

Tourette syndrome & comorbidities



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ESSTS

Athenis 

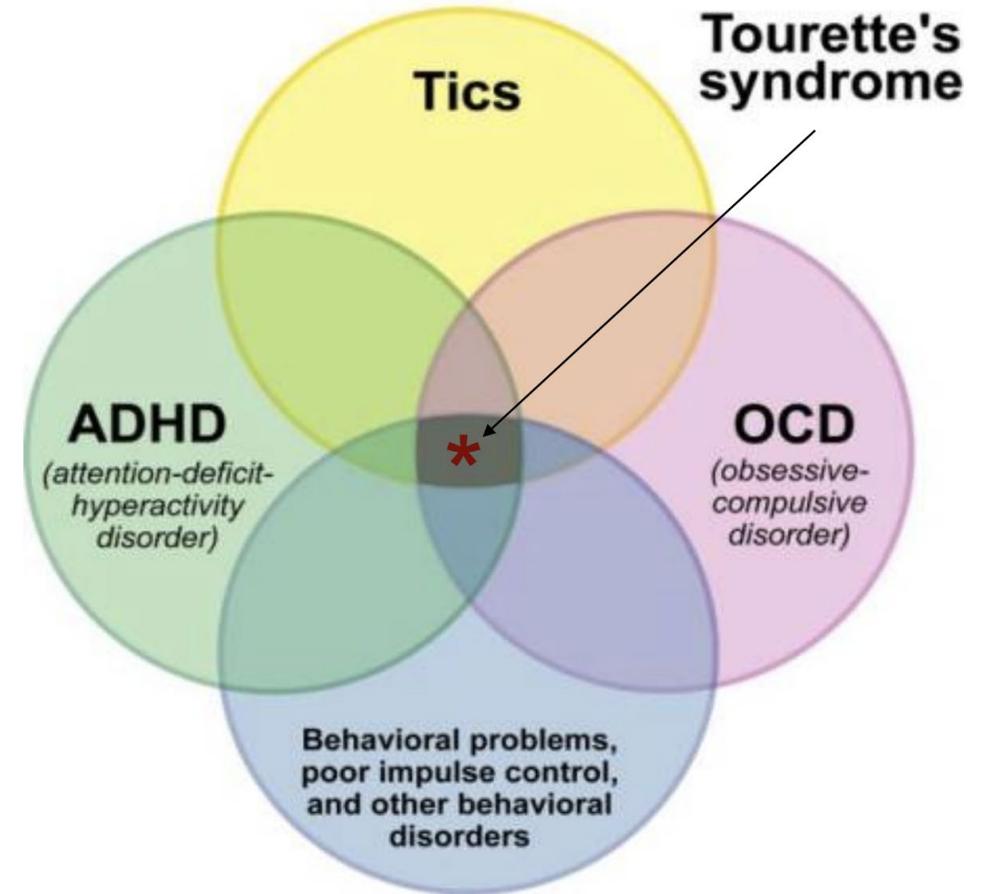
Tourette syndrome (TS) - more than 'just' a movement disorder

JAMA Psychiatry. 2015 April 1; 72(4): 325–333. doi:10.1001/jamapsychiatry.2014.2650.

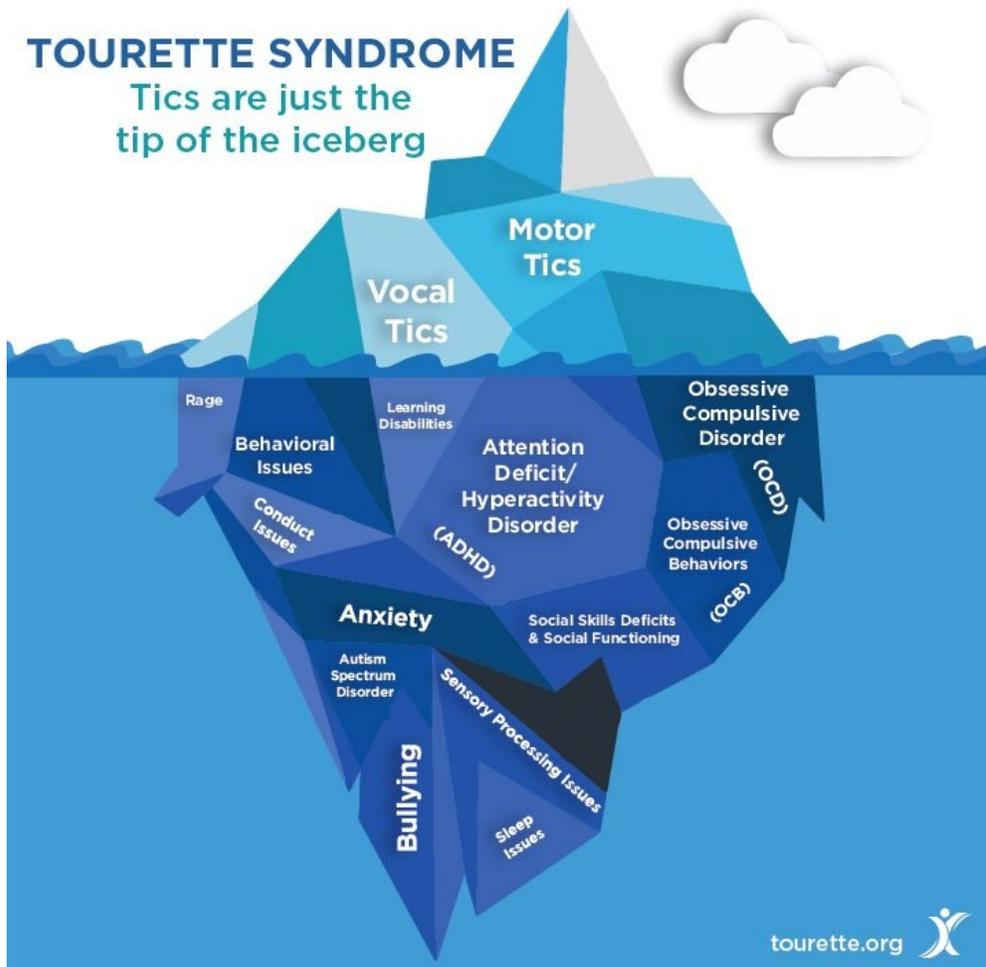
Lifetime Prevalence, Age of Risk, and Etiology of Comorbid Psychiatric Disorders in Tourette Syndrome

