRI to compare brain structure in adult TS volunteers and carefully matched tic-free controls.

Methods

Subjects:

- Subjects were a convenience sample of adult volunteers who had given informed consent prior to participation in a any of several prior PET and MRI studies by the investigators
- A board-certified psychiatrist and movement disorders specialist examined every subject
- 15 neuroleptic-naïve adults with Tourette syndrome or chronic motor tic disorder
 - Ages 19-56 years (mean $\pm$ SD = 33 $\pm$ 11)
- 15 neurologically normal, tic-free controls matched for age, sex and handedness
 - Ages 19-55 (33 $\pm$ 12)
- Exclusion criteria included significant neurological disease (other than TS), current major depression, or lifetime serious psychiatric illness including dementia, psychosis, mania, substance abuse, autism, mental retardation, or social phobia (ADHD, OCD and learning disorders were not excluded in the TS group)

Procedure:

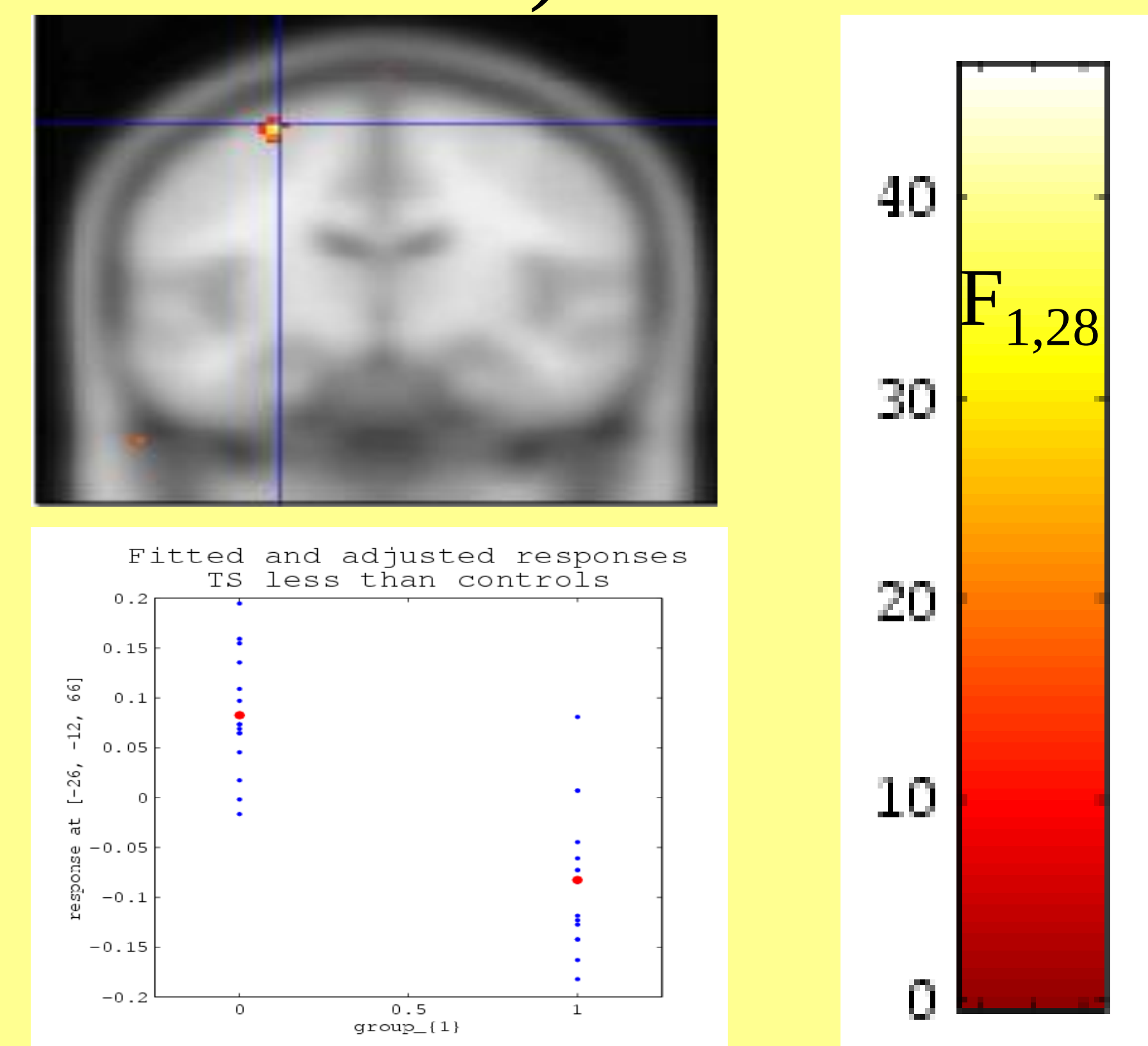
- Name and other identifiers were removed by the physician, and subsequent analyses used a code number only
- High resolution 3D MP-RAGE image (voxel volume 1.25mm³, 1.5T Siemens magnet)
- Nonlinear normalization to the ICBM instantiation of the Talairach and Tournoux stereotactic atlas (SPM99)
- Correction for gradient field inhomogeneity artifact (SPM99)
- Automated classification of each voxel as gray, white, and CSF based on signal intensity and an *a priori* segmentation of the atlas (SPM99)
- Gray matter probability images smoothed with a 3D gaussian filter with **FWHM 13mm** (a second analysis used instead a filter with **FWHM 6mm**)

Analysis:

- Gray matter probability images were compared by a two-sample t test at each voxel followed by correction for multiple comparisons (SPM99, voxel-level correction)

Results

- After correction for multiple comparisons, the primary planned analysis showed no statistically significant difference between the TS and control groups.
- Our initial choice of spatial filtering was typical for VBM analysis but was chosen in the expectation of differences in cortex, and may not be optimal for comparison of smaller (*e.g.* subcortical) structures.
- A second analysis using less spatial filtering showed a trend ($F_{1,28} = 46.2$, corrected $p=0.09$, 2-tailed) for a decrease in gray matter concentration in voxels centered in left precentral gyrus (-26, -12, 66) (primary motor cortex).



- Other regions identified at uncorrected $p < 0.001$ include right postcentral gyrus and left parietal white matter.

Discussion

- Strengths of this work include the neuroleptic-naïve status of TS volunteers and careful matching with controls.
- Weaknesses include sample size, and complications of retrospective analysis including moderate image quality and possible unidentified group differences.
- Hallett and collaborators similarly did not find statistically significant abnormalities in TS using VBM in 30 TS and 30 control subjects (presented at 7th International Congress of Parkinson's Disease and Movement Disorders, Miami Beach, FL, Nov. '02)
- There are several potential explanations for not finding a significant group difference.
 - There is no abnormality in brain structure in TS detectable by T1-weighted MRI. This is unlikely given the positive results of Peterson et al and of other, smaller studies.
 - Experimental error, including imperfect image quality or imperfect group matching on other variables.
 - Abnormalities of brain structure are present early in life in TS, near the age of symptom onset, but wane in adult life. This is consistent with the findings of Peterson et al.
 - Type II error. This is reasonably likely given our relatively small group sizes.
- The trend level finding in motor cortex suggests that further study with a larger number of subjects is warranted.

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