ADHD & tics: clinical overview

PROF. KERSTIN JESSICA VON PLESSEN

So does ADHD….

ICD-10:
F90-Hyperkinetic disorders

(F90-F98) BEHAVIOURAL AND EMOTIONAL DISORDERS USUALLY OCCURRING DURING CHILDHOOD AND ADOLESCENCEC

Behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98)

F90 Hyperkinetic disorders

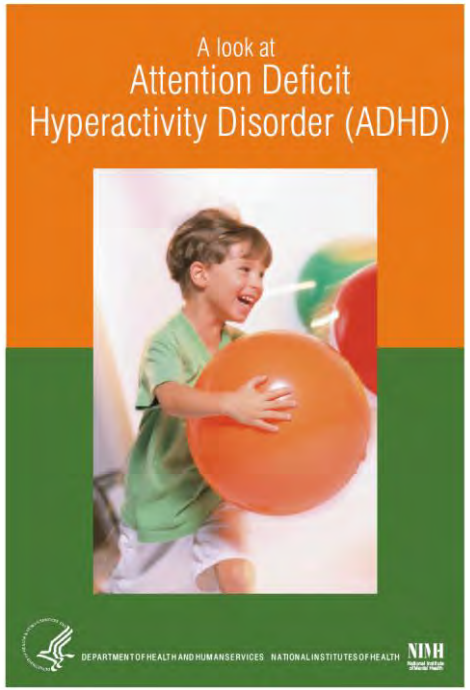
A group of disorders characterized by an early onset (usually in the first five years of life), lack of persistence in activities that require cognitive involvement, and a tendency to move from one activity to another without completing any one, together with disorganized, ill-regulated, and excessive activity. Several other abnormalities may be associated. Hyperkinetic children are often reckless and impulsive, prone to accidents, and find themselves in disciplinary trouble because of unthinking breaches of rules rather than deliberate defiance. Their relationships with adults are often socially disinhibited, with a lack of normal caution and reserve. They are unpopular with other children and may become isolated. Impairment of cognitive functions is common, and specific delays in motor and language development are disproportionately frequent. Secondary complications include dissocial behaviour and low self-esteem.

Excl.: anxiety disorders (F41.-)
mood [affective] disorders (F30-F39)
pervasive developmental disorders (F84.-)
schizophrenia (F20.-)

F90.0 Disturbance of activity and attention

Attention deficit:
- disorder with hyperactivity
- hyperactivity disorder
- syndrome with hyperactivity

Excl.: hyperkinetic disorder associated with conduct disorder (F90.1)



ICD-11

ICD-11 specifies different types of ADHD: combined presentation (both inattentive and hyperactive-impulsive symptoms), predominantly inattentive, and predominantly hyperactive-impulsive, as well as: adds a further two: ‘other specified presentation’ and ‘presentation unspecified’

In ICD-11, Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity that negatively impacts functioning. These symptoms must be present since early to mid-childhood (typically before age 12) and persist for at least 6 months.

Key aspects of the ICD-11 definition:

- **Inattention:** Difficulty sustaining attention, distractibility, and organizational problems.
- **Hyperactivity/Impulsivity:** Excessive motor activity, difficulty remaining still, and impulsivity in actions.
- **Onset:** Symptoms must be present from early to mid-childhood.
- **Duration:** The pattern of symptoms must persist for at least 6 months.
- **Impact:** The symptoms must negatively impact academic, occupational, or social functioning.

ADHD DSM 5

Subtypes
- **Predominantly hyperactive/impulsive**
- **Predominantly inattentive**
- **Combined**

Inattention: Six (or more) of the following symptoms have persisted for at least 6 months *to a degree that does not correspond to the developmental level and has direct negative effects on social and academic/professional activities*

Hyperactivity and impulsivity: Six (or more) of the following symptoms persisted for at least 6 months:

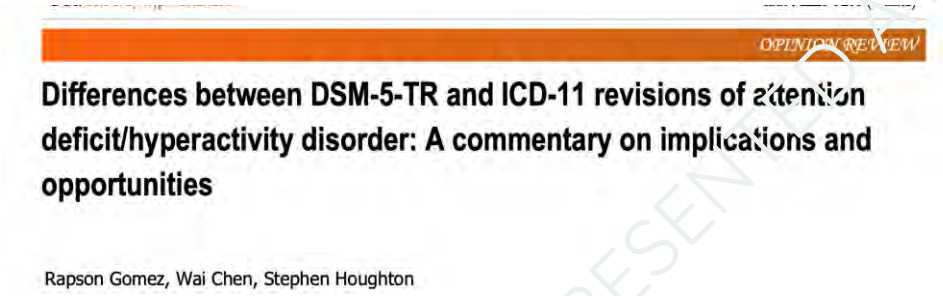
Symptoms present before the age of 12.

Several of the symptoms of inattention or hyperactivity/impulsivity are present in two or more situations

It is clearly evident that symptoms interfere with, or reduce, the quality of social, academic or occupational functioning.

Symptoms are not best explained by another mental disorder

Differences ICD-11 and DSM 5?


OPINION REVIEW

Differences between DSM-5-TR and ICD-11 revisions of attention deficit/hyperactivity disorder: A commentary on implications and opportunities

Rapson Gomez, Wai Chen, Stephen Houghton

- (1) The number of diagnostic criteria for inattention (IA), hyperactivity (HY) and impulsivity (IM) symptoms (i.e., DSM-5-TR has nine IA and nine HY/IM symptoms, whereas ICD-11 has eleven IA and eleven HY/IM symptoms)
- (2) the clarity and standardization of diagnostic thresholds (i.e., the diagnostic thresholds for symptom count in IA and HY/IM domains are explicitly specified in DSM-5-TR, whereas in ICD-11 they are not)
- (3) the partitioning of HY and IM symptoms into sub-dimensions (i.e., difference in partitioning HY and IM symptom domains relates to the differences between the current and previous editions of DSM and ICD, and this has important research implications).

