Tics and Tourette Syndrome

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1


Gilles de la Tourette (1857–1904).

1885

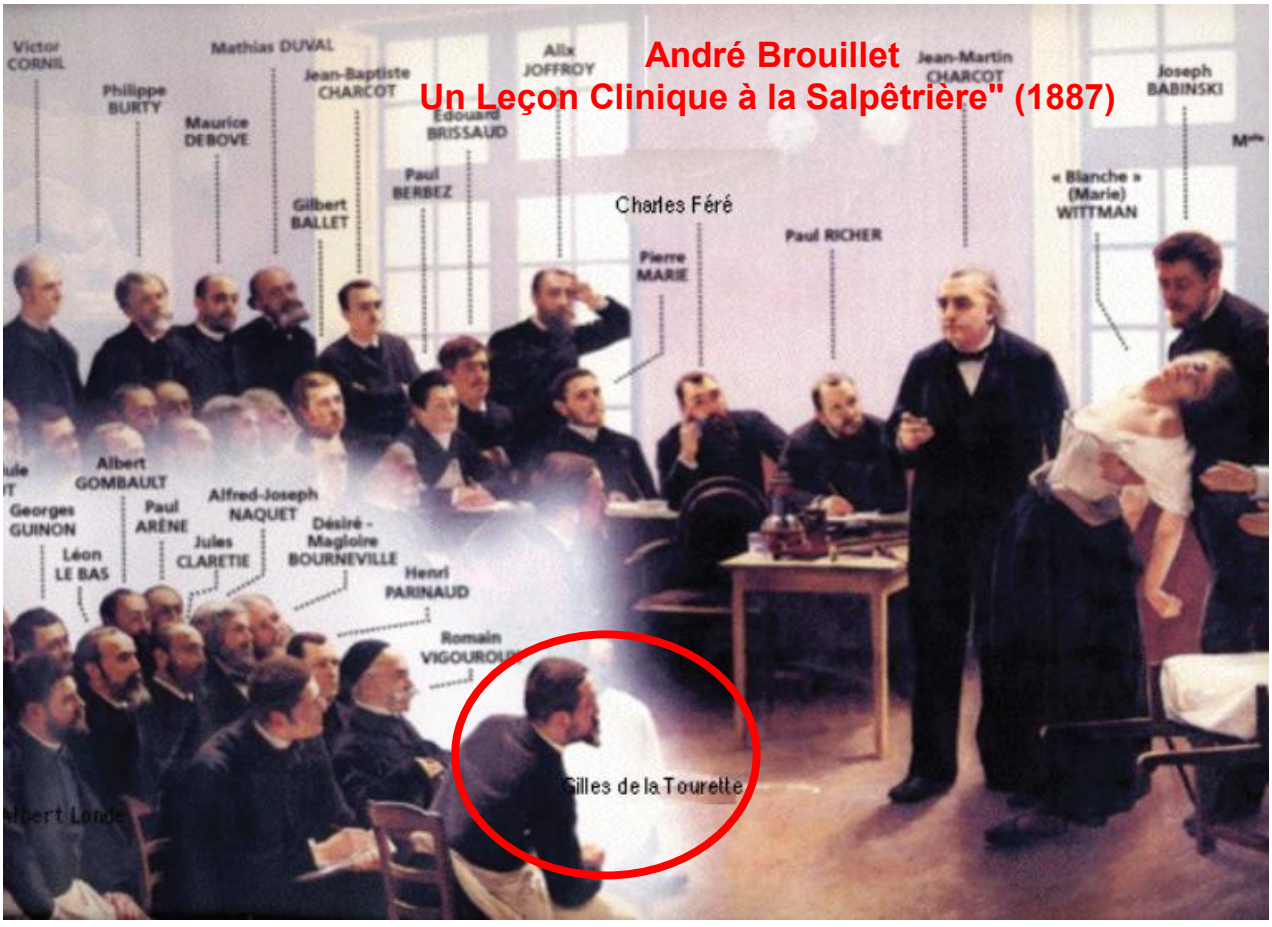
9 patients

9 = motor tics
6 = phonic tics
5 = coprolalia
5 = echolalia
2 = echopraxia

Georges Albert Édouard Brutus Gilles de la Tourette

Gilles de la Tourette G: Étude sur une affection nerveuse caracterisée par de l'incoordination motrice accompagnée d'echolalie et de copralalie. Arch Neurol (Paris)1885;9:158-200
("A study of a neurologic condition characterized by motor incoordination accompanied by echolalia and coprolalia")

