ENIGMA TOURETTE SYNDROME

Enhancing Neuroimaging Genetics through Meta-analysis

A worldwide platform for collaboration on the study of Tourette Syndrome genetics and neuroimaging

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Introduction

Tourette Syndrome (TS) is characterized by multiple motor and vocal tics and high comorbidity rates with other neuropsychiatric disorders. Obsessive Compulsive Disorder (OCD), Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorders (ASD), Major Depressive Disorder (MDD) and Anxiety Disorders (AXD) are among the most prevalent TS comorbidities. To date, studies on TS brain structure and function have been limited in size with efforts mostly fragmented. On the other hand, genetic studies are starting to uncover robust genetic loci for TS. Leveraging an international network of collaborators, existing collections of data, and established infrastructure and pipelines for large-scale neuroimaging and genetics studies, ENIGMA-TS will help close major gaps in our understanding of TS neurobiology and help elucidate the etiological correlations between TS and its frequently comorbid disorders.

ENIGMA-TS

MEMBERS GAIN ACCESS TO OUR JOINT RESOURCES AND DATABASE!

Initial goal: Meta-analysis of structural brain MRI and rsfMRI data for 1,000 patients.

Methods

ENIGMA-TS brings together investigators from around the world with a goal to perform large-scale studies of brain structure and function in TS. Previously collected TS neuroimaging data (structural, diffusion tensor imaging, and resting-state functional MRI) will be analyzed jointly and integrated with genomic data as well as equivalently large and already existing studies of highly comorbid OCD, ADHD, ASD, as well MDD, and AXD. We take advantage of access to data, resources and standardized pipelines from the ENIGMA (Enhancing Neuroimaging Genetics through Meta-Analysis) consortium. Our first goal for joint analysis includes a study of cortical and subcortical neuroanatomical signatures for more than 1,000 patients with TS and equal number of controls.

Join now if you

- would like to work with us on uncovering the cause of Tourette Syndrome and help in improved diagnosis and management.
- can contribute previously collected data on Tourette Syndrome neuroimaging (raw data or summary statistics for meta-analysis).
- are planning to begin collection of Tourette Syndrome neuroimaging data.

Results and conclusions

With 90% of TS patients presenting with additional neuropsychiatric comorbidities, understanding the molecular, pathophysiological and neuroanatomical underpinnings of TS should also extend to investigating relationships to other comorbid disorders. We have performed the largest GWAS for TS (Tsetsos et al. 2021), as well as the largest cross-disorder GWAS meta-analysis for TS, ADHD, ASD, and OCD (Yang et al. 2021). Our work already highlights the power of collaborative efforts and transdiagnostic approaches and points to the existence of different TS subtypes. ENIGMA-TS will offer large-scale, high-powered studies that will lead to important insights towards understanding brain structure and function and genetic effects in TS as well as biomarkers that could help inform improved clinical practice.

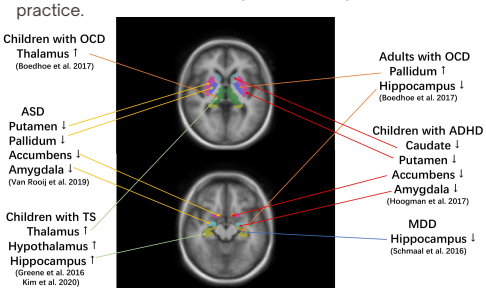

Figure 1. Subcortical brain regions that have been implicated in TS and related disorders through volumetric MRI studies (Yin Jin).

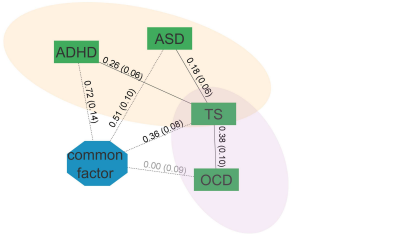

Figure 2. Genomic structural equation modeling factor analysis and pairwise genetic correlation values (LD score regression analysis) for TS, ADHD, ASD, OCD. The solid lines indicate the genetic correlation values (rg) as well as their standard errors in parentheses, while the dashed lines show the common factor values (Yang et al. 2021).

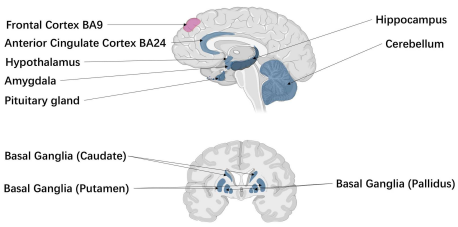

Figure 3. TS-ADHD-ASD GWAS and TS-OCD GWAS cross-disorder tissue specificity analysis, testing 30/53 tissue types from GTEx v7 tissue expression atlas (significant enrichment under Bonferroni correction is shown). Blue color indicates enrichment of gene expression in TS-ADHD-ASD Tissue Specificity Analysis while red also includes significant results for TS-OCD (Yang et al. 2021).

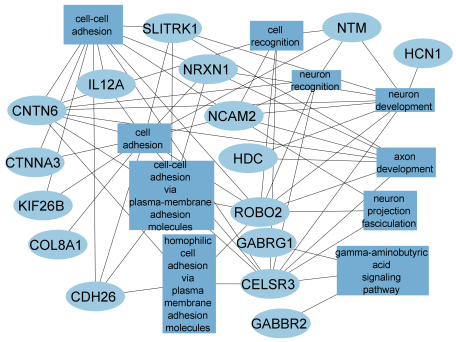

Figure 4. Network of the top 10 GO: Biological Processes (GO:BP) terms from key genes previously implicated in TS based on large-scale studies (reviewed in Levy et al. 2021, analysis by Mary Kaka, Apostolia Topaloudi).

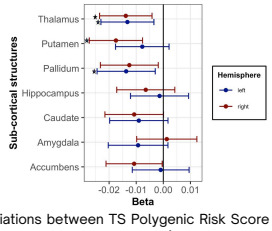

Figure 5. Associations between TS Polygenic Risk Score (PRS) calculated based on latest TS GWAS meta-analysis (Tsetsos et al. 2021) and volume of 14 subcortical brain structures in UK Biobank. (*) Significant association after multiple testing correction using the FDR method (Pritesh Jain).

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