Item	*n*	%
Females	1,259	18.5
Adopted	120	1.8
Twins	106	1.6
TS/tic family history	3,624	51.7
Tic severity mild	2,277	33.7
Tic severity moderate	3,386	50.2
Tic severity severe	1,088	16.1
Pre-/perinatal problems	1,102	16.2
TS-only (no comorbidity)	967	14.2
ADHD comorbid	3,783	55.6
OCD comorbid	1,515	22.3
OCB comorbid	2,219	32.6
ODD/CD comorbid	840	12.3
LD comorbid	1,494	22.0
Mood disorder comorbid	1,152	16.9
Anxiety disorder comorbid	1,141	16.8
PDD comorbid	311	4.6
Mental retardation comorbid	230	3.4
Anger control problems	1,813	27.6
Sleep problems	1,182	17.8
Self-injurious behaviour (SIB)	1,006	14.8
Coprophenomena	885	13.0
Stuttering/speech dysfluency	485	7.1
Social skill deficits	1,268	18.6
Inappropriate sexual behaviour	257	4.3
Trichotillomania	179	2.6
Left-handed	349	9.5
Ambidextrous	133	3.0
Right-handed	3,186	66.9
Child (<18 years)	5,108	75.1
Medication for tics (ever)	3,647	54.2

Freeman et al. 2007

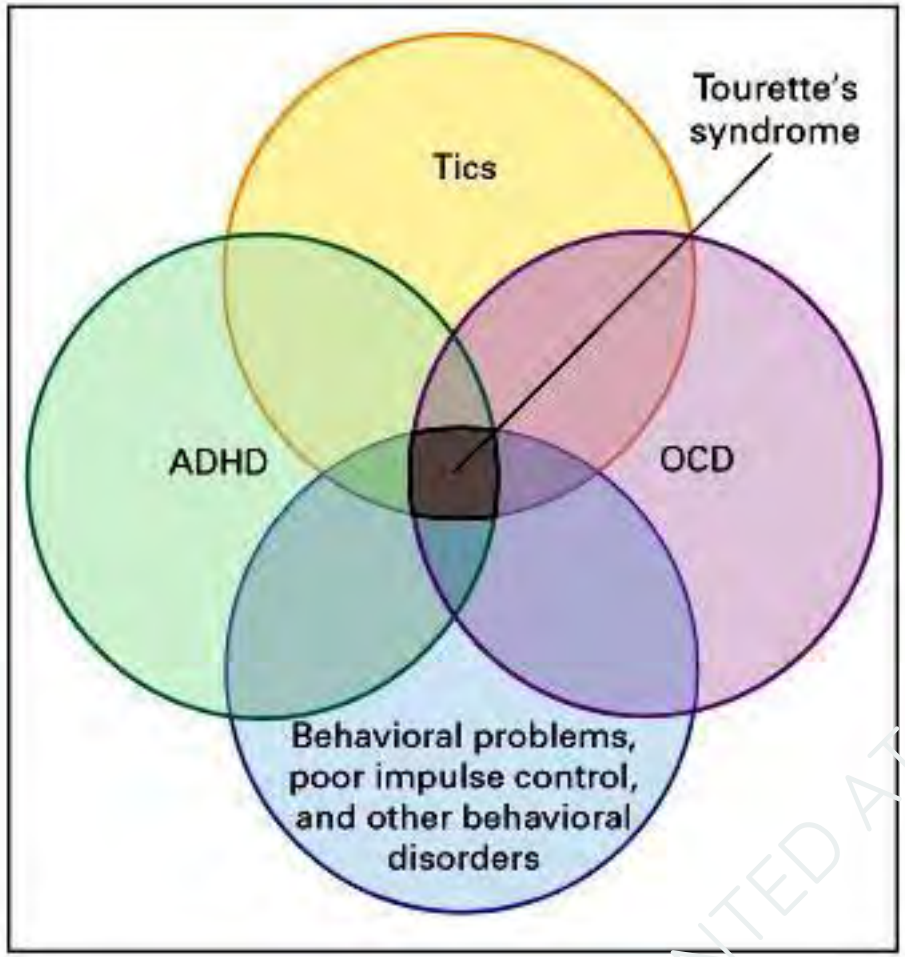
Table 1. Lifetime Prevalence of Psychiatric Disorders by Sex

	No./Total No. With Available Data (%)			
		Sex		
Comorbid Disorder	All TS-Affected Participants	Male	Female	*P* Value[a]
Obsessive-compulsive spectrum[b]	904/1368 (66.1)	645/1001 (64.4)	259/367 (70.6)	.03
Attention-deficit/hyperactivity	713/1314 (54.3)	564/962 (58.6)	149/352 (42.3)	<.001
Mood[c]	277/930 (29.8)	184/690 (26.7)	93/240 (38.8)	<.001
Anxiety[d]	343/949 (36.1)	225/703 (32.0)	118/246 (48.0)	<.001
Disruptive behavior[e]	185/622 (29.7)	157/493 (31.8)	28/129 (21.7)	.03
Eating[f]	19/937 (2.0)	2/693 (0.3)	17/244 (7.0)	<.001
Psychotic[g]	7/931 (0.8)	5/689 (0.7)	2/242 (0.8)	.88
Substance use[h]	59/948 (6.2)	42/701 (6.0)	17/247 (6.9)	.62
Elimination[i]	108/668 (16.2)	90/531 (17.0)	18/137 (13.1)	.28

