17th International Conference on Tourette Syndrome & Tic Disorders

TS school Athens

Tourette syndrome and comorbidities

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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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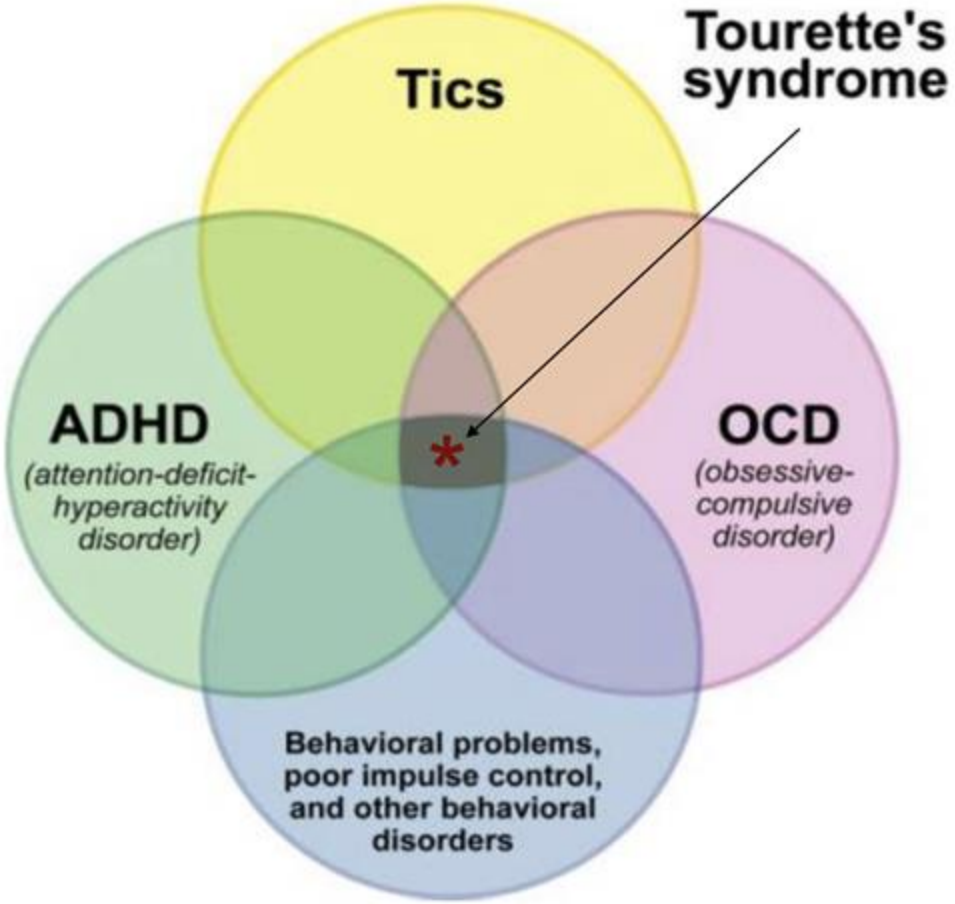
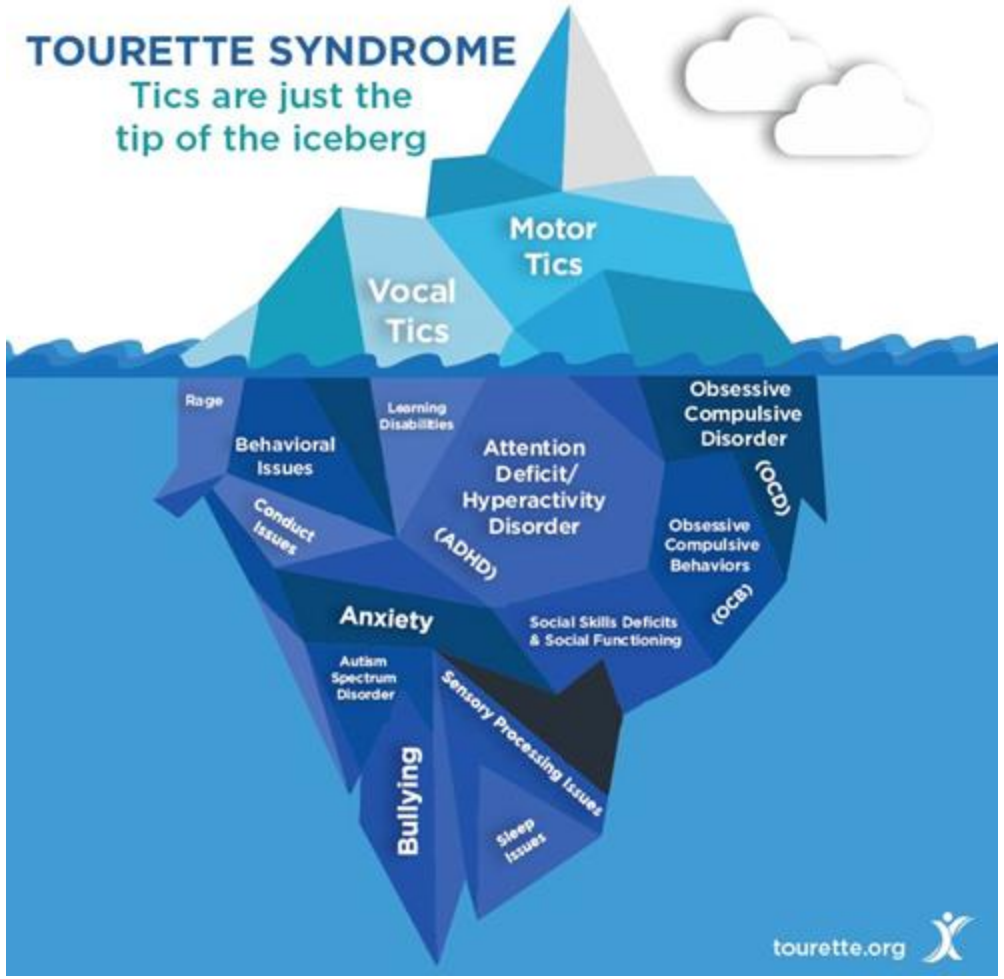