9


André Brouillet
Un Leçon Clinique à la Salpêtrière" (1887)
Victor CORNIL
Mathias DUVAL
Philippe BURTY
Jean-Baptiste CHARCOT
Maurice DEBOVE
Alix JOFFROY
Jean-Martin CHARCOT
Joseph BABINSKI
Édouard BRISSAUD
Paul BERBEZ
Gilbert BALLET
Charles Féré
« Blanche » (Marie) WITTMAN
Paul RICHER
Pierre MARIE
Albert GOMBAULT
Georges GUINON
Paul ARÈNE
Alfred-Joseph NAQUET
Désiré - Magloire BOURNEVILLE
Jules CLARETIE
Léon LE BAS
Henri PARINAUD
Romain VIGOUROUX
Silles de la Tourette

11

Tourette Syndrome

DSM-5 Code: 307.23

- A. Both multiple motor and one or more vocal tics are present at some time during the illness, although not necessarily concurrently.
- B. The tics may wax or wane in frequency but have persisted for more than 1 year since first tic onset.
- C. Onset is before age 18 years.
- D. The disturbance is not attributable to the physiological effects of a substance (e.g. cocaine) or a general medical condition (e.g. Huntington's disease, postviral encephalitis).

ICD-11 Codes:

- Tourette syndrome – F95.2
- Persistent (Chronic) Motor or Vocal Tic Disorder – F95.1
  Single or multiple motor or vocal tics
- Provisional Tic Disorder – F95.0
  Tics present for less than 1 year
  (Replaced "transient tics of childhood", but tics almost always last >1 year)
- Tic disorder, unspecified – F95.9
- Tics of organic origin – G25.69

15

Diagnostic Criteria for Primary Tic Disorders: Time for Reappraisal.

Sarchioto et al. Mov Disord 2024;39:1276-81



17

Tics: Definition

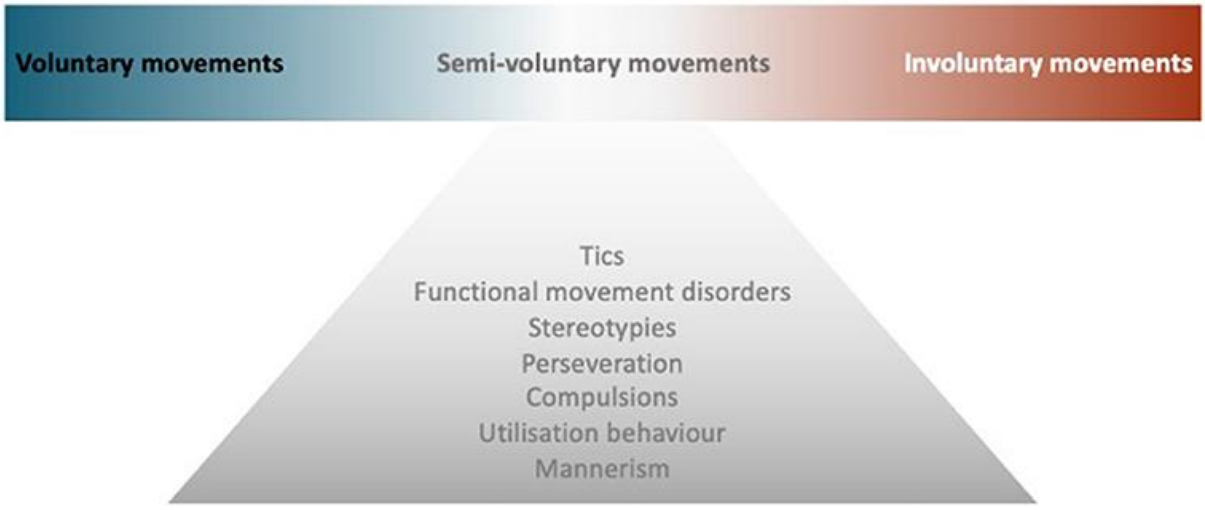
- Sudden, brief, intermittent, repetitive, non-rhythmic, involuntary or semi-voluntary movements or muscle contractions (motor tics) or sounds (phonic tics) which abruptly interrupt otherwise normal motor activity or speech.
- Motor tics
  - Simple or Complex
    - Clonic
    - Dystonic
    - Tonic (isometric)
    - Stereotypic
    - Blocking
    - Compulsive
    - Tic status – continuous tics (tic attack)
- Phonic tics
  - Simple (meaningless sounds/noises)
  - Complex (semantically meaningful utterances - coprolalia)
- Sensory tics
  - Focal sensations (e.g. “tickle”, “itch”)
  - Premonitory sensation or urge (focal, generalized)
  - Sensory hypersensitivity (e.g. misophonia)