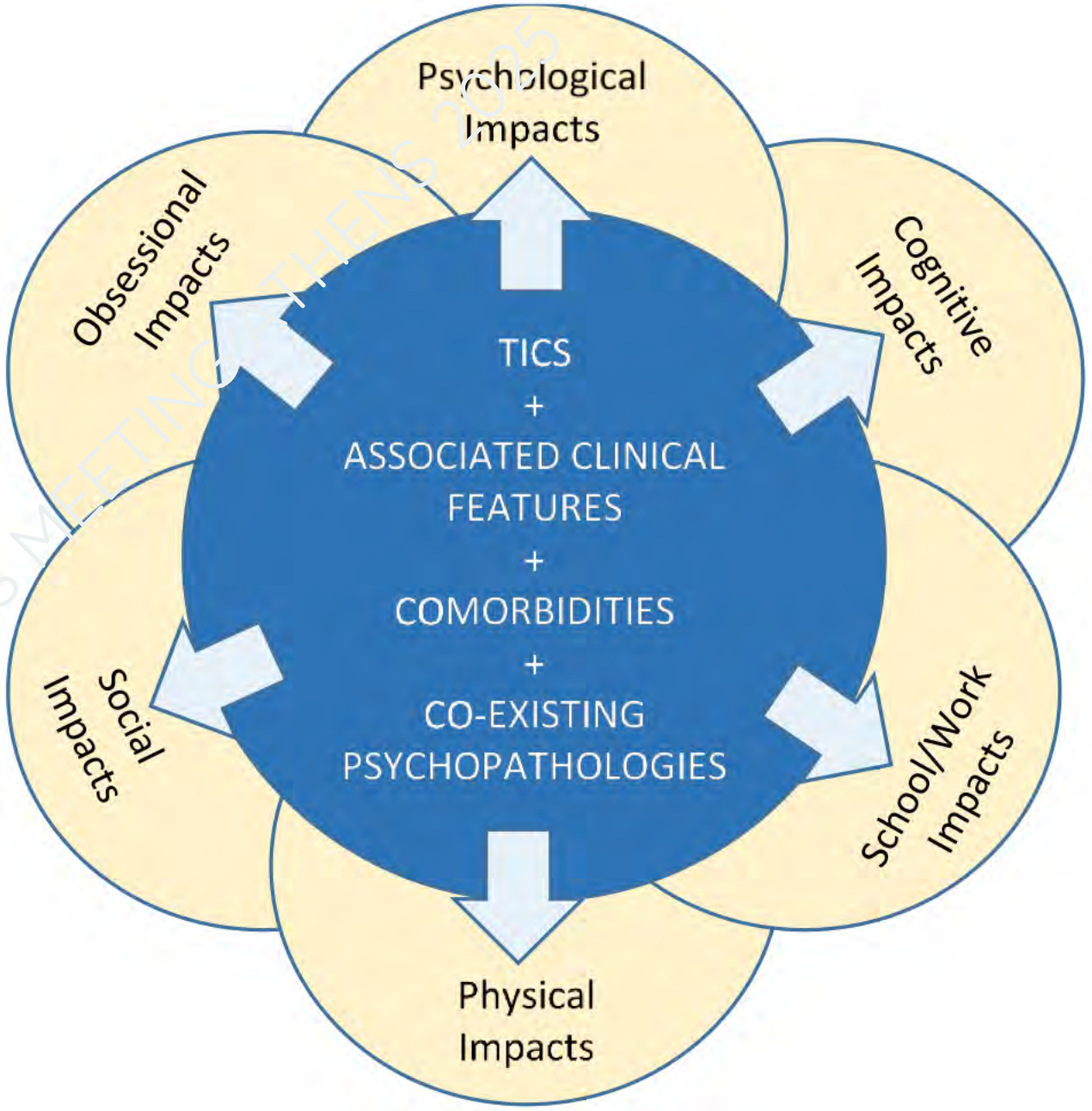
Original Investigation

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

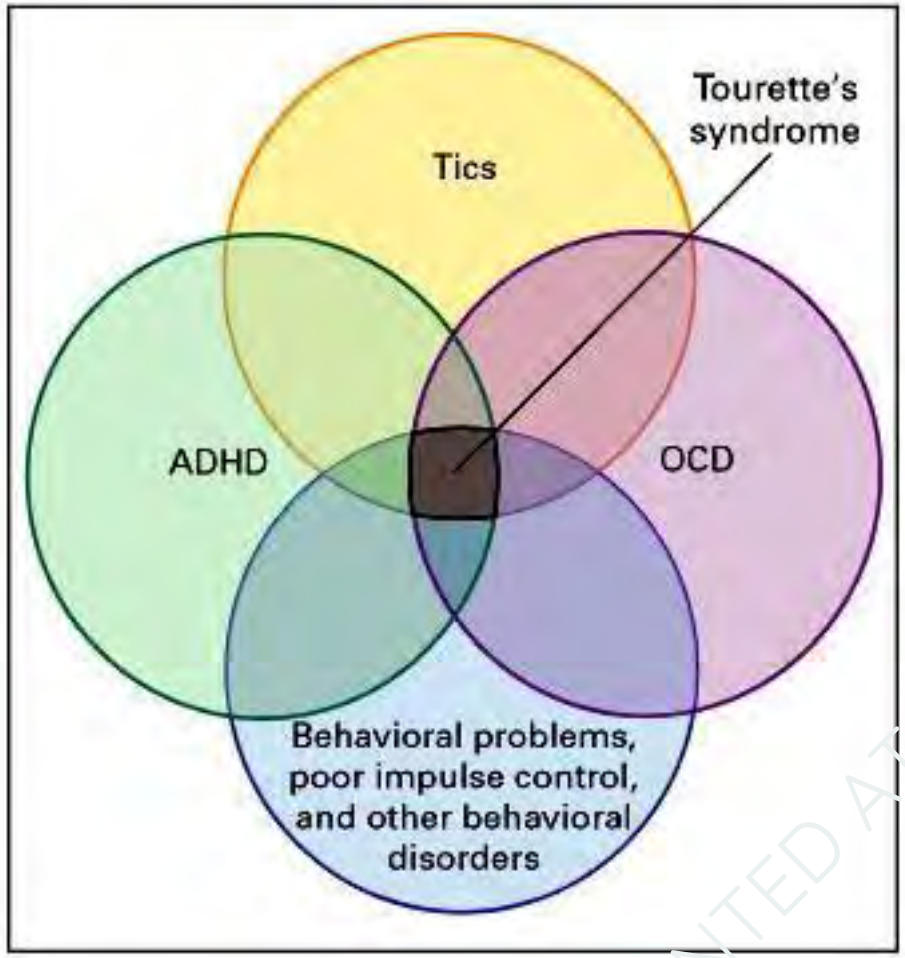
Matthew E. Hirschtritt, MD, MPH; Paul C. Lee, MD, MPH; David L. Pauls, PhD; Yves Dion, MD; Marco A. Grados, MD; Cornelia Illmann, PhD; Robert A. King, MD; Paul Sandor, MD; William M. McMahon, MD; Gholson J. Lyon, MD, PhD; Danielle C. Cath, MD, PhD; Roger Kurlan, MD; Mary M. Robertson, MBChB, MD, DSc(Med), FRCP, FRCPCH, FRCPsych; Lisa Osiecki, BA; Jeremiah M. Scharf, MD, PhD; Carol A. Mathews, MD; for the Tourette Syndrome Association International Consortium for Genetics