- Largest and most comprehensive study of comorbidity in people with TS
- Cross-sectional structured diagnostic interviews, n=1374 with TS, mean age 19.1 years +/-13.5 and 1142 members of unaffected families, from tic disorder specialty clinics in the United States, Canada, Great Britain, and the Netherlands

Jankovic, Joseph, Tourette’s syndrome. N Engl J Med 2001; 345: 1184-1192

TS – a complex neuropsychiatric syndrome



86%

Had ≥ 1 neurodevelopmental or mental health comorbidities

58%

Had two comorbidities

Hirschtritt et al, 201

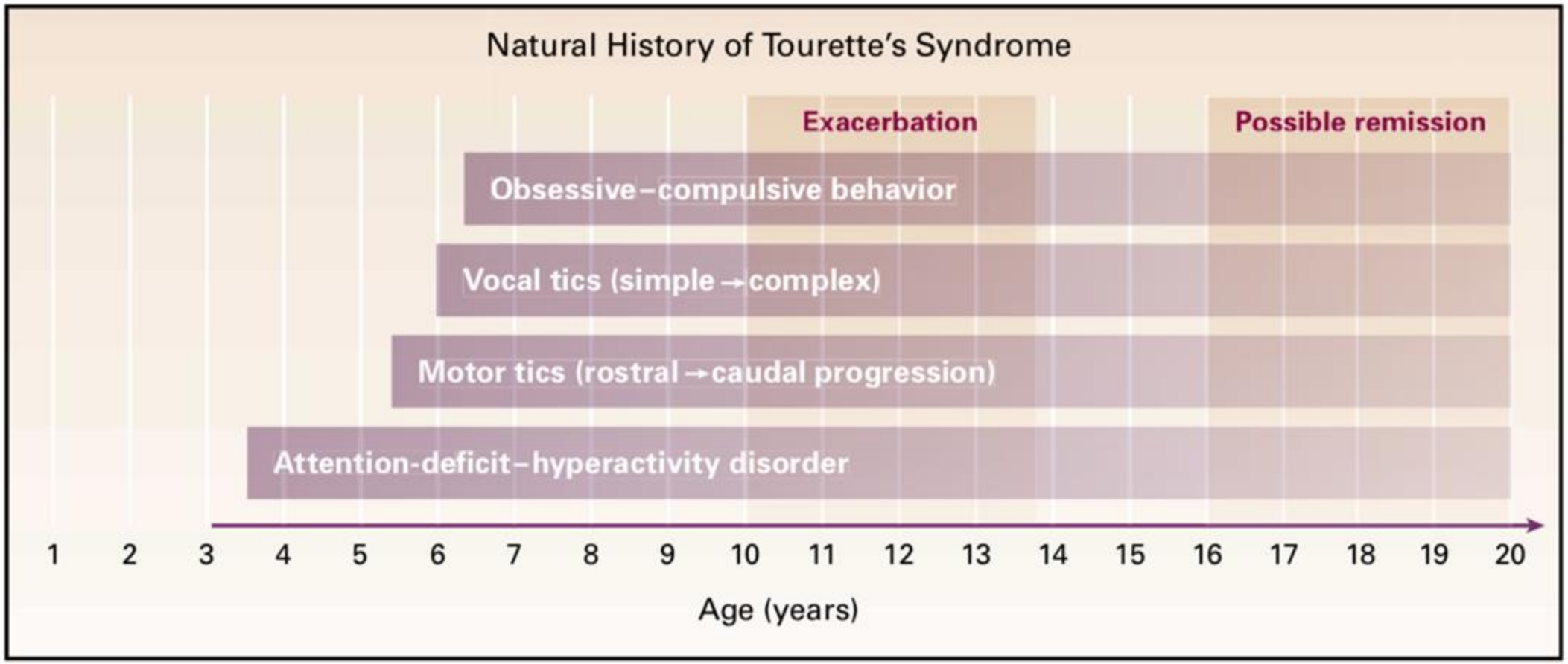
Objectives

- 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%
- Mood disorder 10-20%
- Conduct & ODD 10-30%
- ASD 5-10% (broader phenotype 20%)
- Specific learning difficulties 23%
- Dyspraxia 2-6%
- Injury
- Migraine/headaches
- Sleep disorders
- Stereotyped movements
- Teeth grinding/bruxism
- Trichotillomania, nail biting/skin picking
- Speech delay/stuttering

Onset of comorbidities



Jankovic, 2001

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!!!

[1]Storch et al., 2007; Jalenques et al., 2012 ; [2] Eddy et al., 2011; [3] Muller-Vahl et al., 2010 ; [4]Pringsheim et al., 2009; Ganos and Martino, 2015

ADHD

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)

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

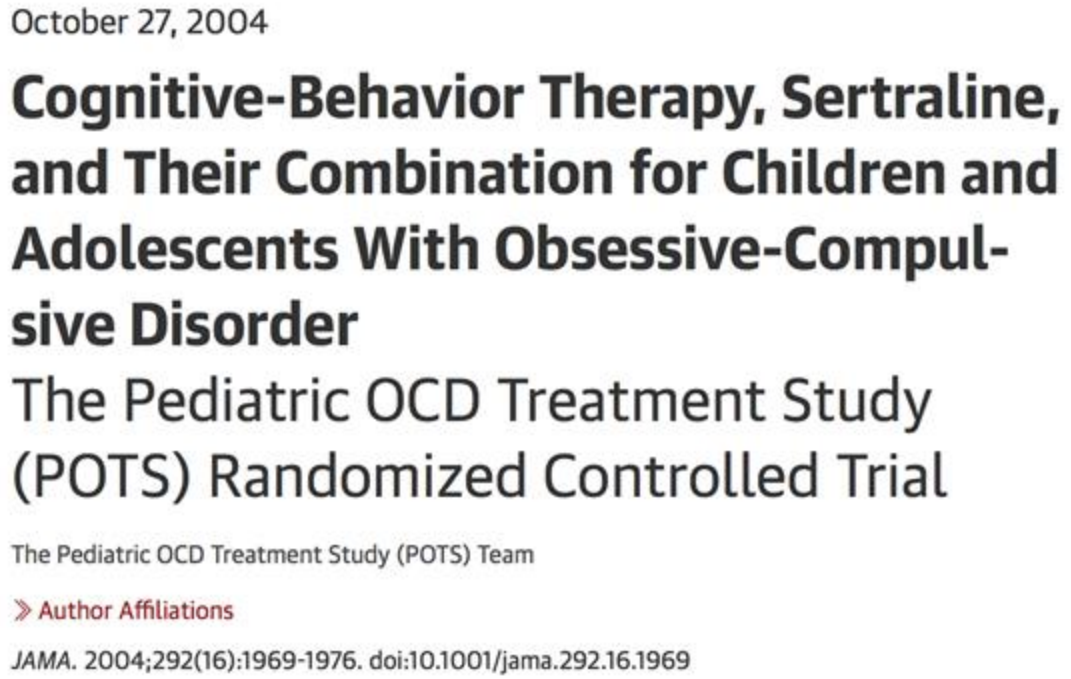
Tic-related compulsive behaviours

- 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]

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

Treatment of OCD in TS

- 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



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

- 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

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

!

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

!

Depressive disorders: 30%

- Variable associations with depression; significant issue in adolescents and adults with TS[5]
- 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.