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- Largest and most comprehensive study of comorbidity in people with TS
- Cross-sectional structured diagnostic interviews, n=1374 with TS, mean age 19.1 years +/-13.5 and 1142 members of unaffected families, from tic disorder specialty clinics in the United States, Canada, Great Britain, and the Netherlands



TS - a complex neuropsychiatric syndrome



86%



Had ≥ 1 neurodevelopmental or mental health comorbidity

58%



Had two comorbidities

Objectives

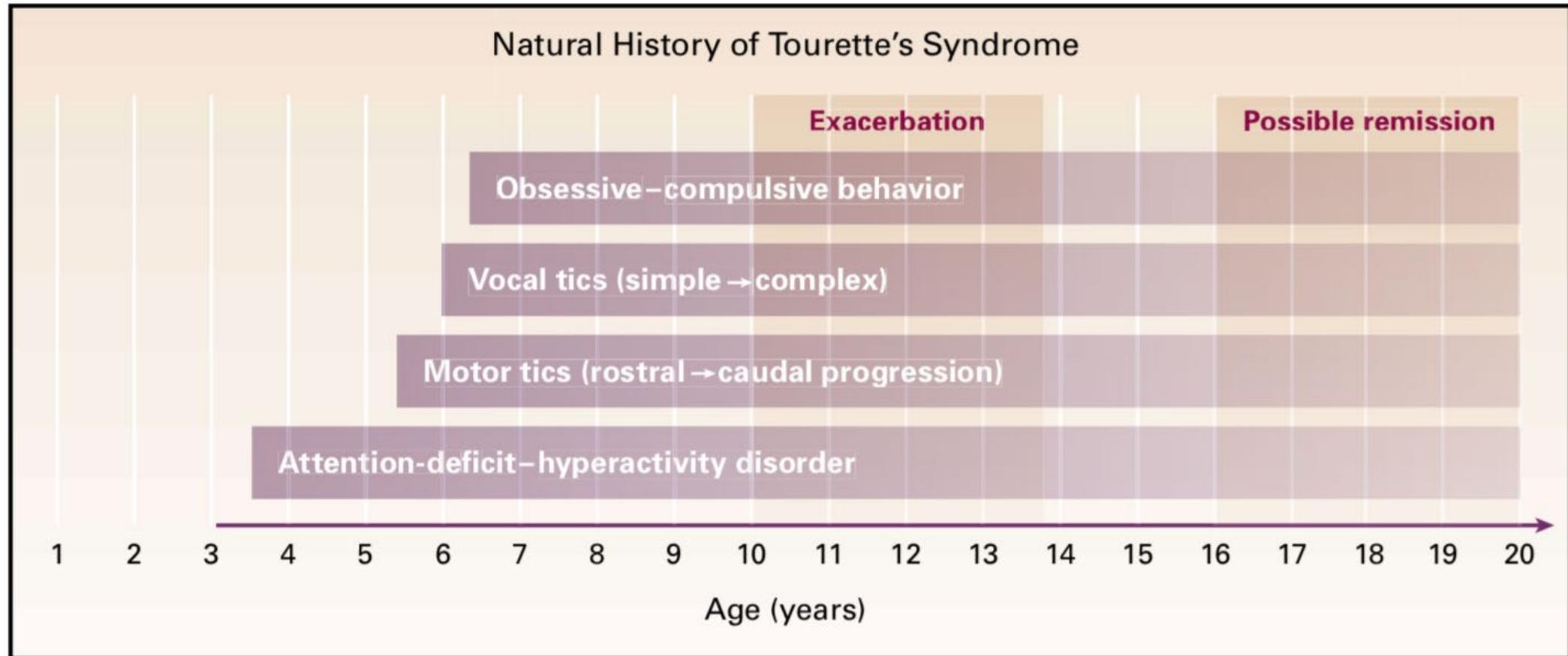
- To discuss the most common comorbid conditions in people with TS.
- To review the specificities of the most common comorbidities in TS in diagnosis and management.

Clinical comorbidities



- ADHD 30-60%
- OCD/OCB 30-40%
- Anxiety disorders 25%-30%
- Conduct & ODD 10-30%
- ASD 5-10% (broader phenotype 20%)
- Mood disorder 10-20%
- Specific learning difficulties 23%
- Dyspraxia 2-6%
- Injury
- Migraine/headaches
- Sleep disorders
- Stereotyped movements
- Substance use disorder
- Trichotillomania, nail biting/skin picking
- Speech delay/stuttering
- Functional tic-like behaviours

Onset of comorbidities



Quality of life in Tourette syndrome

- Lower quality of life than the general healthy population.¹
- Associated psychiatric comorbidities, particularly ADHD and OCD, are often more disabling than tics.²
- In adults with TS, tic severity contributed little to quality of life.³

Screening and management of TS comorbidities are therefore crucial goals in this population.⁴



Treat behavioral co-morbidities first if these are the main source of disability!!!

¹Storch et al., 2007; Jalenques et al., 2012 ; ²Eddy et al., 2011; ³Muller-Vahl et al., 2010 ;

⁴Pringsheim et al., 2009; Ganos and Martino, 2015

ADHD

DSM 5 Criteria for ADHD

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

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

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

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

Interference with, or reduction of the **quality of, social, school, or work functioning.**

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

- 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 loses things necessary for tasks and activities.
- Is often easily distracted.
- Is often forgetful in daily activities.



Six or more symptoms of **hyperactivity-impulsivity** <16, or five or more for 17+

- Often **fidgets** with or taps hands or feet, or squirms in seat.
- 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 5 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.