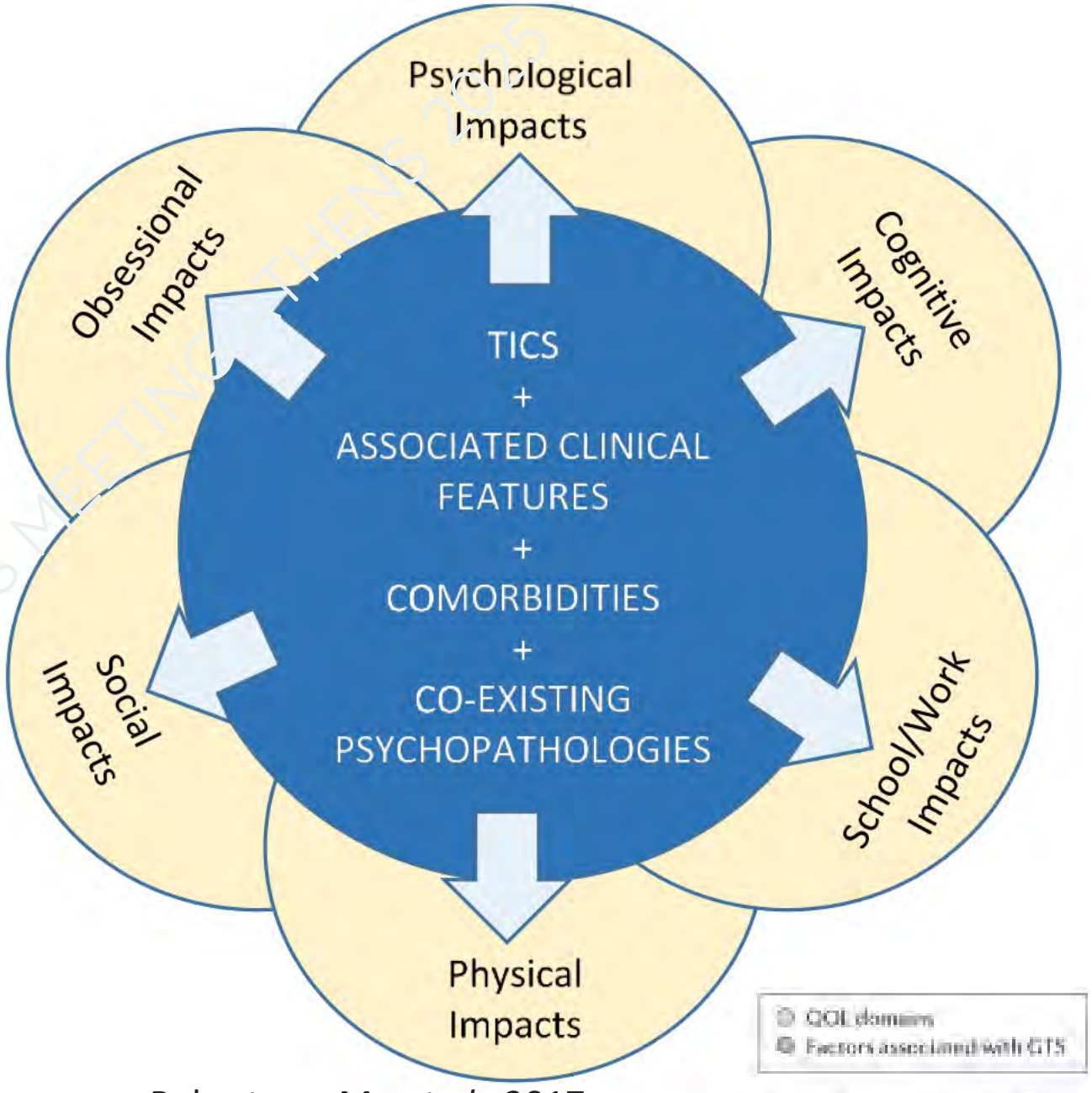
Jankovic, NEJM, 2001



Robertson, M., *et al.*, 2017



Jankovic, NEJM, 2001



Robertson, M., *et al.*, 2017

Comorbidity measured in clinical samples

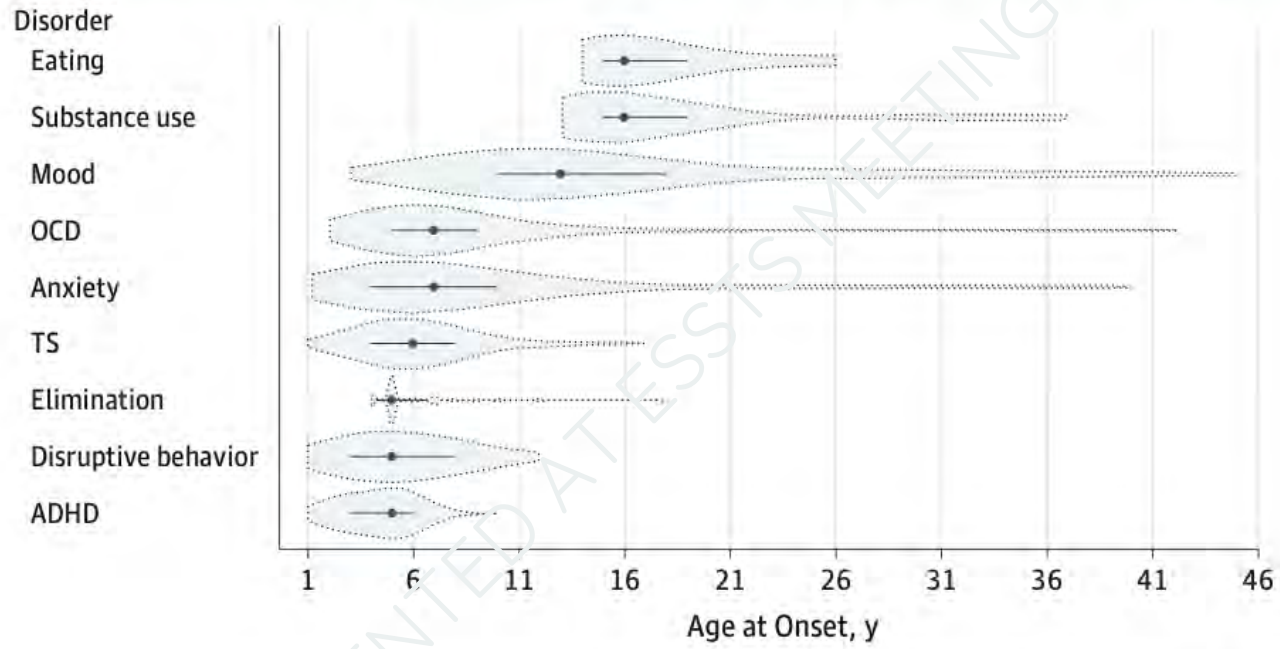
- TS and ADHD: 69%[1] . Varies, however, from 21%-90% [2,3,4,]
- ADHD and TS: 34%[5]

Depends on who's watching and who's counting!

[1]Leckman et al., 1998
[2]Singer, 2005
[3]Robertson, 2006
[4] Hirschtritt et al., 2015
[5]Spencer et al., 1999

Constellations of Co-morbidities

Figure 2. Ages at Onset for Comorbid Disorders Among Individuals With Tourette Syndrome (TS)



Hirschtritt et al., 2015

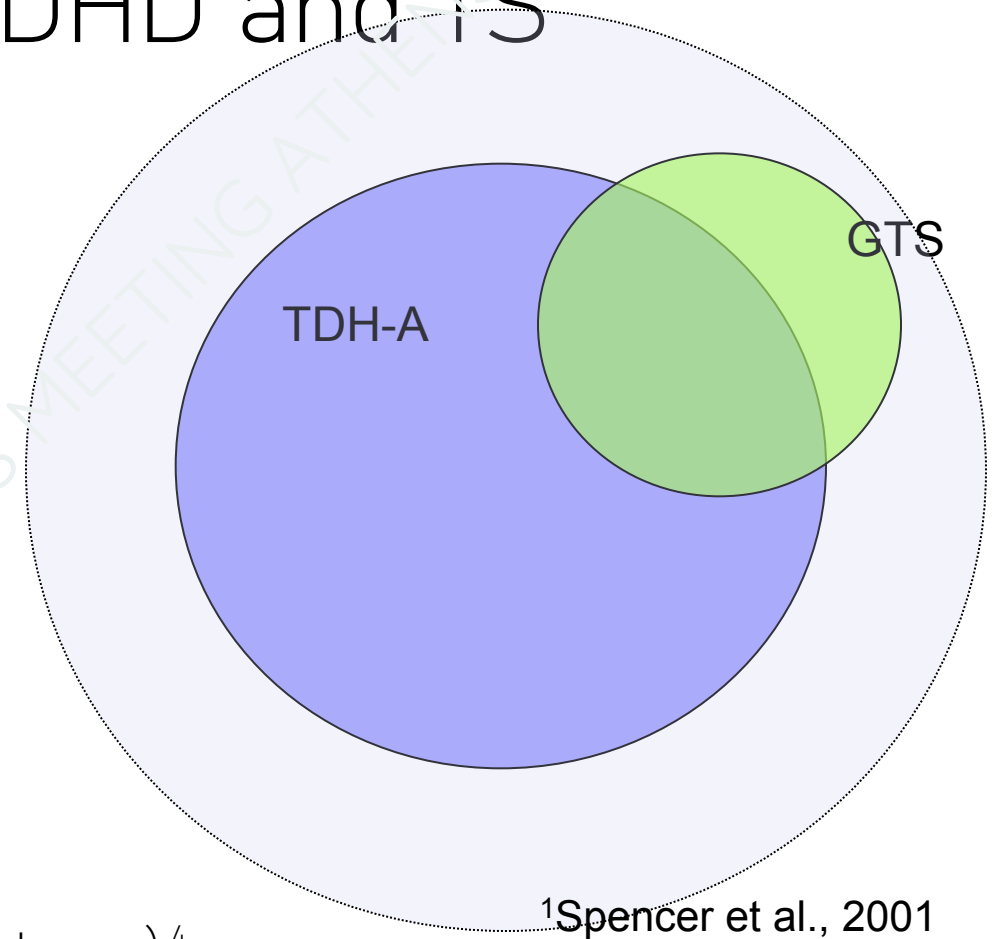
Clinical observations of ADHD/TS

- Comorbidity better explored in children with primary TS (and ADHD) than in children with ADHD as a primary diagnosis
- On average, TS is diagnosed 3 1/2 years earlier if there is co-morbidity with ADHD.[1]
- There is no association between the severity of tics and a diagnosis of ADHD in children[2] or adults.[3]
- Tics can be even more distracting for children with ADHD [4]
- Tics can disappear in situations that require concentration

[1]Freeman et al., 2007
[2]Poncin et al, 2007
[3]Haddad et al, 2009
[4]Cavanna et al, 2009

Relationship between ADHD and TS

Additional tics have
less influence on ADHD [1]
ADHD supplement
at the TS[2]



Deficits in executive functions

because of co-morbid ADHD [3]

Identification of ADHD improves final function (outcome) [4]

[1]Spencer et al., 2001
[2]Pringsheim et al, 2009
[3]Verte et al., 2005
[4]Carter et al., 2000

How do children with TS progress later in life?