[1]Lewin et al., 2012, [2]Rizzo et al., 2017, [3]Lewin et al., 2012, [4]Fernández de la Cruz et al., 2017, [5]Chou et al, 2013

Oppositional Defiant Disorder (11-54%)

- Severe and persistent negative, defiant, hostile and oppositional behavour
- Conduct disorder: violation of the rights of others or societal norms
  - Higher frequency **with age and in boys**
- Associated with ADHD

Eapen and Robertson, 2008, Hirschtritt et al., 2015, Maughan et al, 2004

DSM 5 Criteria for Autism spectrum disorder (1)

A. Persistent deficits in social communication and social interaction across multiple contexts:

1) Deficits in social-emotional reciprocity.
2) Deficits in nonverbal communicative behaviors used for social interaction
3) Deficits in developing, maintaining, and understanding relationships

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following:

1) Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behavior
2) Highly restricted, fixated interests that are abnormal in intensity or focus
3) Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment

DSM 5 Criteria for Autism spectrum disorder (2)

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay (intellectual disability and ASD frequently co-occur)

ASD and TS (10-25%)

Overlap:

- **Stereotyped repetitive behaviors** that are aggravated or worsened by heightened emotional states (tics and stereotypies)
- Higher proportion of **males**
- Children with ASDs appear similar to children without ASDs with respect to **overall tic severity**

Tools

- Social Responsiveness Scale (SRS)
- Social Communication Questionnaire (SCQ); Children's Communication Checklist.
- ADI-R (semi-structured interview) and/or ADOS (observation)

Comorbidities

- Children with tic disorders + ASDs have greater overall rates of comorbidity (ADHD, rage attacks, ODD) compared with children with tics without ASDs

Treatment

- Neuroleptics?

Eapen and Robertson, 2008, Hirschtritt et al., 2015, Maughan et al, 2004, Pringsheim and Hammer, 2013

Impulsive behaviour: rage/ explosive outbursts

Reported in 35% of children with TS and 8% of adults[1]

- 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]**

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

Trichotillomania (3-6%)

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

Bloch et al 2007

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.**

Screening for drug/alcohol use should be part of the standard clinical routine, especially if comorbid ADHD

Sleep disturbances: 25% in TS, maybe more?

Especially in the case of comorbid ADHD[1]

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

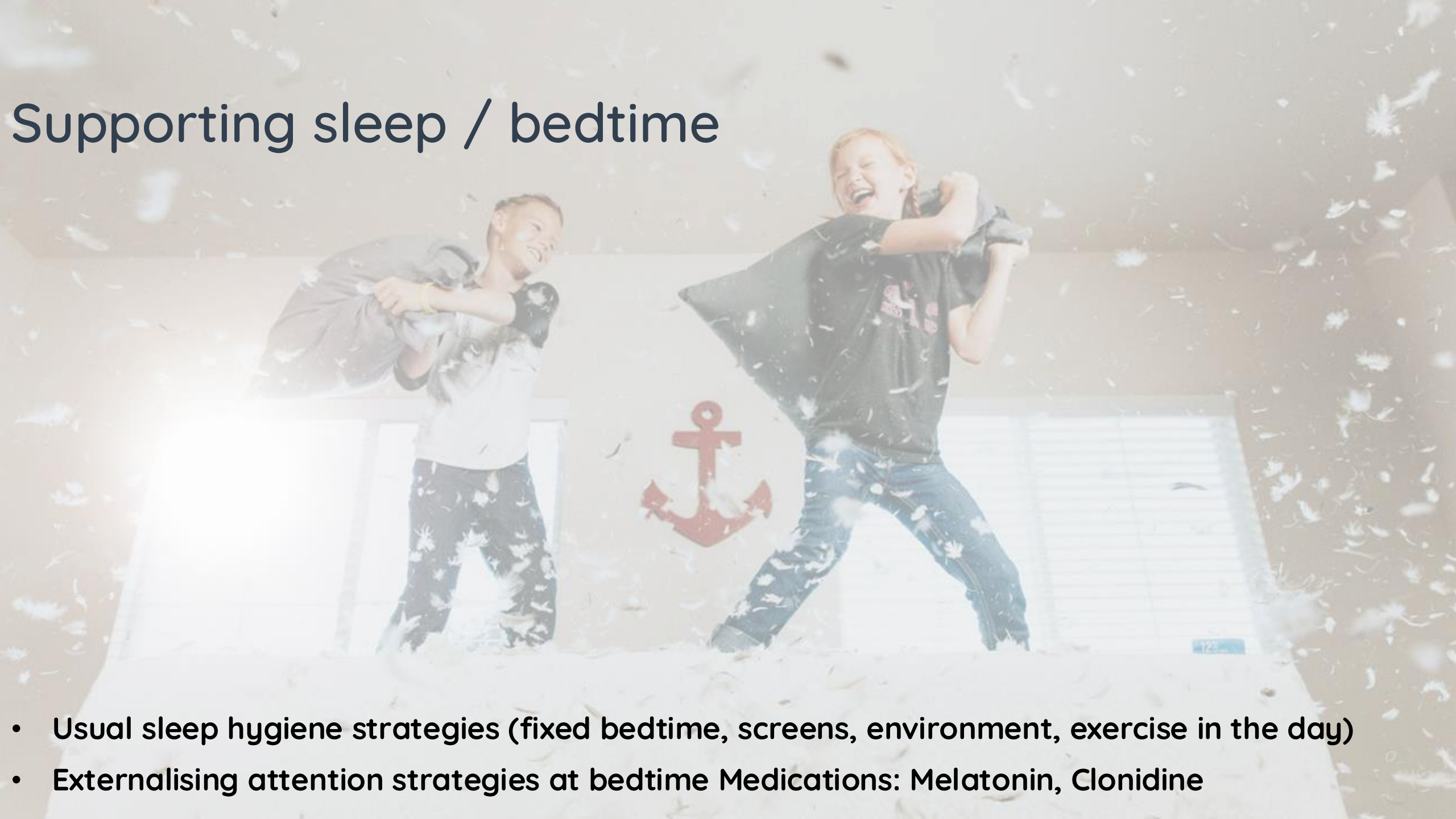
A study using a prospective questionnaire in 123 youth with TS reported a **65% prevalence of sleep disorders irrespective of comorbid ADHD.** [2]

