

Treatment of ADHD in people with TS and/or OCD

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Objectives

1. To discuss the epidemiology, clinical characteristics and natural history of ADHD in people with TS and OCD

2. To review treatment strategies for ADHD and how these may be affected by comorbid TS and OCD diagnoses

Why are we talking about this?

ADHD symptoms appear to be more common in people with TS and/or OCD

Treatment of ADHD symptoms in people with TS and/or OCD may be complicated by worsening tics or OCBs

DSM V Criteria for ADHD

People with ADHD show a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development

Inattention: Six or more symptoms of inattention < 16, or five or more for 17+

Symptoms of inattention have been present for at least 6 months, and they are inappropriate for developmental level

Hyperactivity and Impulsivity: Six or more symptoms of hyperactivity-impulsivity < 16 years, or five or more for 17+

Symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for the person's developmental level

Inattention

Often fails to give close attention to details or makes careless mistakes

Often has trouble holding attention on tasks or play activities.

Often does not seem to listen when spoken to directly.

Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace

Often has trouble organizing tasks and activities.

Often avoids, dislikes, or is reluctant to do tasks that require mental effort over long periods

Often loses things necessary for tasks and activities

Is often easily distracted

Is often forgetful in daily activities.

Hyperactivity/Impulsivity

Often fidgets with or taps hands or feet, or squirms in seat.

Often leaves seat in situations when remaining seated is expected.

Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).

Often unable to play or take part in leisure activities quietly.

Is often "on the go" acting as if "driven by a motor".

Often talks excessively.

Often blurts out an answer before a question has been completed.

Often has trouble waiting their turn.

Often interrupts or intrudes on others (e.g., butts into conversations or games)

DSM V Criteria for ADHD

Several inattentive or hyperactive-impulsive symptoms were present before age 12 years.

Several symptoms are present in two or more settings, (such as at home, school or work).

There is clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning.

The symptoms are not better explained by another mental disorder (such as a mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

The symptoms do not happen only during the course of schizophrenia or another psychotic disorder.

DSM V Criteria for ADHD

Combined Presentation: if enough symptoms of both criteria inattention and hyperactivity-impulsivity were present for the past 6 months

Predominantly Inattentive Presentation: if enough symptoms of inattention, but not hyperactivity-impulsivity, were present for the past six months

Predominantly Hyperactive-Impulsive Presentation: if enough symptoms of hyperactivity-impulsivity, but not inattention, were present for the past six months.

Tourette syndrome

Childhood onset neurodevelopmental disorder characterized by motor and vocal tics

More common in boys than girls 3:1

Multiple motor tics *and* at least one vocal tic

Present for at least a year, demonstrating a waxing and waning pattern

DSM V Criteria for OCD

A. Presence of obsessions, compulsions, or both:

Obsessions are defined by (1) and (2):

1. Recurrent and persistent thoughts, urges, or impulses that are experienced as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).

Compulsions are defined by (1) and (2):

1. Repetitive behaviors or mental acts that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.

DSM 5 Criteria for OCD

Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder

Comorbid ADHD in people with TS

Approximately 50%
of people with TS
are diagnosed with
ADHD

ADHD symptoms
and diagnosis
usually precede tic
onset

Lower rates of
comorbidity are
seen in community
derived samples 25-
35%

Comorbidity rates
between tics and
ADHD are higher
with more severe tic
disorders

transient tics <
chronic motor tic
disorder < chronic
vocal tic disorder <
TS

TS and ADHD: Shared Symptomatology

Impairment in attention

Impairment in control

Hyperactivity

Anxiety

Behaviour problems

Obsessive compulsive behaviours

Sensory processing issues

Depression

Sleep disturbances

Impairment in socialization and communication

Repetitive patterns of behaviour

TS and ADHD: Shared Etiology?

Evidence suggests similar neuropathology between TS and ADHD - long-range underconnectivity and short-range overconnectivity

In normal brain development, a shift occurs from local processing (short-range connectivity) to more global processing (long-range connectivity)

With age there is pruning of local connectivity and strengthening of long-range connectivity

Brain connectivity issues could be due to neuronal insult or genetically determined

Deficits in brain connectivity correlate with both tic and ADHD symptom severity

Contrasting TS+ADHD vs ADHD only

ADHD severity is minimally greater in children with TS+ ADHD compared to children with ADHD only

Age of ADHD onset is similar

Frequency of mood disorders, anxiety disorders and disruptive behaviour disorders is similar in children with TS+ADHD and ADHD only

Frequency of OCD is higher in children with TS+ADHD than children with ADHD only

How does the co-occurrence of ADHD impact children with TS?