ADHD: most common comorbidity in TS

- **Onset** : 3-5 years.¹
- Lifetime diagnosis: **54%**.²
- **May improve** in adolescence.³
- **In adults**: 26% in women, 21% in men.⁴
 - Difficulties with executive functions in daily life and relating to peers.
 - Continue to require support.⁵



¹Martino et al., 2017, ²Hirschtritt et al., 2015, ³Groth et al., 2017, ⁴Lewin et al., 2012, ⁵Groth et al., 2017

TS and ADHD: shared symptomatology

- Attentional problems
 - Increased attentional focus on internal **sensory 'tic' information** may contribute to reduced resources available for external attention tasks
 - Engaging in **tic suppression**
 - **Compulsions** or mental rituals/obsessional thoughts
- Impairment in control
- Hyperactivity
- Anxiety, depression
- Behaviour problems
- Sensory processing issues
- Sleep disturbances
- Impairment in socialization and communication
- Repetitive patterns of behaviour

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 (greater overall psychosocial impairment?)
- Co-occurring ADHD may impair tic suppression
- Mental effort to suppress tics may accentuate inattention in ADHD
- Moderation of the effectiveness of **alpha agonists** for the treatment of tics ?
- Risk for aggressive and delinquent behaviour and conduct difficulties

Underdiagnosis of girls?

- **Males > females** (59% vs 42%; $P < 0.01$)^{1,2}
- Higher M/F ratios in clinical versus population-based samples.
- Similar severity.³
- Inattentive presentation: females > males.³

Externalising behavioural problems were predictors of diagnosis and treatment in females, whereas males may be prescribed medication based on ADHD diagnostic status alone.³



¹Hirschtritt et al., 2015 ; ²Girgis et al., 2022, ³Mowlem et al., 2019 (Parents of 19,804 twins (50.64% male) from the Swedish population completed dimensional assessments of ADHD symptoms)

Managing ADHD with tics

Alpha agonists

- Showed efficacy against tics, ADHD and oppositional behavior
- But moderate effect size and long latency of effect

Stimulants

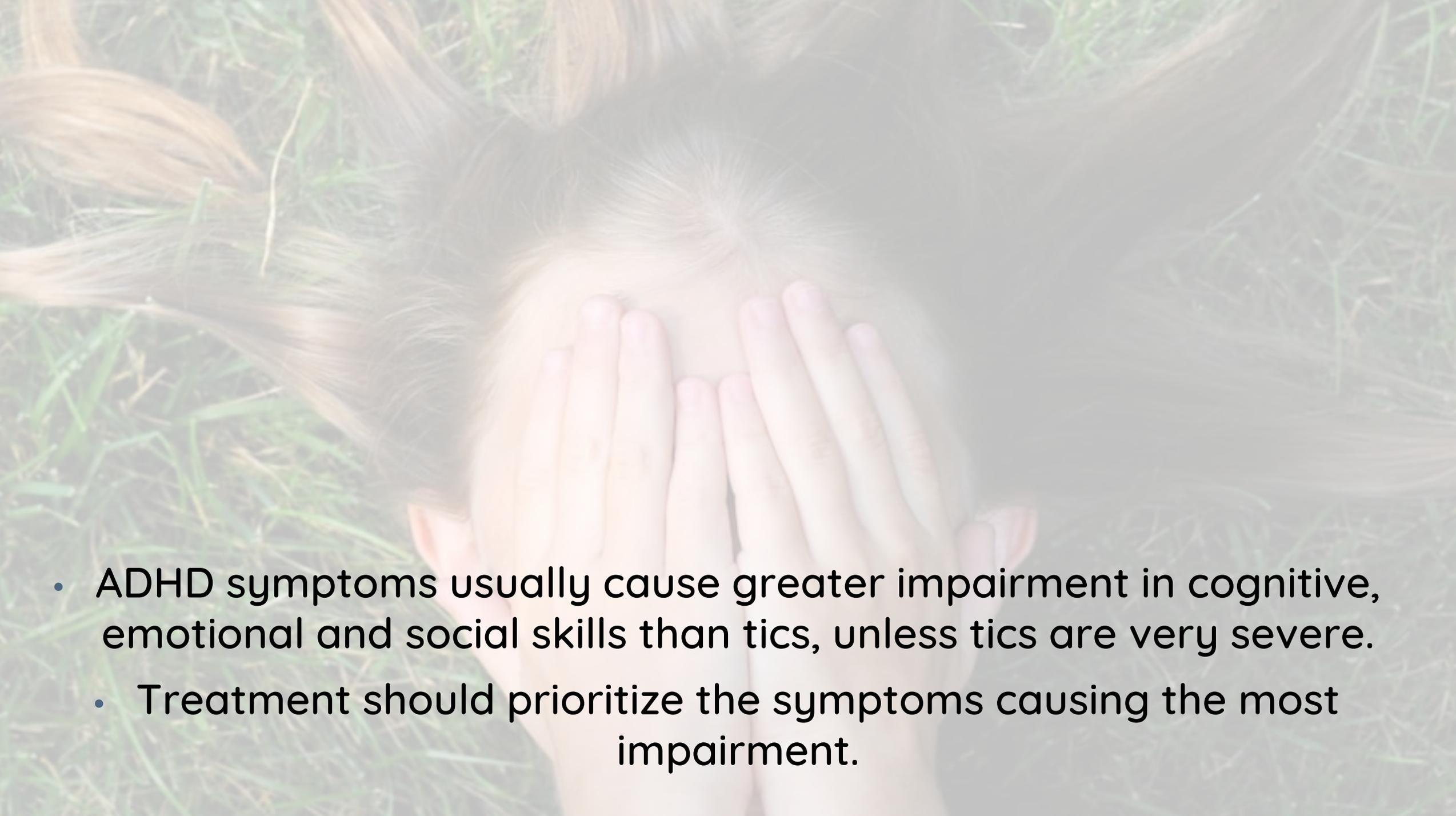
Exacerbation of tics?

Gorman, Gardner, Murphy, et al., 2015, Weisman et al., 2013.