Factors affecting sleep:

- tic severity
- comorbid neurodevelopmental disorders
- medication use.

[1] Freeman et al., 2000, [2] Ghosh et al., 2014

Supporting sleep / bedtime



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

Pain

Table 1: Classification of Pain in Relation to Tic Disorders

1. Pain Caused by Tics or Compulsions
   - A) Exertional
     - i) Muscular pain due to excessive contraction
     - ii) Skeletal or joint pain
     - iii) Neuropathic pain (due to spinal cord, radicular or peripheral nerve compression)
   - B) Traumatic
     - i) Pain in a body part struck by a moving limb
     - ii) Pain in a moving body part striking something nearby
     - iii) Self-mutilation (including biting)
     - iv) Pain from compulsive touching of hot or sharp objects
     - v) Pain inflicted on others from tics or compulsions
2. Pain Caused by Suppression of Tics
3. Pain Relieving Tics

- premonitory urge-related pain
- associated primary pain syndromes.

Riley and Lang., 1989, Green et al, 2025 (comprehensive review), Lavenstein et al, 2016

- Pain is reported by 47%–60% of individuals with TS
- Negatively impacts quality of life.
- Carpal tunnel syndrome, myelopathy

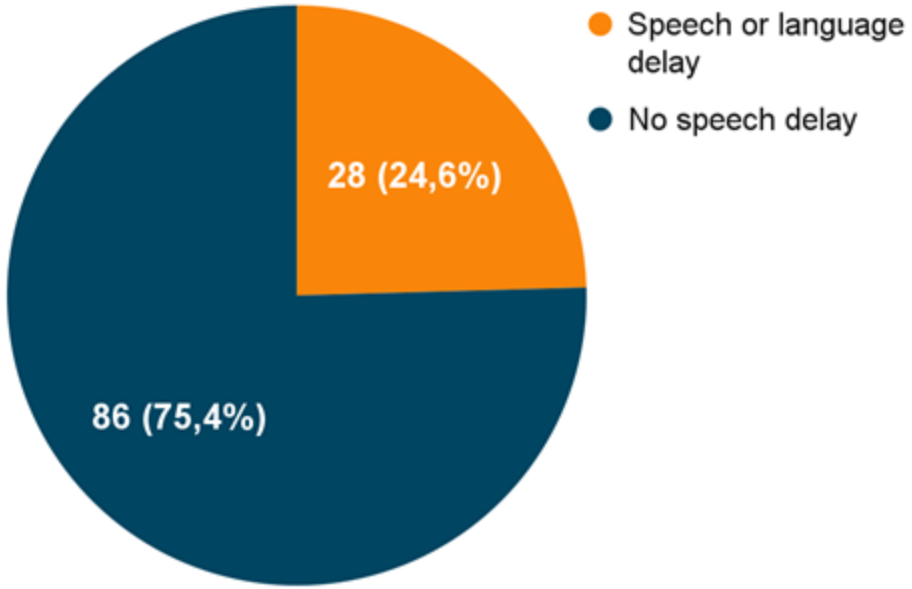
Review

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 children[1]

[1]Shriberg et al., 1999

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]