Children with ADHD+TS seem to be treated for TS symptoms earlier, without having greater tic severity. May be related to greater overall psychosocial impairment.

Co-occurring ADHD may impair tic suppression

Mental effort to suppress tics may accentuate inattention in ADHD

Presence of comorbid ADHD may moderate the effectiveness of alpha agonists for the treatment of tics - studies suggest greater effect of alpha agonists for tics in children with TS+ADHD

Risk for aggressive and delinquent behaviour and conduct difficulties in children with TS is posed largely by the presence of ADHD

Greatest independent predictor of psychosocial quality of life in children with TS is ADHD symptom severity

Treatment priority: TS vs ADHD

ADHD symptoms usually cause greater impairment in cognitive, emotional and social skills than tics, unless tics are very severe

Treatment should prioritize the symptoms causing the most impairment

Treating ADHD in children with tics



Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders

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Treating ADHD in children with tics

Objective: To assess the effects of pharmacological treatments for ADHD in children with comorbid tic disorders on symptoms of ADHD and tics

Methods: Systematic review of randomized controlled trials of any pharmacological treatment for ADHD used specifically in children with ADHD+TS

Treating ADHD in children with tics

8 randomized controlled trials with 510 participants - 443 boys, 67 girls

All studies performed in USA

Trial length ranged from 3 to 22 weeks

Several trials assessed multiple agents

Medications assessed included methylphenidate, clonidine, desipramine, dextroamphetamine, guanfacine, atomoxetine and deprenyl

Methylphenidate

Outcomes	Effect of treatment	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
<p>ADHD symptom-related behavior</p> <p>Measured by standardized rating scales: Conners' Abbreviated Teacher Rating Scale, Conners' Abbreviated Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Mothers' Objective Method for Subgrouping, Continuous Performance Task, Conners' Teacher Rating Scale, Conners' Continuous Performance Task</p>	<p>Tourette's Syndrome Study Group 2002 showed a significant treatment effect using the Conners' Abbreviated Teacher Rating Scale (3.3 points, 98.3% CI -0.2 to 6.8; P = 0.02).</p> <hr/> <p>Gadow 2007 showed that all doses (0.1 mg/kg, 0.3 mg/kg, 0.5 mg/kg) of methylphenidate were superior to placebo on all rating scales (Conners' Abbreviated Teacher/Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Mothers' Objective Method for Subgrouping, Continuous Performance Test), with a dose-dependent effect (F = 24.7; P = 0.001)</p> <hr/> <p>Castellanos 1997 showed significantly decreased hyperactivity at all doses (15 mg, 25 mg, 45 mg).</p>	229 (3 studies)	⊕⊕⊕⊖ Low^a	-

Methylphenidate

Tic severity

Measured by standardized rating scales: Yale Global Tic Severity Scale, Tourette Syndrome Severity Scale, Tourette Syndrome Clinical Global Impression Scale, Global Tic Rating Scale, 2-Minute Tic and Habit Count, Tic Symptom Self-Report

[Tourette's Syndrome Study Group 2002](#) found a significant treatment effect using the Yale Global Tic Severity Scale (11.0 points, 98.3% CI 2.1 to 19.8; $P = 0.003$).

[Gadow 2007](#) found no difference on the Yale Global Tic Severity Scale but found an improvement in tic severity at all doses (0.1 mg/kg, 0.3 mg/kg, 0.5 mg/kg) on the Global Tic Rating Scale completed by teachers ($F = 5.33$; $P = 0.002$)

[Castellanos 1997](#) found no effect of drug on tic severity for second and third cohorts. Tic severity was significantly greater during week 2 in the first cohort ($P < 0.01$)

229 (3 studies)

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Low^a

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Tourette syndrome study group

RCT in 136 children with TS+ADHD for 16 weeks

Randomized to clonidine alone, methylphenidate alone, combined clonidine and methylphenidate, or placebo

ADHD symptom improvement on ASQ-Teacher

Clonidine alone vs placebo 3.3 (-0.2, 6.8)