Table 1 Comparison of Children's Global Assessment Scale (CGAS), Vineland Socialization Domain and Child Behaviour Checklist (CBCL) scores in participants with Tourette syndrome and community controls

	Tourette syndrome	Controls				Controlling for a lifetime diagnosis of ADHD		
	Mean (s.d.)	Mean (s.d)	*F*	d.f.	*P*	*F*	d.f.	*P*
CGAS Consensus score	56.4 (12.1)	70.4 (12.3)	39.4	1, 126	**10^{-8}**	9.4	1, 125	**<0.01**
Vineland Socialization domain standard score	84.5 (23.8)	101.1 (14.7)	19.8	1, 119	**$<10^{-4}$**	5.7	1, 118	**0.02**
CBCL, t-scores								
Activities[a]	44.5 (6.7)	47.1 (8.2)	2.8	1, 104	0.1	2.8	1, 103	0.1
Social[a]	42.5 (10.0)	51.2 (6.2)	27.2	1, 94	**10^{-6}**	11.3	1, 93	**0.001**
School[a]	40.7 (9.2)	50.2 (5.8)	38.4	1, 106	**10^{-8}**	13.8	1, 105	**<0.001**
Withdrawn	57.7 (9.0)	52.8 (6.4)	8.9	1, 111	**<0.01**	3.7	1, 110	0.06
Somatic complaints	57.8 (9.6)	55.0 (5.4)	2.0	1, 111	0.2	0.2	1, 110	0.7
Anxious/depressed	59.8 (9.5)	53.0 (5.4)	21.5	1, 111	**10^{-5}**	7.8	1, 110	**0.01**
Social problems	59.9 (9.7)	52.4 (5.1)	25.4	1, 111	**$<10^{-5}$**	8.3	1, 110	**0.01**
Thought problems	61.7 (10.9)	52.7 (6.0)	27.8	1, 111	**10^{-6}**	13.1	1, 110	**<0.001**
Attention problems	63.7 (11.2)	52.8 (6.1)	38.8	1, 111	**10^{-8}**	11.4	1, 110	**0.001**
Delinquent behaviour	56.3 (9.5)	52.7 (4.6)	5.1	1, 111	**0.03**	0.2	1, 110	0.6
Aggressive behaviour	58.3 (11.7)	51.9 (4.5)	13.2	1, 111	**<0.001**	3.3	1, 110	0.07
Internalising	56.9 (12.9)	47.4 (11.0)	15.7	1, 111	**10^{-4}**	5.5	1, 110	**0.02**
Externalising	54.1 (14.1)	45.2 (9.6)	13.8	1, 111	**<0.001**	2.4	1, 110	0.1
Total problems	58.0 (13.7)	45.3 (11.4)	26.2	1, 111	**10^{-6}**	7.6	1, 110	**0.01**

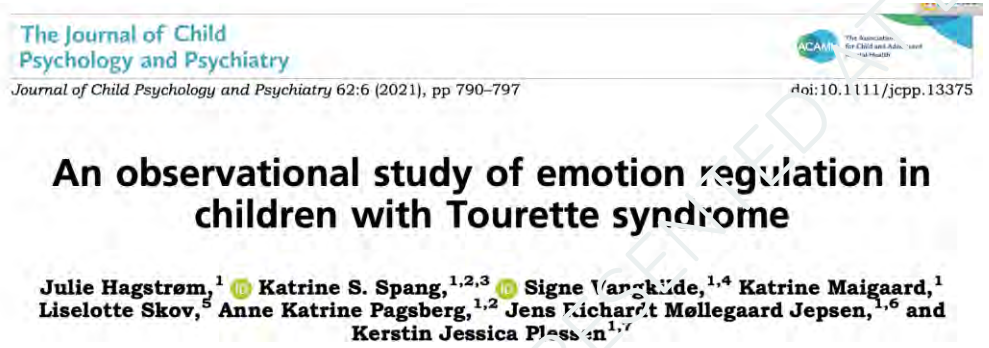
ADHD, attention-deficit hyperactivity disorder.
a. Competence subscales.
Significant results are shown in bold ($P \leqslant 0.05$).

Gorman et al. 2010

Context for emotional problems

- Rage attacks, aggression and explosive behaviour are associated with several neuropsychiatric disorders (Sukhodolsky & Scahill, 2007).
- In children with TS, these symptoms are present in 25-70% of cases (Budman et al., 2000).
- TS is associated with emotional problems, peer problems and an increased prevalence of depression and behavioural problems in adulthood - even after the tics have stopped (Hoekstra et al., 2012; Gorman et al., 2010).
- ADHD comorbidity and the most disruptive (Leclerc et al., 2011)
- There are only a few studies on the TS and the regulation of emotions without any direct measurement.