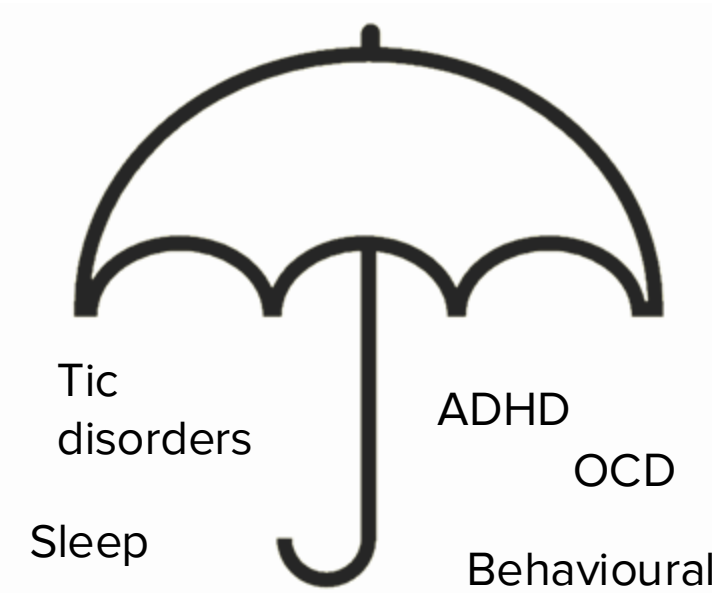
[1]Comings & Comings, 1987; [2] Pauls et al., 1993 ; [3] Freeman et al., 2000; [4] Mol Debes et al., 2008