Methylphenidate alone vs placebo 3.3 (-0.2, 6.8)

Clonidine + methylphenidate vs placebo 6.3 (2.8, 9.8)

Tourette syndrome study group

Tic severity on Yale Global Tic Severity Scale

Clonidine vs placebo 10.9 (2.1, 19.7)

Methylphenidate vs placebo 9.4 (0.7, 18.1)

Clonidine + Methylphenidate vs placebo 11.0 (2.1, 19.8)

Tourette syndrome study group

Worsening tics reported as an adverse effect in:

20% of children receiving methylphenidate

22% of children receiving placebo

26% of children receiving clonidine alone

Tourette syndrome study group

Tics limited further dosage increases more often for participants assigned to methylphenidate alone (35%), than participants assigned to methylphenidate plus clonidine (15%), clonidine alone (18%) or placebo (19%)



Tourette syndrome study group

Data from Tourette syndrome study group suggest methylphenidate and clonidine have similar efficacy in treating ADHD symptoms, and that their combination is superior to either treatment alone

These findings are contrary to clinical experience, in which stimulants are more effective than alpha agonists in most patients

Unexpected result may be due to low doses of methylphenidate used in the study of 25 mg/day

Dextroamphetamine

One placebo-controlled crossover study of dextroamphetamine including 20 children

Assessed doses of 7.5 mg BID, 15 mg BID or 22.5 mg BID

Increased tic severity seen with 15 mg BID and 22.5 mg BID dose

Improved ADHD symptom severity seen with all three doses

Clonidine

Outcomes	Effect of treatment	Number of participants (studies)	Quality of the evidence (GRADE)
<p>ADHD symptom-related behavior</p> <p>Measured by standardized rating scales: Conners' Abbreviated Teacher Rating Scale, Conners' Abbreviated Parent Rating Scale, IOWA Conners' Teacher Rating Scale, Conners' Continuous Performance Task, Child Behaviour Checklist, Gordon Diagnostic System, Clinical Evaluation of Language Function, Matching Familiar Figures Test, Porteus Maze Test, Restricted Academic Test</p>	<p>Tourette's Syndrome Study Group 2002 found a significant treatment effect using the Conners' Abbreviated Teacher Rating Scale (3.3 points, 98.3% CI -0.2 to 6.8; P = 0.02).</p> <hr/> <p>Singer 1995 found no significant difference on any ADHD outcome measures, except the nervous/overactive subscale of the Child Behaviour Checklist (boys aged 6-11 years).</p>	170 (2 studies)	⊕⊕⊕⊖ Low^a

Clonidine

Tic severity

Measured by standardized rating scales: Yale Global Tic Severity Scale, Tourette Syndrome Severity Scale, Global Tic Rating Scale, Tic Symptom Self-Report, Hopkins Motor/Vocal Scale

[Tourette's Syndrome Study Group 2002](#) showed a significant treatment effect using the Yale Global Tic Severity Scale (10.9 points, 98.3% CI 2.1 to 19.7; P = 0.003).

[Singer 1995](#) found no significant difference on measures of tic severity.

170 (2 studies)

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Low^a

Guanfacine

One 8 week parallel group trial of guanfacine vs placebo in 34 children

Guanfacine significantly reduced symptoms of ADHD on the ADHD Rating Scale Total Score (teacher) and tics on the YGTSS Total Tic Score

Atomoxetine

Parallel group study of atomoxetine in 148 children for 18 weeks

Primary objective - to test the hypothesis that atomoxetine does not worsen tics in children with TS+ADHD relative to placebo

Significant improvement in ADHD symptoms on the ADHD Rating Scale total score with atomoxetine compared to placebo

Atomoxetine was non-inferior to placebo on the YGTSS total tic score

Tics decreased by 5.5 points in the atomoxetine group and 3 points in the placebo group

Conclusions from systematic review

Psychostimulants should be considered first line treatment of ADHD in children with tics

More evidence to support use of methylphenidate than dextroamphetamine

Lowest effective dose should be used as dose of methylphenidate in studies was at lower end, and higher doses of dextroamphetamine worsened tics

If tics are exacerbated by psychostimulants, evidence to support the use of clonidine and guanfacine for ADHD and tic symptoms, and atomoxetine for ADHD symptoms