19

Phenomenology of Tics

- **Dystonic tics**
  Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J. J Neurol 2022;269:5312-8
- **Oromandibular tics**
  Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J. J Neurol 2023;270:2591-6
- **Blocking tics**
  Baizabal-Carvallo JF, Jankovic J. J Mov Disord 2023;16:163-7
- **Oculogyric tics**
  Baizabal-Carvallo JF, Jankovic J. Acta Neurol Belg 2022;122:925-30
- **Secondary tics**
  Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J. J Neural Transm 2023:1–6
- **Beyond tics**
  Baizabal-Carvallo JF, Jankovic J. J Neural Transm 2021;128:1177-83
- **Self-injurious behaviors**
  Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J. J Neurol 2022;269:2453-9
- **Tic emergencies and malignant TS**
  Baizabal-Carvallo JF, Cavanna AE, Jankovic J. Neurosci Biobehav Rev 2024;159:105609
- **Axial tics**
  Baizabal-Carvallo JF, Jankovic J. J Neurol 2024;271:7232-8
- **Phonic tics**
  Baizabal-Carvallo JF, Jankovic J. Brain Sci 2025;15:620

Semivoluntary or Unvoluntary Movements



Virameteekul et al. Front Neurol 2022;13:834217

… also akathisia, restless legs syndrome, leg stereotypy syndrome, etc

Nilles et al. Semin Neurol 2023;43:123-46

Yilmaz AY, Ruzicka E, Jankovic J. J Neurol 2024;271:5519-24

29

Tics: Characteristics

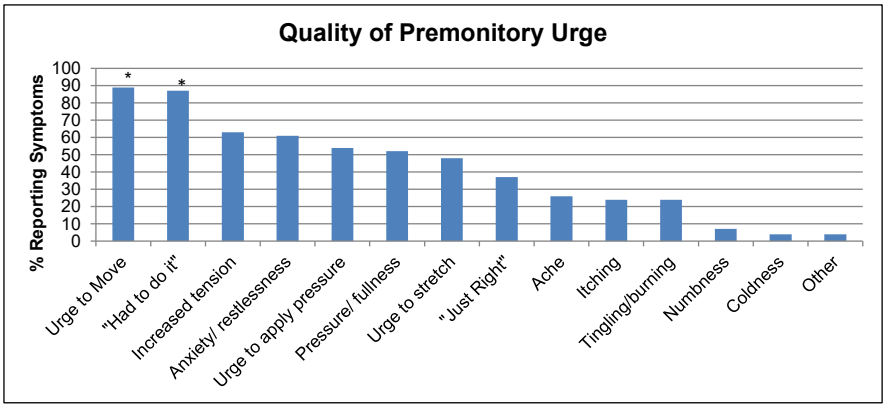
- **Premonitory feelings, sensations or urges**
- **Regional or generalized sensory or mental phenomena or an urge that precede tics and are temporarily reduced by performance of tics.**

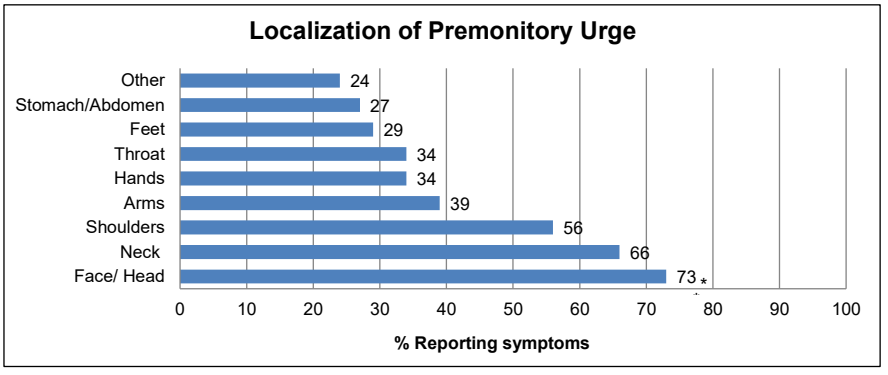


- **Premonitory urges and tic severity are significantly associated**.
  Brandt et al. Mov Disord Clin Pract 2023;10:922-32

PREMONITORY PHENOMENA

(reported by 92% of 50 patients)