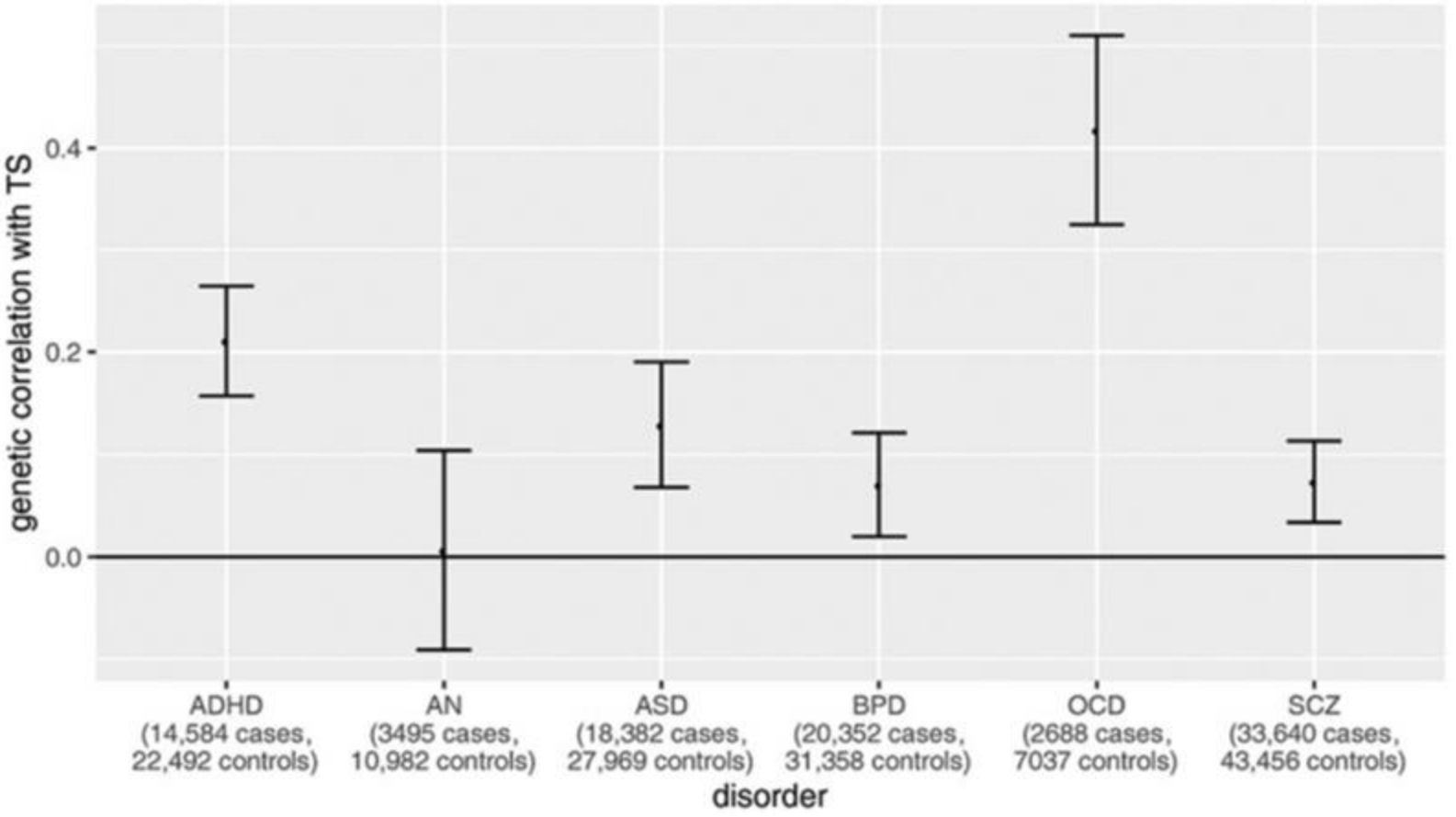
Specific disfluency pattern in TS

- **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





Domènech *et al*, 2021

Functional tic-like behaviours