Stimulants do **NOT** appear to worsen tics compared to placebo

- However, despite there being no overall group effect of stimulants on tics, clinical reports indicate that tics **may be exacerbated in certain individuals** (20%), at higher stimulant doses, with tic worsening reversible by dose reduction (in 2 to 3 weeks)
 - Comorbid ASD: more likely to have the sustained tic worsening
 - Improvement with methylphenidate in both ADHD and tic symptoms
- **Psychostimulants remain the first-line treatment for ADHD in patients with TS** (methylphenidate > dextroamphetamine)
- 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

- 
- 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.

OCD/OCBs

DSM 5 Criteria for OCD (1)

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 (2)

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

Specify if: tic-related, the individual has a current or past history of a tic disorder

OCD in Tourette syndrome

- **Onset:** 4-10 years ¹
- **Women++** ^{2,3}
- Prevalence: 30-50%³ (sometimes lower in community- based studies)^{4,5}
- Associated with **increased tic severity**
- **Compulsions are different from tics** ⁶ (respond to urges)



¹Bloch et Leckman, 2009, ²Lewin et al., 2012, ³Hirschtritt et al., 2015, ⁴Kurlan et al., 2002, ⁵Khalifa and Von Knorring, 2006, ⁶Martino et al., 2017

Tic-related compulsive behaviours

- Can be close phenomenologically with compulsions
- *Just-right* phenomena
- E.g. touching, tapping, grooming, evening-up^{1,2}
- More common in patients with co-existing tics and OCD.³

¹Leckman J F et al., 1994, ²Worbe et al., 2010, ³Cath et al, 2001



Treatment of OCD in TS

October 27, 2004

Cognitive-Behavior Therapy, Sertraline, and Their Combination for Children and Adolescents With Obsessive-Compulsive Disorder

The Pediatric OCD Treatment Study (POTS) Randomized Controlled Trial

The Pediatric OCD Treatment Study (POTS) Team

» Author Affiliations

JAMA. 2004;292(16):1969-1976. doi:10.1001/jama.292.16.1969

- First line treatment of OCD in individuals with (or without) tics should be **cognitive behavioural therapy**
- One RCT (POTS1) suggested that individuals with tics **may not respond as well as those without tics to SSRIs** for OCD symptoms
- Meta-analysis of 20 RCTs of CBT and SSRIs for pediatric OCD found that tic-related OCD moderates CBT efficacy, **suggesting that youth with TS may be more responsive to CBT**

Other psychiatric
comorbidities

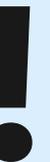
Anxiety disorders: 25-30%

- Women++¹
- Associated with tic severity^{2,3}
- Anxiety worsens tics
- Higher rates of tic-like attacks in this group
- Managing Parental/sibling anxiety – whole family / systemic approach

¹Hirschtritt et al., 2015, ²Coffey et al., 2000, ³Johnco et al., 2016

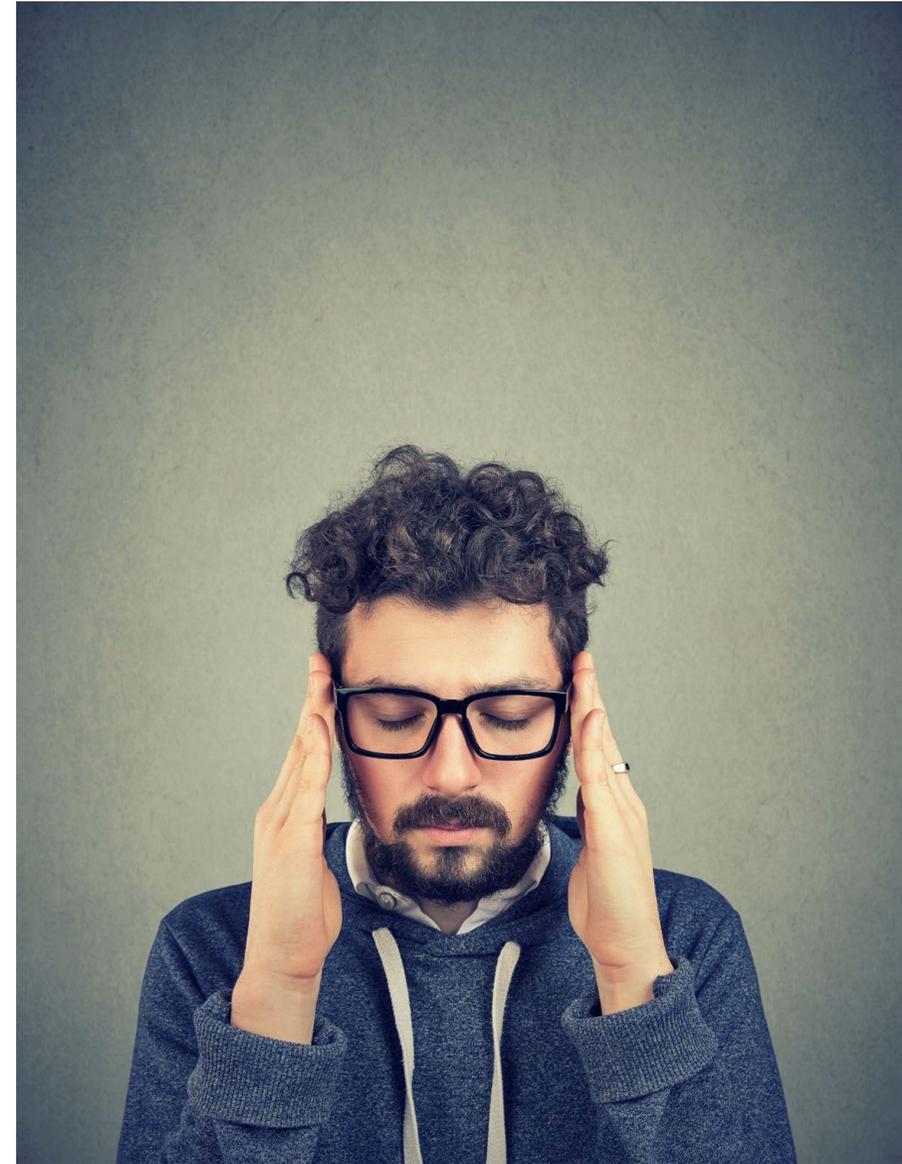


Anxiety/a distressing event does not start a tic disorder but may make it noticeable for the first time.



