ADHD

- Childhood onset before age 12
- Prevalence 5%
- 3 subtype
  - Inattentive
  - Hyperactive-impulsive
  - Combined
ADHD and TS prevalence

- Population study: minimum 20% of TS has ADHD (Scharf et al., 2012)
- Clinical studies: approx 55% (Freeman et al. 2000, Hirschtritt et al., 2015)
What if ADHD is also present in TS?

• ADHD is linked with various **impulsive behaviors** in TS patients (Palumbo and Kurlan, 2007; Yamamuro et al., 2015)

• ADHD is most associated with **anger problems** in TS (Freeman, 2000)

• **Distruptive behavior**: low frustration tolerance, outbursts, noncompliance and aggression (Roessner et al., 2007)

• **peer relationships**, internalising/externalising behaviors and **academic achievement** (Poh et al., 2018)

• **Sleep** problems (Freeman, 2007)

• Comorbid ADHD is associated with a **lower ability to suppress tics** (Sambrani et al. 2016)
Common neurobiology?

Large number of studies investigating the question

- the responsible complex pathways are not clear

- ADHD-TS vs TS-OCD abnormalities in glutamatergic neurochemistry in the fronto-striatal circuitry

Naaijen et al, 2016
Shared genetic basis?

Investigating Shared Genetic Basis Across Tourette Syndrome and Comorbid Neurodevelopmental Disorders Along the Impulsivity-Compulsivity Spectrum


ABSTRACT
BACKGROUND: Tourette syndrome (TS) is often found comorbid with other neurodevelopmental disorders across the impulsivity-compulsivity spectrum, with attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and obsessive-compulsive disorder (OCD) as most prevalent. This points to the possibility of a common etiological thread along an impulsivity-compulsivity continuum.

METHODS: Investigating the shared genetic basis across TS, ADHD, ASD, and OCD, we undertook an evaluation of cross-disorder genetic architecture and systematic meta-analysis, integrating summary statistics from the latest genome-wide association studies (GWAS) of 4,375,716 individuals, 6,748,510 markers.

RESULTS: As previously identified, a common etiological factor connects TS, ADHD, and ASD, while TS and OCD show the highest genetic correlation in pairwise testing among these disorders. Thanks to a more homogeneous set of disorders and a targeted approach that is guided by genetic correlations, we were able to identify multiple novel hits and regions that seem to play a pleiotropic role for the specific disorders analyzed here and could not be identified through previous studies. In the TS-ADHD-ASD-GWAS genome-wide association study single nucleotide polymorphism-based and gene-based meta-analysis, we uncovered 13 genome-wide significant regions that host single nucleotide polymorphisms with a high posterior probability for association with all three studied disorders (p-value > 0.81), 11 of which were not identified in previous cross-disorder analyses. In contrast, we also identified two additional pleiotropic regions in the TS-OCD meta-analysis. Through conditional analysis, we highlighted genes and genetic regions that play a specific role in a TS-ADHD-ASD genetic factor versus TS-OCD. Cross-disorder tissue specificity analysis implicated the hypothalamus-pituitary-adrenal gland axis in TS-ADHD-ASD.

CONCLUSIONS: Our work underlines the value of redefining the framework for research across traditional diagnostic categories.


Tourette syndrome (TS) is a common childhood-onset neurodevelopmental disorder that is often comorbid with other neurodevelopmental disorders along the impulsivity-compulsivity spectrum. In fact, only 16% of cases of TS appear as pure TS, while up to 54.3% of patients are also diagnosed with attention-deficit/hyperactivity disorder (ADHD), 58% with obsessive-compulsive disorder (OCD), and up to 28% with comorbid autism spectrum disorder (ASD) [1-3]. The high comorbidity rates among these disorders have led to the hypothesis that TS, OCD, ADHD, and ASD might actually lie on an impulsivity-compulsivity continuum, sharing overlapping etiologies that converge in dysfunctional brain circuits [4].

Here, pursuing a transdiagnostic approach, we seek to identify the common genetic factors and neural underpinnings across this spectrum of phenotypes. TS, ADHD, ASD, and OCD all have a complex and highly heterogeneous genetic architecture, with both common and rare genetic variants contributing to their etiology [5-9]. Over the past five years, 12 genome-wide significant loci have been identified for ADHD [10], and five genome-wide significant loci were described for AS [11,12]. For OCD, no genome-wide significant loci have been detected to date [13], while one genome-wide significant locus was recently reported for TS [14].
Shared genetic basis?

• the existence of a **unifying genetic factor** across TS, ADHD, and ASD is confirmed

• the high genetic correlation of TS and OCD appears to be **separate from the TS-ADHD-ASD factor**

• **Cross-disorder tissue specificity analysis** implicated the **hypothalamus-pituitary-adrenal gland axis in TS-ADHD-ASD**
Neuropsychology in ADHD-TS

• May be weaknesses in motor skills, cognitive flexibility, working memory and attention when ADHD is also present (Termine et al., 2016)

• Response inhibition abilities may be predictive of the success of behavioural therapy for tic management (Deckersbach et al., 2006).
inhibitory deficit

• Inhibition of a prepotent, automatic or ongoing response

Inhibitory control improve with age
Inhibitory deficits were associated with tic severity (YGTSS total tic score)
ADHD exacerbate inhibitory deficits

• TS alone vs Control
  • TS has a small effect on inhibitory control
  • TS + ADHD vs. healthy controls:
    • Medium effect on inhibitory control
  • TS+OCD vs healthy controls:
    • Not enough studies

Morand-Beaulieu et al. 2017 review
Impaired response inhibition during a stop-signal task in children with Tourette syndrome is related to ADHD symptoms: A functional magnetic resonance imaging study

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Tic suppression ability and the urge are independent

(Ganos et al, 2012)
Clinical implications

• some features of TS might look like ADHD-like symptoms!!

• the ability to maintain attention could be impaired
  • by the tics themselves,
  • by efforts to inhibit the tics,
  • or by distractions from comorbid anxiety or OCD

(Erenberg, 2005).
Behavioral therapy in ADHD-TS

- Attentional problems may predict poor tic treatment outcome (Himle and Woods, 2005)
- Preference to treat ADHD first (Döpfner and Rothenberger, 2007),
- When ADHD is stable positive treatment effects are observed (Piacentini et al., 2010)
- ADHD/anxiety does not impact on outcome following CBIT, suggesting that CBIT is effective for tics in patients with co-occurring conditions (Sukhodolsky, Woods ea., 2017)
- TS patients with ADHD are able to suppress tics (Lyon et al 2010, Conelea et al., 2018)
Behavioral therapy in ADHD-TS
Solutions for the problems

- Distracted
- Wanting to talk, run around
- Sessions take too long/boredom
- Not doing homework
- Parental ADHD
- Executive dysfunction

- Parental support
- Involve parents/partners/co-therapist
- Practice in an environment free of distractions
- HRT is more practical
- For ERP, good results have been reported changing the therapist halfway the session (Verdellen et al., 2008a)
- Practice in small pieces of time
- Short sessions-practice little and often
- Physical activity breaks
- Immediate reward and praise (Fosco et al., 2015)
- Clear visual aids, schedules
- Promote recommendations for school
Thank you!