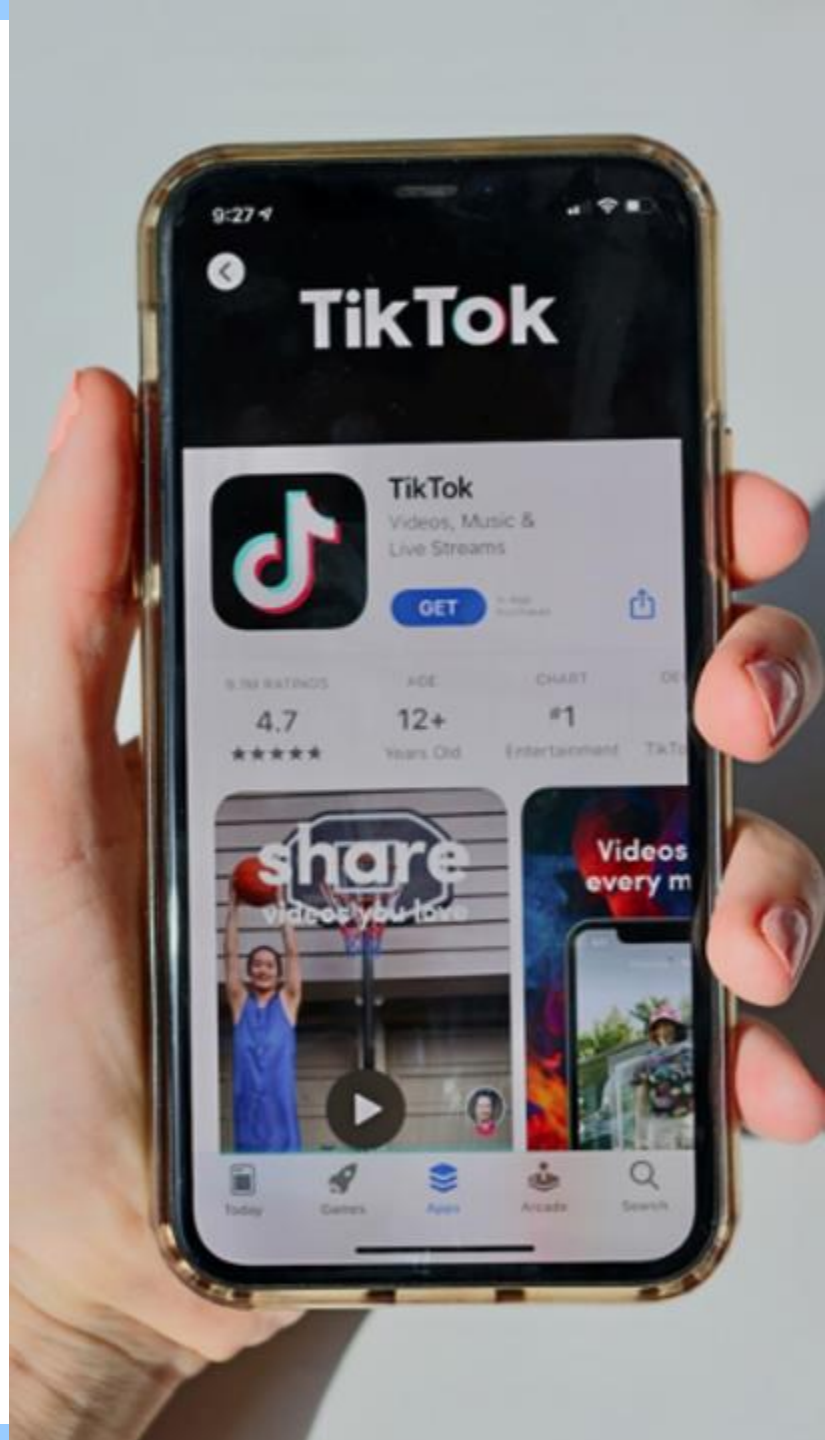
Functional tic-like behaviours (FTLBs)

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



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)