Depression: 30%

- Variable associations with depression; significant issue in adolescents and adults with TS⁵
- Women++¹
- Associated with tic severity^{2,3}
- **Increased risk of both dying by suicide (OR=4.4) and attempting suicide (OR=3.9)⁴**
 - This risk was reduced but remained substantial even after adjusting for psychiatric comorbidities.
 - Persistence of tics beyond young adulthood was a predictor of death by suicide.



Oppositional Defiant Disorder

- Severe and persistent negative, defiant, hostile behaviour; diff from conduct.
- 11%–54% of youth with TS
- Disruptive behaviors in 30%
- ADHD
- A higher frequency of conduct disorder was reported **with age and in boys**

Autism spectrum disorder

Overlap in symptoms:

- Stereotypies
- Sensory sensitivities
- Compulsions
- Just right perceptions

Impulsive behavior: rage/ explosive outbursts

Reported in 35% of children with TS
and 8% of adults¹

- Out of proportion to trigger
- Difficulty calming down
- Can persist in adolescence/adulthood
- Significantly associated with greater tic severity, & younger age of tic onset.²
- **More common when ADHD, OCD present.³**

¹Bundman et al 2000; ² Chen et al., 2013 ; ³Mol Debes et al., 2008



Trichotillomania (OC spectrum)

More common in TS-plus.
Can be **impairing**.

- The hair pulling can be automatic as well as focussed
- Can be related to obsessive need to pull combined with impulsivity, tic-like for some, can be rewarding
- CBT/ ERP with Habit reversal can help
- Medication: mixed results but Clomipramine can help



Substance use

Increased risk of any subsequent substance misuse outcomes

- alcohol-related disorder
- drug-related disorder
- substance-related death

(A Swedish cohort of 7832 individuals with a chronic tic disorder, mean age 13.4years, Virtanen et al., 2021).

The risk of different substance misuse outcomes in TS **remained significant after controlling for psychiatric comorbidity.**



Sleep disturbances: 25% in TS, maybe more?

Especially in the case of comorbid ADHD¹

- The number of arousals from sleep: higher in children with ADHD ?

A study using a prospective questionnaire in 123 youth with TS reported a **65% prevalence of sleep disorders irrespective of comorbid ADHD.**²

Factors affecting sleep:

- tic severity
- comorbid neurodevelopmental disorders
- medication use.

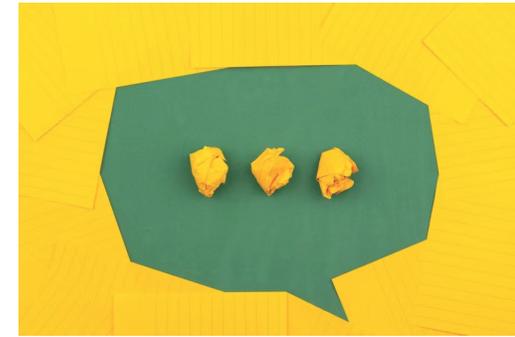
Supporting sleep / bedtime

- Usual sleep hygiene strategies (fixed bedtime, screens, environment, exercise in the day)
- Externalising attention strategies at bedtime Medications: Melatonin, Clonidine

Review

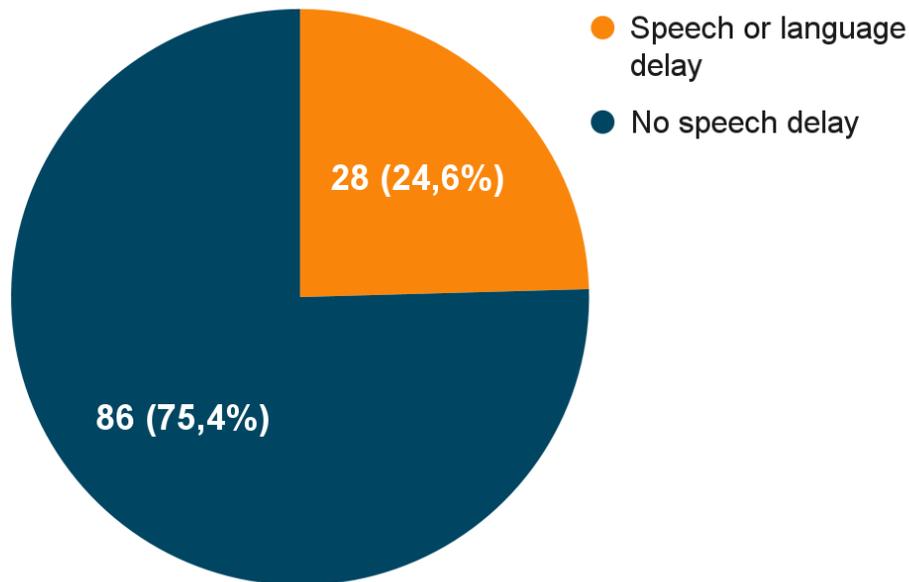
Developmental stuttering, physical concomitants associated with stuttering, and Tourette syndrome: A scoping review

Christelle Nilles^a, Lindsay Berg^a, Cassidy Fleming^b, Davide Martino^{c,d,e},
Tamara Pringsheim^{a,c,d,e,*}



Speech delay

Child Tic Disorder Registry, n=114 children



25/114 (22%) required speech therapy.