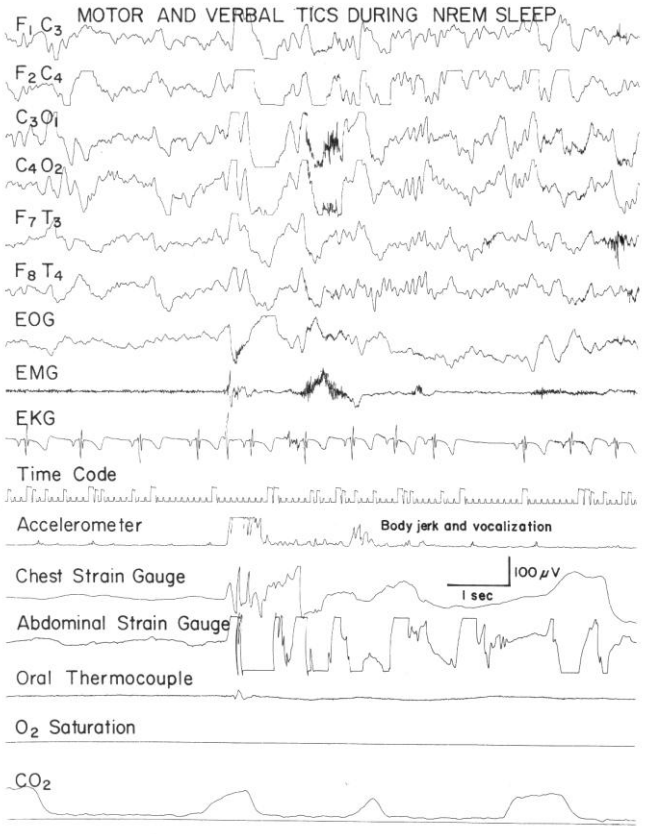


Kwak and Jankovic. Mov Disord 2003;18:1530-3

41

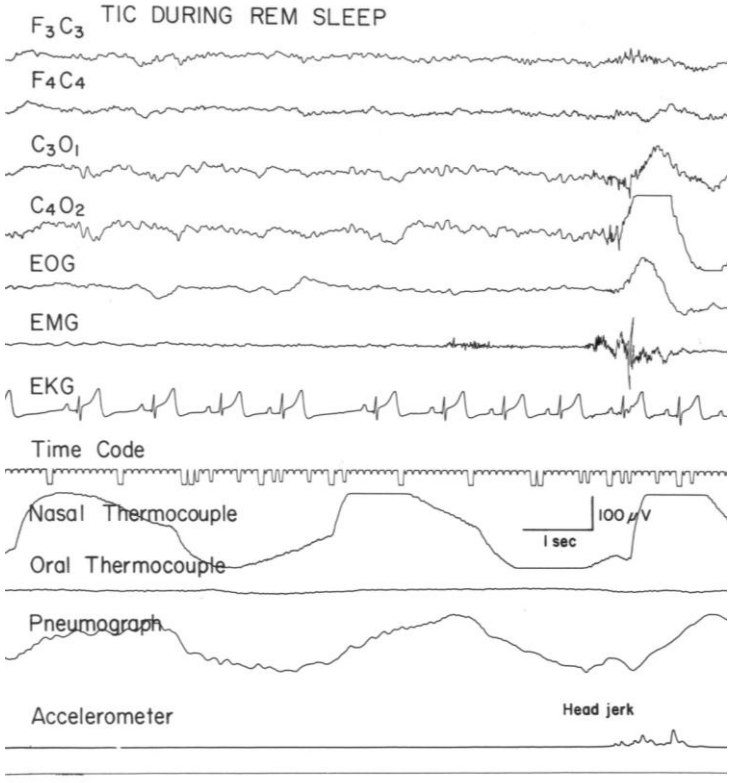
Tics: Characteristics

- Premonitory feelings or sensations
- **Brief and intermittent**
- **Repetitive (stereotypic)**
- **Temporarily suppressible**
- **Suggestible**
- **Increase with stress**
- **Increase during relaxation after stress (rebound)**
- **Decrease with distraction and with concentration**
- **Change location, intensity, wax and wane, may remit for months or years**
- **Persist during sleep**



Glaze DG, Frost JD, Jankovic J. Neurology 1983;33:586-92

45



Glaze DG, Frost JD, Jankovic J. Neurology 1983;33:586-92

46

Polysomnography in TS

First Author/Yr	N	Age	REM	Arousal	Tics
Mendelson 1980	6	10-20	0	---	---
Glaze 1983	14	8-23	↓	↑	+
Jankovic 1987	34	<28	↓	↑	+
Drake 1982	7	10-36	↓	↑	---
Silvestri 1995	9	11-32	↓	↑	+
Voderholzer 1997	7	31±11	↓	↑	---
Rotheberg 2000	13	8-16	?	↑	+

Hanna and Jankovic. Sleep and Movement Disorders 2003;464-71

Insomnia, excessive daytime sleepiness, disorders of arousal (sleepwalking, sleeptalking, sleep terrors, and enuresis), persistence of tics during sleep, periodic limb movements during sleep