Instructions



The Journal of Child Psychology and Psychiatry

Journal of Child Psychology and Psychiatry 62:6 (2021), pp 790–797 doi:10.1111/jcpp.13375

An observational study of emotion regulation in children with Tourette syndrome

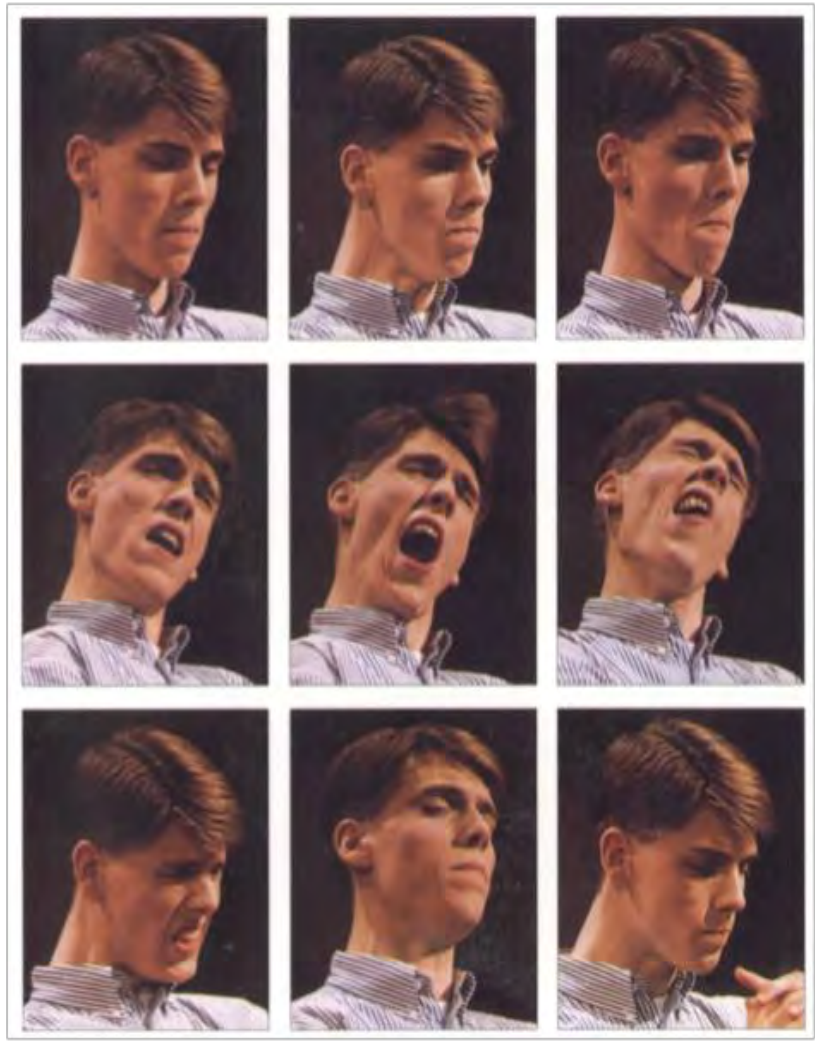
Julie Hagstrøm,[1] Katrine S. Spang,[1,2,3] Signe Vangkilde,[1,4] Katrine Maigaard,[1] Liselotte Skov,[5] Anne Katrine Pagsberg,[1,2] Jens Richardt Møllegaard Jepsen,[1,6] and Kerstin Jessica Plessen[1,7]

- To the child: "Look, here's a jigsaw puzzle. You can make lots of different shapes with this puzzle. It's your job to make as many of these shapes with these puzzle pieces as you can over the next five minutes."
- For the parent: "You're here to support your child, but you're only here to help if it's really necessary. You get the solutions for yourself, but you don't have to show them to the child".

Aggression

The Study

- 49 children with TS, 16 children with GTS+ADHD, 23 children with ADHD, 62 controls, all 8-12 y.
- The control group did significantly better than the ADHD group (p= .012) and the TS + ADHD group (p= .010), but not the TS only group.
- The TS only group presented with significantly better ER scores than the ADHD group (p= .037) and the TS + ADHD group (p= .029).
- A high frequency of parental tension was present in 2% of parents in the TS group and not present at all in the control group and the TS + ADHD group, whereas 17% of parents in the ADHD group were tense 'sometimes' or 'often'.



ORIGINAL CONTRIBUTION

Behavior Therapy for Children With Tourette Disorder

A Randomized Controlled Trial

John Piacentini, PhD

Total vocal	10.1 (4.5)	10.0 (4.7)
Other diagnoses[c]		
Attention-deficit/hyperactivity disorder	20 (32.8)	13 (20.0)
Obsessive-compulsive disorder	8 (13.1)	16 (24.6)
Generalized anxiety	10 (16.4)	15 (23.1)
Separation anxiety	6 (9.8)	5 (7.7)
Social anxiety	13 (21.3)	14 (21.5)

Piacentini et al., 2010

Tics and Stimulants

- Tics are not normally aggravated by stimulants (methylphenidate) [1,2,3,4]
- Metylphenidate (25 mg/day) and Clonidin (0.25 mg/day) were validated for children with GTS and ADHD [3]
- Children with TS and ADHD had a better effect with a combination of the two medications than with a single medication.[3]

Monitor tics for a period of 3 months before making any decision about ADHD treatment (ECAP)
If the tics are related to stimulants, reduce the stimulant dose or consider switching to guanfacine (in children ≥5 years of age and adolescents only), atomoxetine or clonidine; add an antipsychotic agent (ECAP); or discontinue treatment[5].