Speech or language delay :

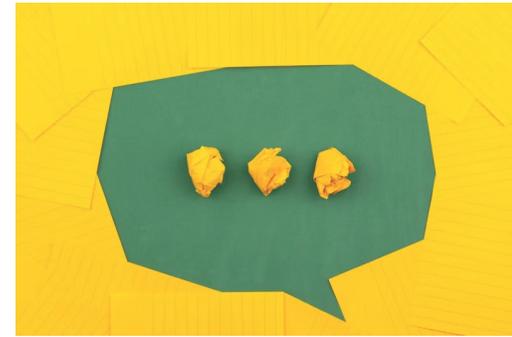
- No association with severity of tics
- No association with comorbid ADHD.

Prevalence in the overall population:

- Speech delay: 3.8% (95% CI 2.9-5.0%)

in 1,328 6-yo English-speaking children¹

Developmental stuttering & Tourette



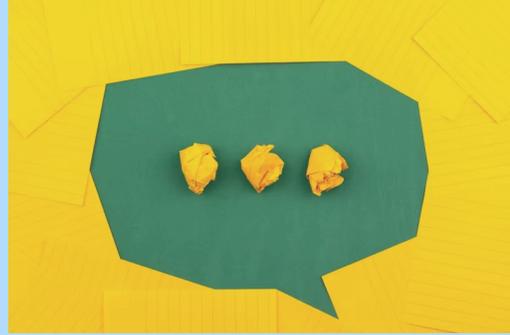
Prevalence

- **31%** stuttered or had stuttered (n=246 patients with TS vs controls, $p < 0.0005$)¹
- **15%** diagnosed with DS (n=85 adults with TS) ²
- **8%** exhibited stuttering (large multisite study)
- **15%** had been stuttering for > 6 months (n=314 children with TS)

Similarities

- Frequent neurodevelopmental disorders, male predominance, comorbidities, waxing and waning course, good prognosis
- Preceded by an anticipatory sensation, +/- suppressible, response to neuroleptics and CBT.
- Polygenic disorders, dysfunction of the cortico-basal ganglia-thalamocortical loop.⁴

Specific disfluency pattern in TS

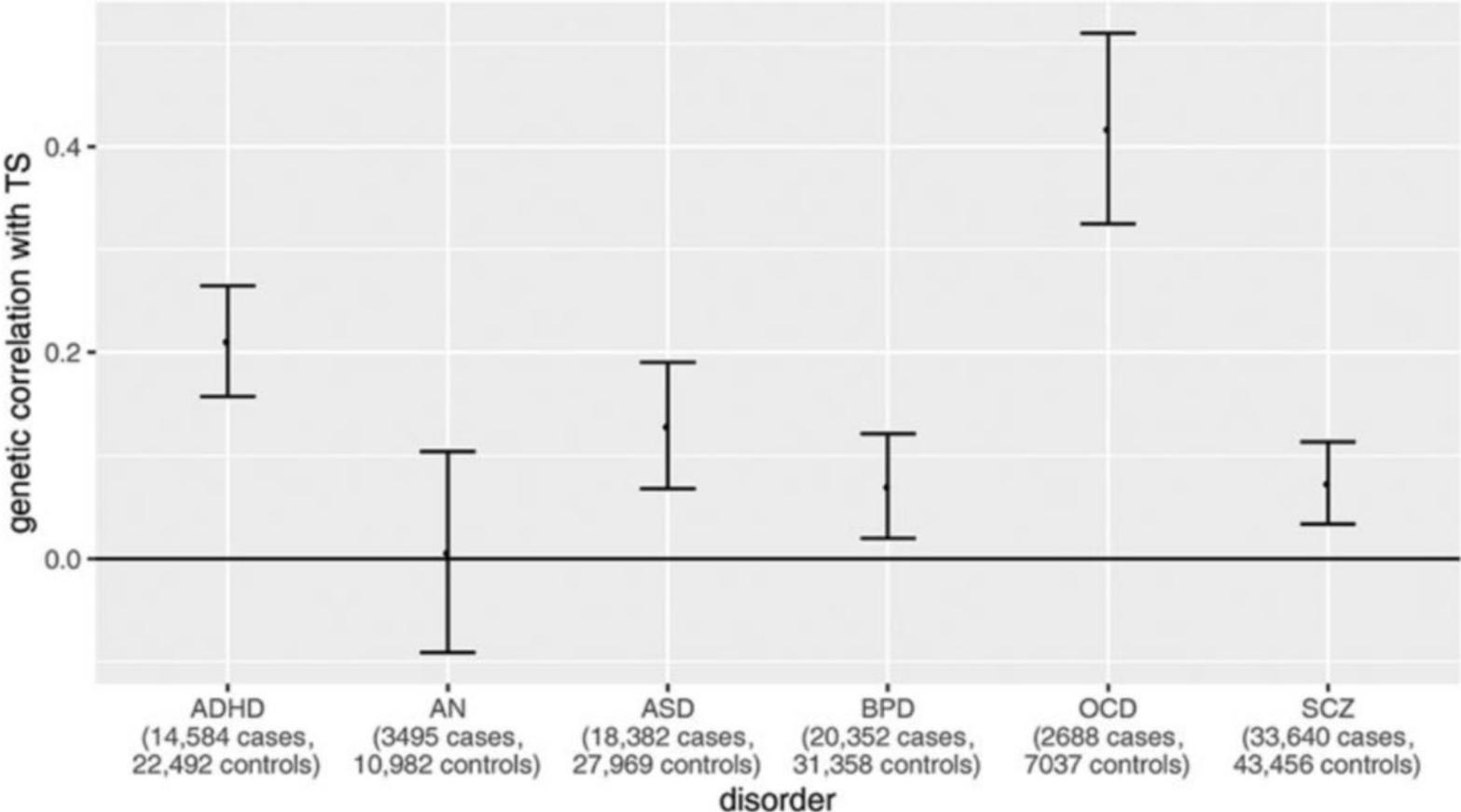
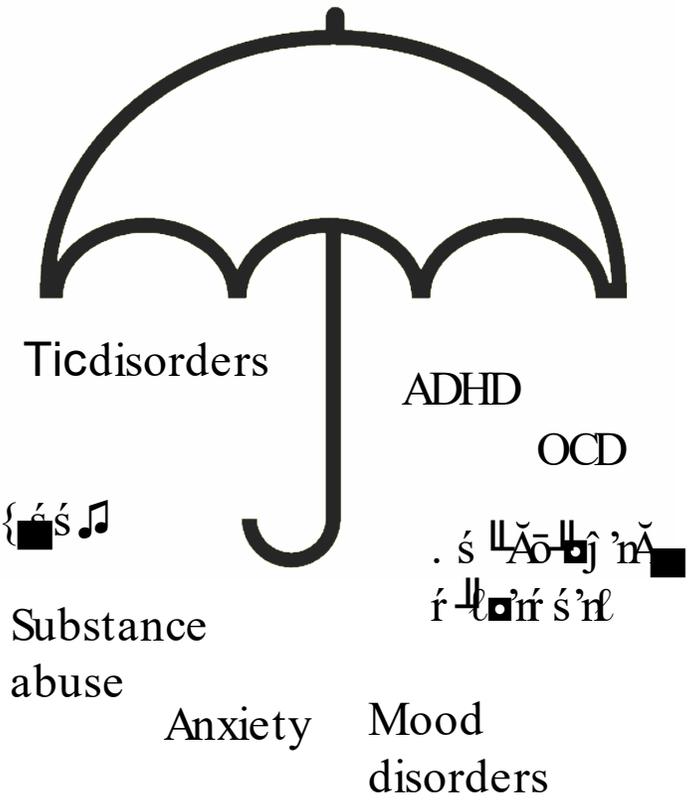