Jiménez-Jiménez et al. Sleep Med Rev 2020;53:101335
Bailey et al. JNNP 2021;92:723-6
Isomura et al. Mov Disord 2022;37:392-400
Blaty JL, DelRosso LM. Biomed J 2022;45:240-9
Mi et al. Front Pediatr 2022;10:911343

47



50



53



56



57



59

14 y/o boy with stereotypic complex tics, anxiety and OCD



62

Complex tics released when examiner leaves the room



63

Coprophenomenon in TS

Freeman et al. Devel Med Child Neurol 2009;51:218-27

- **A specialized data collection form was completed for 558 consecutive new cases of TS, 15 sites, 7 countries**
- **Coprolalia occurred at some point in 19.3% of males and 14.6% of females; copropraxia in 5.9% of males and 4.9% of females**
- **Mean age at onset of coprolalia was at 11 years and 10 years for copropraxia**
- **The mean age for onset of coprophenomena was 5 years after the onset of tics; in 11% of those with coprolalia this was the initial symptom of TS**
- **17/149 (11.4%)**
  Baizabal-Carvallo JF, Jankovic J. Brain Sci 2025;15:620
- **17/169 (10.1%) reported coprophenomena had higher tic severity.**
  Myers et al. Neurol Clin Pract 2025;15:e200369

Coprolalia consists of uttering (swearing) obscenities (foul, repulsive, language, often with sexual or scatological meaning); more common than profanities (cursing with religious meaning), although some have racist, sexist, or vulgar (coarse or crude) meaning. Mental coprolalia > verbal coprolalia.

70

‘I Swear’ Review: Surviving and Thriving Against the Odds

The British actor Robert Aramayo rises above the clichés in a biographical drama about a man living with Tourette’s syndrome.

Listen · 6:24 min

Share full article 1



Robert Aramayo as John Davidson in “I Swear.” Graeme Hunter/Sony Pictures Classics

https://www.nytimes.com/2026/04/23/movies/i-swear-review-tourettes-syndrome.html?smid=nytcore-ios-share

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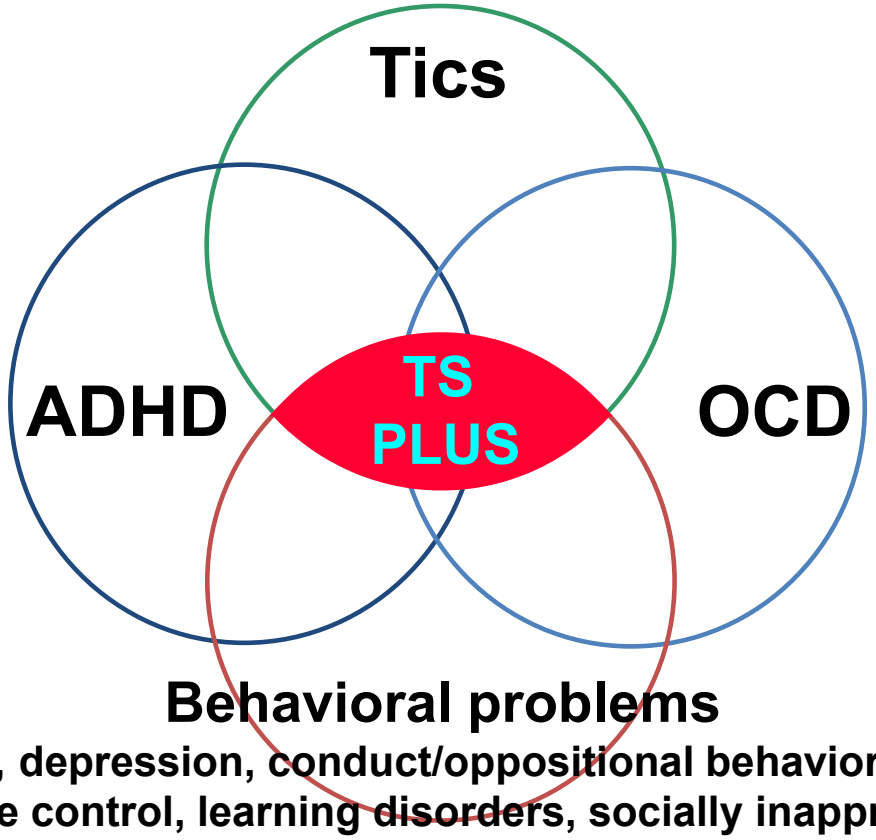
Copropraxia



79



80



Behavioral problems

Anxiety, depression, conduct/oppositional behavior, loss of impulse control, learning disorders, socially inappropriate and self-injurious behaviors