Comorbid ADHD in people with OCD

- Reports are highly inconsistent, especially in pediatric studies
- Range from 0-60%
- Lower comorbid rates reported in adolescents and adults compared to children
- Several important methodological issues with studies reporting comorbid ADHD in people with OCD
 - Most studies examine clinical samples from specialty clinics rather than community-based samples
 - Inconsistent inclusion/exclusion criteria
 - Gender ratios

Comorbid OCD in people with ADHD

Few studies have reported the occurrence of OCD in people with ADHD

There is less variation from reported studies, with comorbid OCD in 3 to 7.5% of children with ADHD

One study in adults using a nationally representative US sample reported that 2.7% of patients with ADHD had comorbid OCD, which resembles the prevalence in the general population (2-3%)

Phenomenology of OCD and ADHD

OCD

Estimated heritability 40%

Onset before 18 years in 25-50%

Internalizing disorder

Characterized by obsessions and compulsions

Associated with harm/risk avoidance, restrained behaviour, withdrawal, and avoidance of novel stimuli

Lower levels of behavioural impulsivity than controls

Positive response to SSRIs and antipsychotics

ADHD

Estimated heritability 70%

Childhood onset

Externalizing disorder

Characterized by inattention, impulsivity, hyperactivity

Associated with risk-taking and novelty seeking

Positive response to psychostimulants

Hollander's Impulsive-Compulsive Continuum



IMPULSIVE

Behaviours lacking forethought

Limited ability to inhibit or postpone behaviours

Risk taking

COMPULSIVE

Carefully planned rituals

Performed according to rigid rules

Harm avoidance

Risk-averse behaviour

Neurobiology of ADHD and OCD

Abnormal pattern of brain activity in the frontostriatal system and network in both disorders

Functional abnormalities contrast sharply between the disorders

OCD is associated with abnormally **INCREASED** activity (hypermetabolism) in frontal and striatal regions - orbitofrontal cortex, basal ganglia and thalamus, and hyperactivated frontostriatal functional connectivity

ADHD is associated with **DECREASED** activity (hypometabolism) in prefrontal and striatal brain regions, with reduced frontostriatal connectivity

Neuropsychology of ADHD and OCD

Individuals with ADHD and OCD underperform relative to controls on tasks of executive function – working memory, planning and response inhibition

Neuropsychological findings in ADHD are highly consistent; in OCD are highly variable

Deficient performance of people with ADHD and people with OCD on neuropsychological tests may stem from different mechanisms

Concomitant ADHD-OCD as a familial subtype

One study (Geller et al 2007) found evidence to suggest that comorbid ADHD-OCD is a distinct condition in which the two disorders are genetically transmitted together

By looking at a sample of children with ADHD alone, ADHD + OCD, and controls:

Relatives of children with ADHD with and without OCD had similar and higher rates of ADHD than relatives of controls

The risk of OCD was elevated only among relatives of children with ADHD + OCD

The Executive Overload Model of OCD

Proposed by Abramovitch et al 2012

Focuses on the cognitive cost of obsessions in OCD

Overflow of obsessive thoughts in OCD may overload the executive system, resulting in neuropsychological deficits

Neuropsychological impairments in OCD should be considered an epiphenomenon associated with state-dependent symptom severity

Suggests that ADHD symptoms in OCD might actually be ADHD-like symptoms - may be behavioural manifestations of OCD-related neurocognitive impairment

Such ADHD-like symptoms may be especially pronounced in children due to maturational abnormality in children with OCD

Treatment of ADHD in OCD

Be rigorous in your diagnostic approach: are these ADHD symptoms or ADHD-like symptoms?

Be cautious: psychostimulants can worsen OCD symptoms, titrate slowly and monitor response

Consider treating OCD symptoms first, especially if there is significant impairment

Re-evaluate ADHD symptoms after OCD symptoms have improved

Summary

ADHD + TS

Symptomatic overlap between conditions
ADHD symptoms usually more impairing than tics

More evidence to support use of methylphenidate than dextroamphetamine

Alpha agonists used adjunctively or alone to treat both conditions

ADHD + OCD

Rate of co-occurrence highly variable but ADHD appears more common, especially in children

Evaluate carefully - ADHD vs ADHD-like symptoms secondary to OCD

Treat OCD first and re-evaluate ADHD symptoms