- **Majority of typical disfluencies:** interjections, repetitions and revisions
- Cluttering behaviours
- **Complex phonic tics** (end of speech)
- Atypical disfluencies (but no prolongations and blocks)
- Speech or language delay
- Probably underdiagnosed -> not addressed specifically in speech therapy.
- Specific management?



Why such an overlap of disorders?

The neurodevelopmental umbrella



Functional tic-like behaviours

Baking with Tourette's



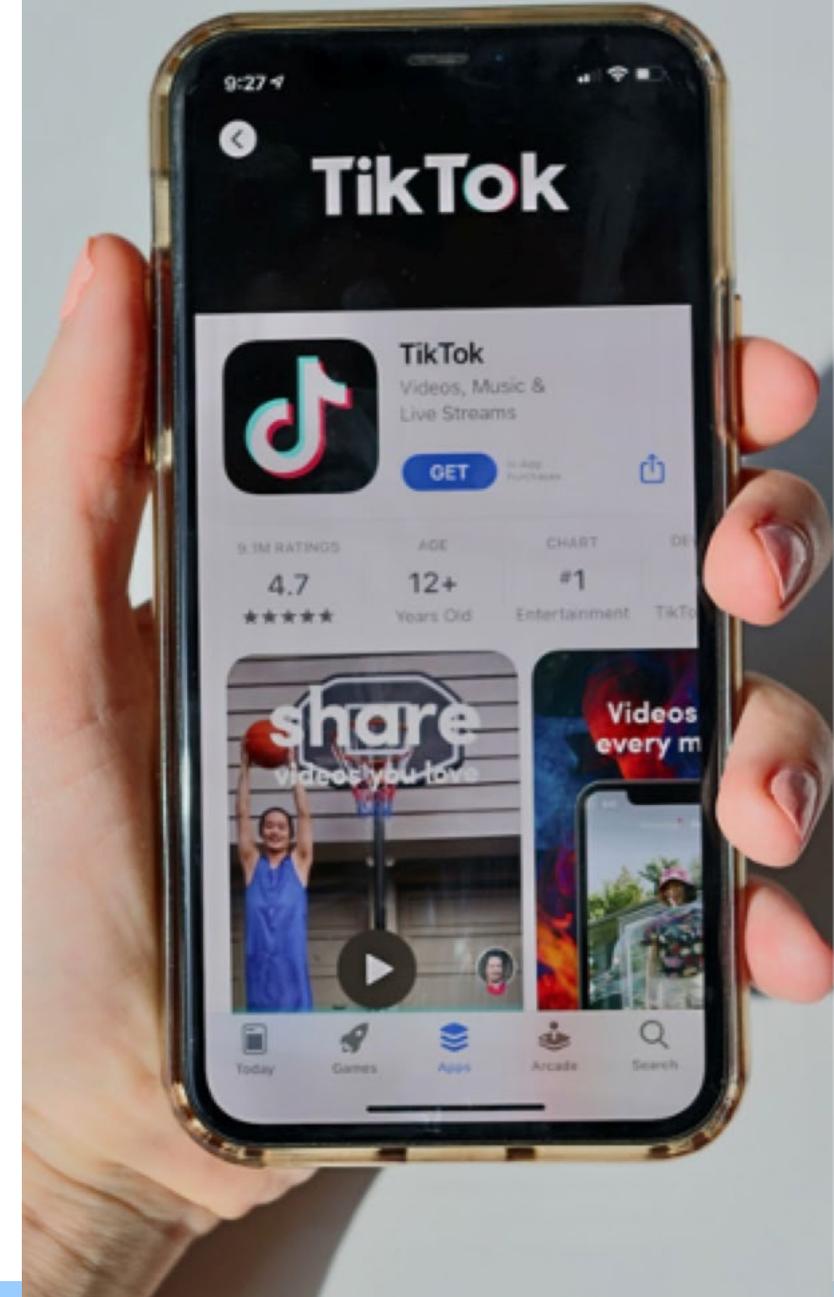
Functional tic-like behaviours (FTLBs)

Movements or vocalizations that resemble tics.

Unlike Tourette syndrome:

- **Late** and **rapid** onset
- Large-amplitude arm movements, self-injurious behaviour, **coprophenomena**, bizarre words and phrases.
- **Complex tics** > simple tics
- May be influenced by popular references (**TikTok**).