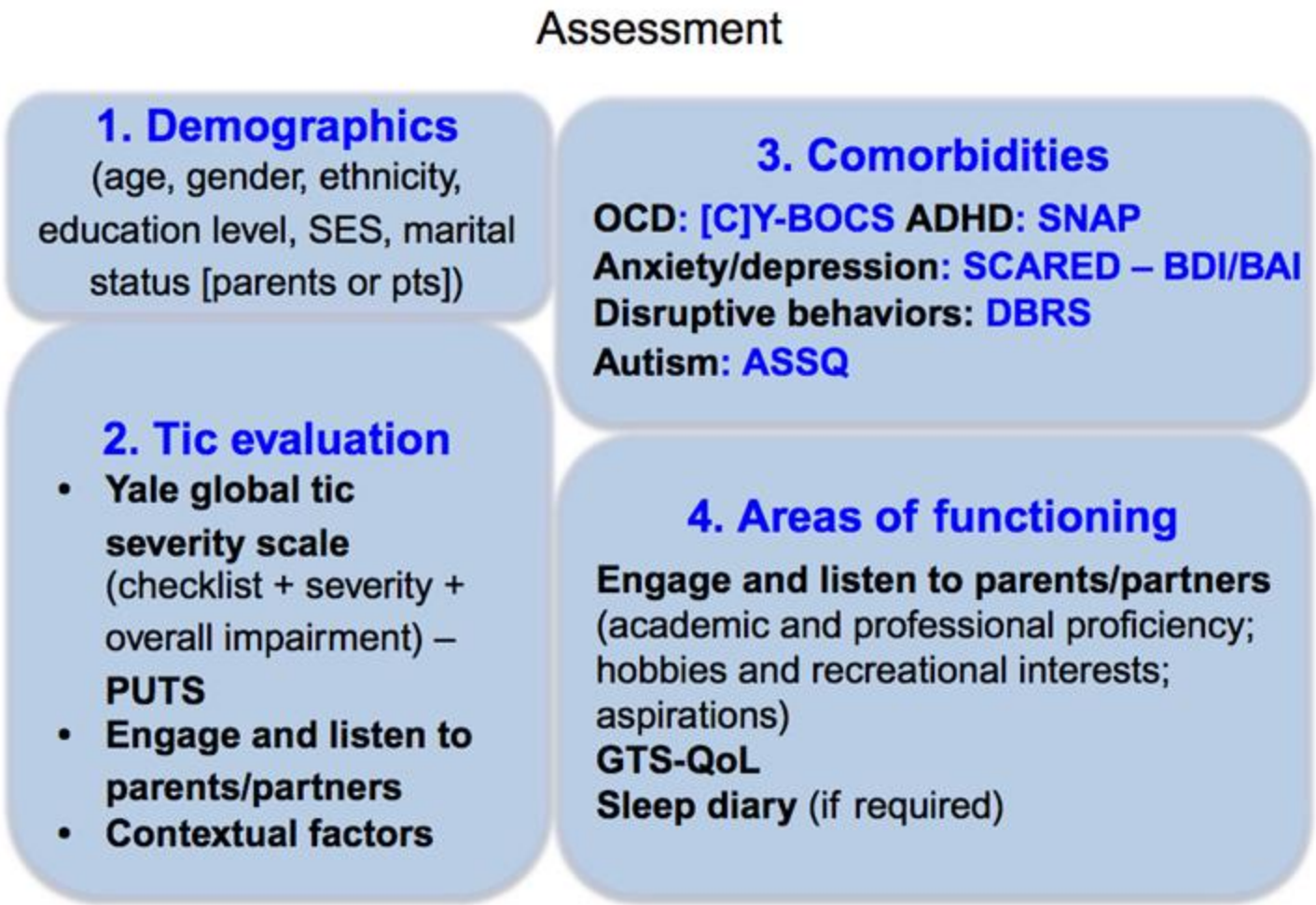
- **Compared to a large TS sample, patients with TS + FTB were more likely to**
  - be female
  - have coprophenomena-like symptoms
  - have atypical influential factors
  - have atypical descriptions of premonitory sensations
  - have higher rates of comorbid obsessive-compulsive disorder
  - have self-injurious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

In Adults

The Calgary and Paris Adult Tic Registry

Comorbidities, n (%)	N=218
Anxiety	**108 (49.5%)**
ADHD	**78 (35.8%)**
Depression	**75 (34.4%)**
OCD	**43 (19.7%)**
Schizophrenia	2 (0.9%)
Bipolar disorder	2 (0.9%)
Personality disorder	4 (1.8%)
Substance use disorder	6 (2.8%)
None	**46 (21.1%)**

Assessment of comorbidities



- ADHD: Conners (parents and teachers)
- Anxiety: MASC

Martino et al, 2017

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)