

# A large-scale study of rare copy number variation identifies novel loci associated with Tourette's syndrome

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## INTRODUCTION AND OBJECTIVES

The role of large, rare copy number variations (CNVs) has been highlighted across a wide variety of neurodevelopmental disorders, including Tourette's syndrome (TS). However, previous studies involving TS have been limited largely by sample size<sup>1,2</sup>. To investigate the contribution of CNVs to the genetic etiology of TS, we evaluated a large cohort of clinically diagnosed TS patients using dense genome-wide single nucleotide polymorphism (SNP) arrays.

## METHODS

All samples were genotyped on the Illumina OmniExpress or OmniExpress + Exome chips and, to reduce platform variability, only SNPs present on both arrays were used. After extensive sample and CNV-level quality control, a total of 2,764 cases and 2,852 ethnically-matched controls were used to generate CNV calls using PennCNV. We limited our analysis to large (>400KB), rare (

## RESULTS AND DISCUSSION

We observed a substantial overlap with CNV regions identified in other neurodevelopmental disorders, and identified in TS cases several recurrent CNVs in genomic regions previously implicated in TS. Two of these loci that also contain gene-coding regions demonstrated enrichment in cases compared to controls: *NRXN1* (1-sided Fisher's exact,  $p=0.007$ ) and *CNTN4* ( $p=0.029$ ). Consistent with previously published reports, all CNVs involving *NRXN1* detected in this study were deletions. We also detected a suggestive enrichment of CNVs spanning *PARK2*, a gene previously implicated in TS and significantly associated with attention-deficit hyperactivity disorder.

## CONCLUSIONS

In the largest study performed to date, we report the first statistically significant CNV in a single locus associated with TS. Future analyses involving larger sample sizes will be needed to refine the role of large, rare CNVs in the genetic architecture of TS. We continue to evaluate the robustness of our results by the incorporation of additional controls and are investigating pathways enriched for genic CNVs.

## REFERENCES

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