Pringsheim et al., 2021; Müller-Vahl et al., 2021



How to diagnose FTLBs

Pringsheim et al, 2022

Clinically definite diagnosis : 3 major criteria

Clinically probable diagnosis : 2 major criteria + 1 minor criterion

Major criteria	Age onset \geq 12 yr
	Rapid onset and evolution of symptoms
	Phenomenology : 4/9
Minor criteria	Comorbid depression or anxiety disorder
	Other functional neurological symptoms/ somatoform disorders

Complex > simple tic-like behaviours

Variable reproduction

Complex tic-like behaviours: banging chest/head, tapping, hitting others, sign language, throwing objects, offensive gestures, drop attacks, context dependent, self- injury or injury to others

Do not to follow the typical rostrocaudal progression

Coprolalia, context-dependant words, statements

Popular culture references

Large variation in symptom frequency and intensity in a day

Tic-like behaviours change rapidly

More tic-like behaviours during the examination

Urbans

Comorbid functional tic-like behaviours in TS

Data from international Registry, 294 patients with FTLBs (97% adolescents/young adults, 87% females)
(Martino et al, 2023)

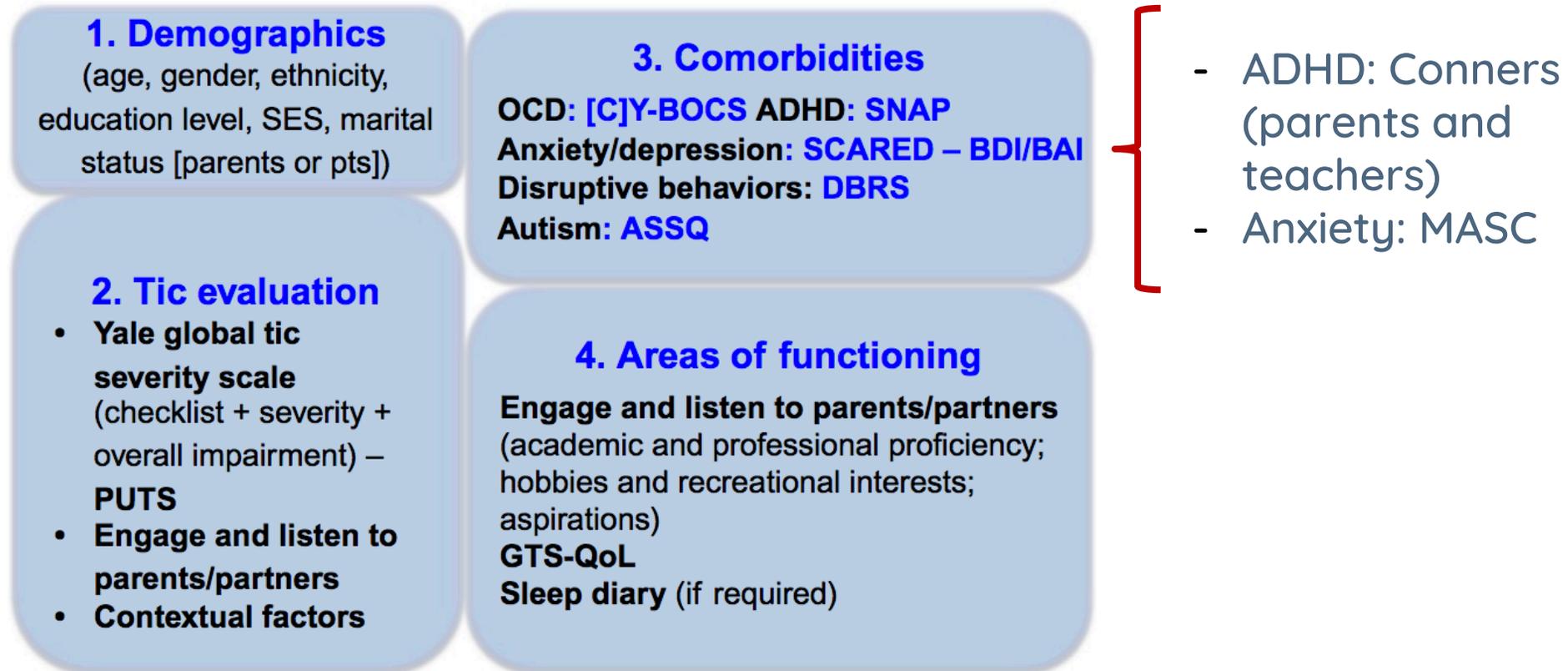
Around 20% of patients had pre-existing primary tic disorder

Sample of 71 patients (38.0% female, mean age: 21.5y) with TS + FTLB. (Müller-Vahl et al, 2024)

- Compared to a large TS sample, patients with TS + FTB were more likely to
 - be female
 - have coprophenomena-like symptoms
 - have atypical influential factors
 - have atypical descriptions of premonitory sensations
 - have higher rates of comorbid obsessive-compulsive disorder
 - have self-injurious behaviors.

Assessment of comorbidities

Assessment



In conclusion

- Having mental health comorbidities is the rule, not the exception in Tourette syndrome
- Most common: ADHD and OCD in children
- Often more impairing than the tics
- Screening and multidisciplinary management is crucial

On the beach
by Benjamin Edwards (age 11)



Acknowledgements

Varese



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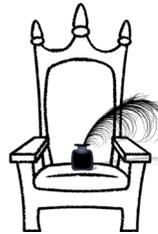
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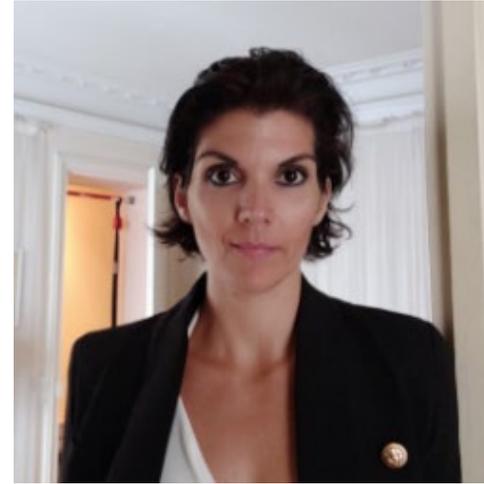


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