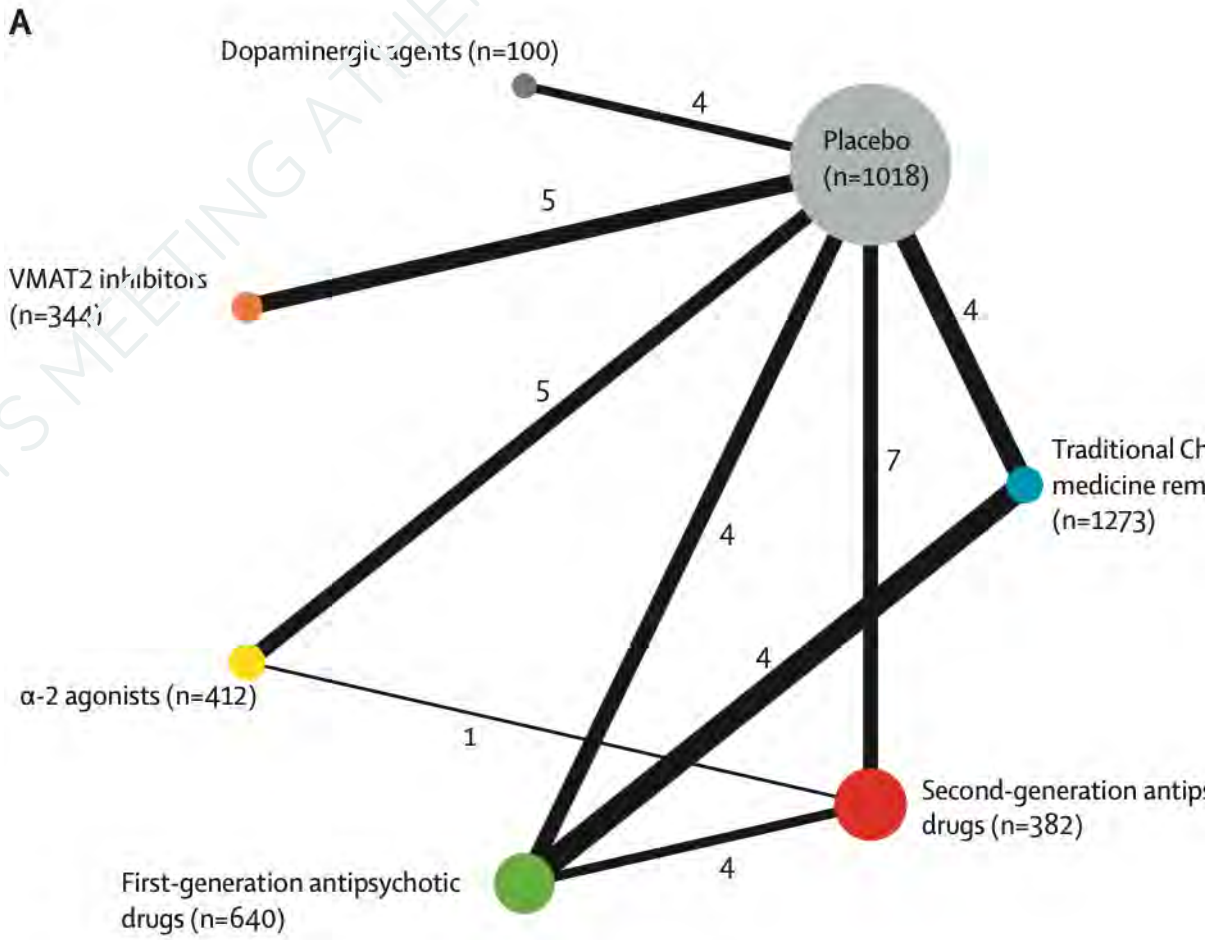
[1] Roessner et al. 2006
[2] Scahill et al., 2006
[3] Tourette's syndrome study group, 2002
[4] Bloch et al., 2009
[5] Roessner et al., 2022

Recommandation of Alpha -2 agonists (Guanfacin and Clonidin)

The balance of clinical benefits to harm favors the α-2 adrenergic receptor agonists clonidine and guanfacine

Substantial heterogeneity with studies with transdermal application of clonidine being less effective compared to oral administration.

the effect size of α-2 adrenergic agonist on tic reduction is larger in children with tics plus ADHD than those without ADHD



Whittington et al., JCPP, 2016; Weissman et al., Neurosci Biobehav Rev 2013

Farhat et al. , JCAP 2024

Cochrane Library
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

Sydney T Osland[1], Thomas DL Steeves[2], Tamara Pringsheim[3]

- Included eight randomized controlled trials (four cross-over) with 510 children (mostly boys) with both ADHD and a chronic tic disorder.
- Conducted in the USA, studies lasted 3 to 22 weeks.
- A meta-analysis wasn't possible due to important clinical heterogeneity.
- The trials assessed methylphenidate, clonidine, desipramine, dextroamphetamine, guanfacine, atomoxetine, and deprenyl.
- Evidence quality was low for methylphenidate, atomoxetine, and clonidine, and very low for the others in treating ADHD in children with tics.
- Tic symptoms also improved with guanfacine, desipramine, methylphenidate, clonidine, and a methylphenidate/clonidine combination.
- However, tics limited methylphenidate dosage increases in one study, and high-dose dextroamphetamine worsened tics in a short study (duration 3 weeks)

Pringsheim T, Steeves T 2011, Osland et al., update 2018

Cochrane Library
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

Sydney T Osland[1], Thomas DL Steeves[2], Tamara Pringsheim[3]

- Included eight randomized controlled trials (four cross-over) with 510 children (mostly boys) with both ADHD and a chronic tic disorder.
- Conducted in the USA, studies lasted 3 to 22 weeks.
- A meta-analysis wasn't possible due to important clinical heterogeneity.
- The trials assessed methylphenidate, clonidine, desipramine, dextroamphetamine, guanfacine, atomoxetine, and deprenyl.
- Evidence quality was low for methylphenidate, atomoxetine, and clonidine, and very low for the others in treating ADHD in children with tics.
- Tic symptoms also improved with guanfacine, desipramine, methylphenidate, clonidine, and a methylphenidate/clonidine combination.
- However, tics limited methylphenidate dosage increases in one study, and high-dose dextroamphetamine worsened tics in a short study (duration 3 weeks)


Meta-Analysis: Risk of Tics Associated With Psychostimulant Use in Randomized, Placebo-Controlled Trials

Stephanie C. Cohen, BA, Jilian M. Mulqueen, BA, Eduardo Ferracioli-Oda, Zachary D. Stuckelman, Catherine G. Coughlin, BS, James F. Leckman, MD, PhD, Michael H. Bloch, MD, MS

Pringsheim T, Steeves T 2011, Osland et al., update 2018

Comorbidity TS and ADHD

- Important to map all comorbidities for the individual longterm outcome
- ADHD is more relevant for the lifecourse than tics
- Individualising the treatment is key
- Treat the ADHD, also pharmacologically
- More research is needed for the problems of emotional regulations linked to ADHD, in children, adolescents and adults