Jankovic. Tourette's syndrome. N Engl J Med 2001;345:1184-92

81

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

Hirschtritt et al. JAMA Psychiatry 2015;72:325-33

- **Cross-sectional structured diagnostic interviews in 1374 TS patients and 1142 in TS-unaffected family members.**
- **Lifetime prevalence of comorbid DSM-IV-TR disorders in 85.7%; 57.7% of the population had 2 or more psychiatric disorders.**
- **72.1% of the individuals met the criteria for OCD or ADHD.**
- **Other disorders, including mood, anxiety, and disruptive behavior, each occurred in approximately 30% of the participants.**
- **The age at greatest risk for the onset of most comorbid psychiatric disorders was between 4 and 10 years, with the exception of eating and substance use disorders, which began in adolescence.**

88

Association of Tourette Syndrome and Chronic Tic Disorders With Objective Indicators of Educational Attainment: A Population-Based Sibling Comparison Study.

Perez-Vigil et al. JAMA Neurol 2018;75:1098-1105

- **Of the 2,115, 554 individuals in the Swedish cohort, 3,590 had registered a diagnosis of Tourette syndrome or a chronic tic disorder in specialist care (78.6% were male; median age at first diagnosis 14.0 years).**
- **Help-seeking individuals with Tourette syndrome or chronic tic disorders seen in specialist settings experience substantial academic underachievement across all educational levels, spanning from compulsory school to university, even after accounting for multiple confounding factors and psychiatric comorbidities.**

90

Malignant Tourette Syndrome

Cheung MC, Shahed J, Jankovic J. Mov Disord 2007;22:1743-50

- **Malignant TS defined as ≥ 2 emergency room visits or ≥ 1 hospitalizations for TS symptoms or its associated behavioral co-morbidities; refractory to treatments.**
- **Of 332 TS patients evaluated during the three-year period, 17 (5.1%) met criteria for malignant TS.**
- **Compared to patients with non-malignant TS, those with malignant TS were significantly more likely to have a personal history of obsessive compulsive behavior/disorder, complex phonic tics, coprolalia, copropraxia, self-injurious behavior, mood disorder, suicidal ideation, and poor response to medications.**

93

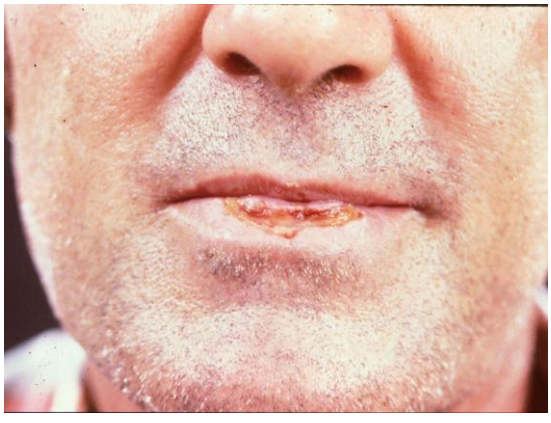


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Hitting his face and teeth (knocked his upper teeth out), blind in the L eye because of detached retina, abrasions in his hands, etc, etc







96



97



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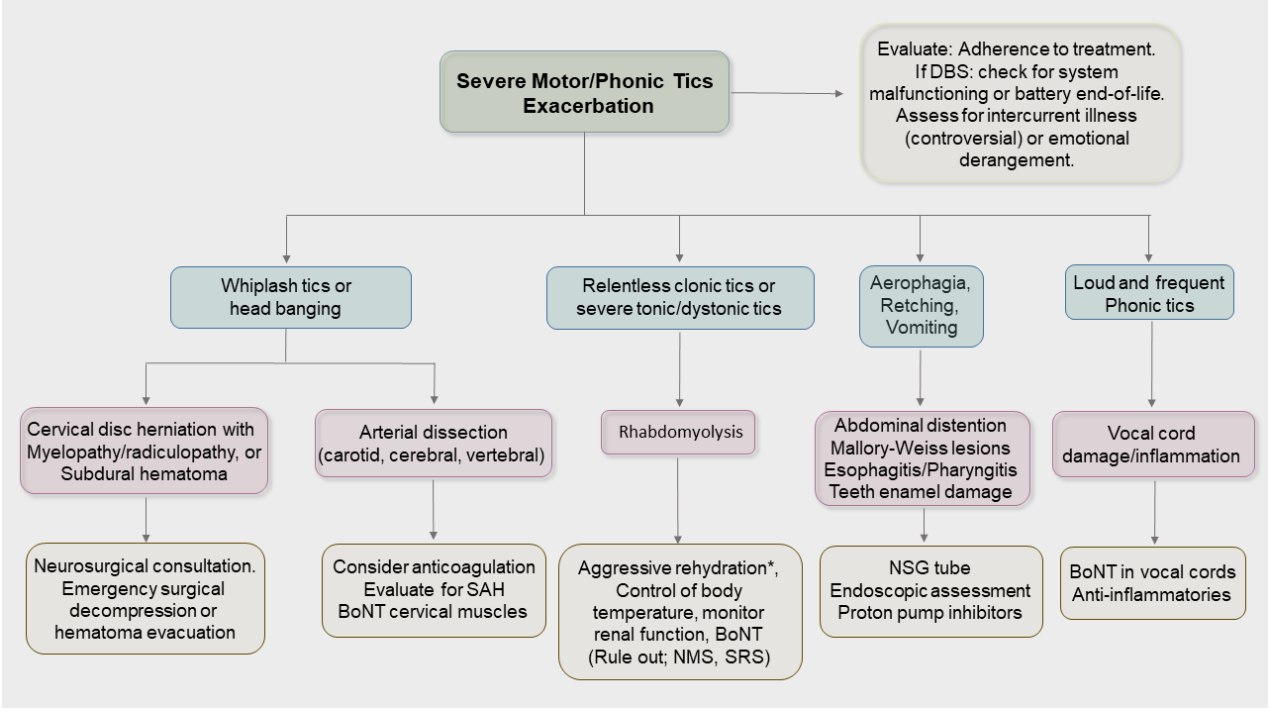
102

Self-injurious behavior in Tourette syndrome

- **34/201 (17%) patients with SIB; 11.4% experienced self-directed damage; while others had outward-directed (3.5%) or tic-related SIB (2%). The presence of complex motor tics, OCD and greater severity of tics was related to the presence of SIB.**
  Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J. J Neurol 2022;269:2453-9
- **Based on Meta-Analysis and Systematic Reviews of Observational Studies in Epidemiology of 20 cohort studies, SIB was present in 35% of patients with TS. OCD appears to be associated with SIB in patients with TS.**
  Stafford M, Cavanna AE. Neurosci Biobehav Rev 2020;113:299-307
- **Treatment: behavioral therapy, antipsychotics, anti-epileptics, clonidine, n-acetylcysteine, naltrexone, amantadine, mirtazapine, topical anesthetics, botulinum toxin, and deep brain stimulation.**
  Sabus et al. Pharmacotherapy 2019;39:645-64
  Hull M, Parnes M, Jankovic J. Botulinum Neurotoxin Injections in Children with Self-Injurious Behaviors. Toxins 2023;15:236

108

Tic-related injuries



Baizabal-Carvallo JF, Cavanna AE, Jankovic J. Neurosci Biobehav Rev 2024;159:105609

109

Tourette Syndrome and the Legal System

- **Individuals with TS are significantly more likely (2x) not only to experience assault but also to be perpetrators of violent (including sexual) assaults (3x).**
  Mataix-Cols et al. JAMA Neurol 2022;79:459-67; Martino et al. JAMA Neurol 2022;79:442-4
- **Impulsive behavior, coprophenomenon, rage outbursts, intrusive behavior (e.g. forced touching), alcohol and substance abuse may trigger or eventually lead to involvement with the law-enforcement and legal system.**
  Jankovic et al. J Neuropsychiatry Clin Neurosci 2006;18:86-95
  Virtanen et al. Biol Psychiatry 2021;89:407-14
  Andersen et al. Pediatr Neurol 2023;145:88-93
- **As children with TS mature and start driving, because of their tics, such as blinking and blepharospasm, or dystonic neck and trunk tics, and a variety of other complex tics, coupled with co-morbid attention deficit, they should be screened for such troublesome symptoms that could possibly put them or others in danger while driving.**
  Makhoul K, Jankovic J. Mov Disord Clin Pract 2021;8:763-8
  Makhoul K, Jankovic J. Mov Disord Clin Pract 2023;10:369-81

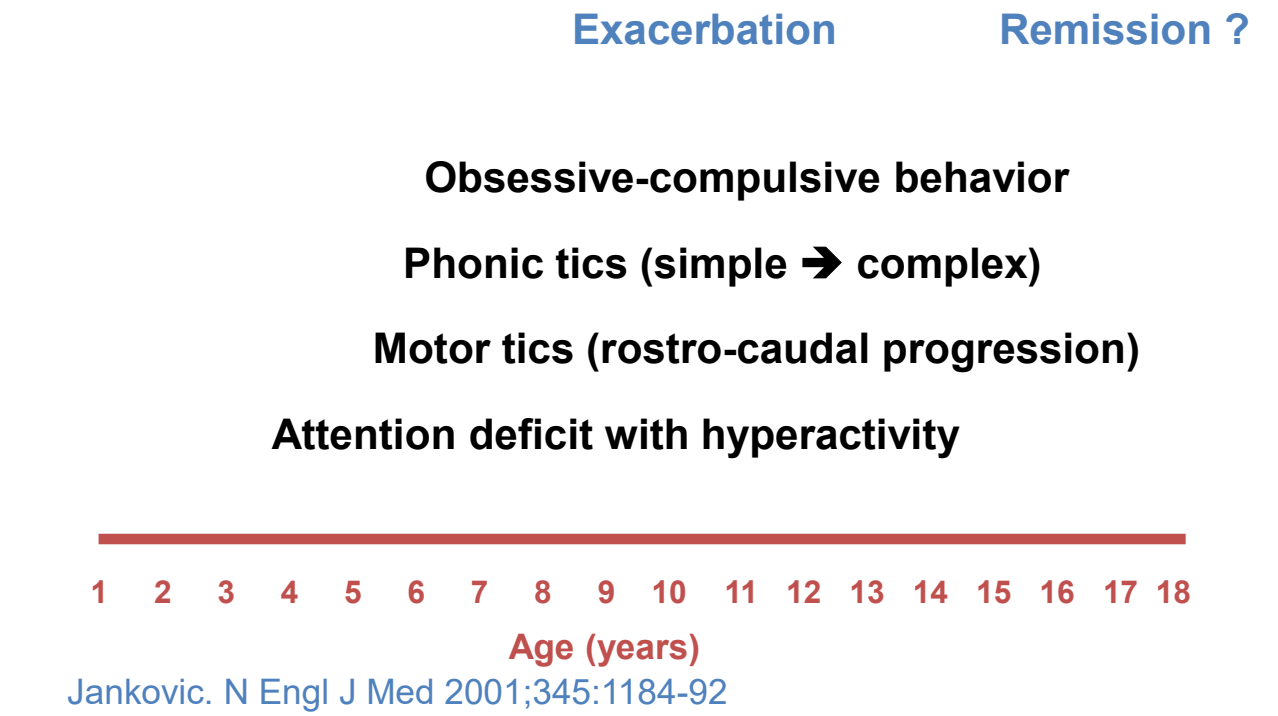
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Tics while driving



114

Natural History of Tourette Syndrome



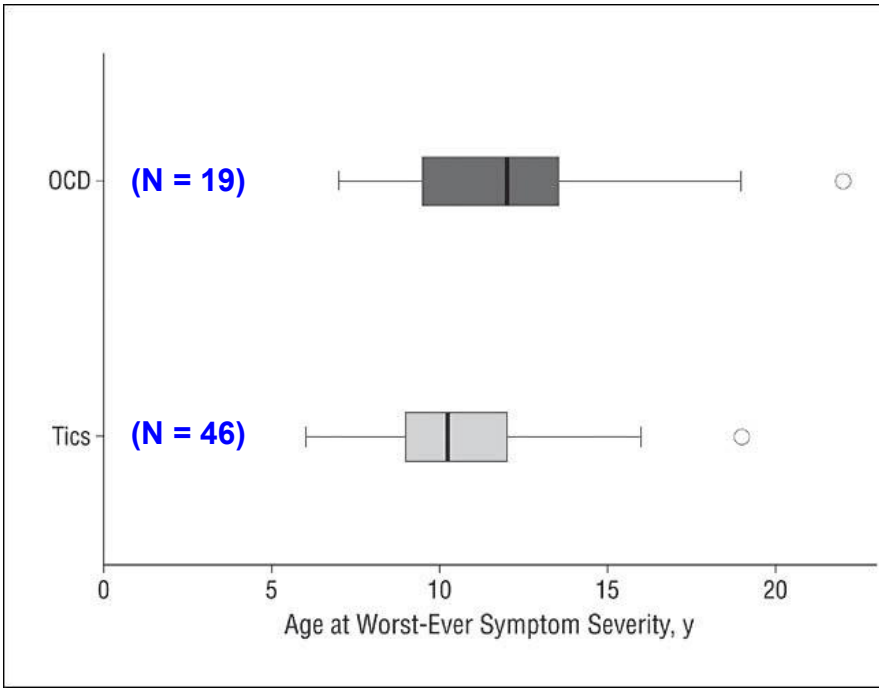
Jankovic. N Engl J Med 2001;345:1184-92

117

Age When Tic and OCD Symptoms Are at Their Worst

46 children with TS

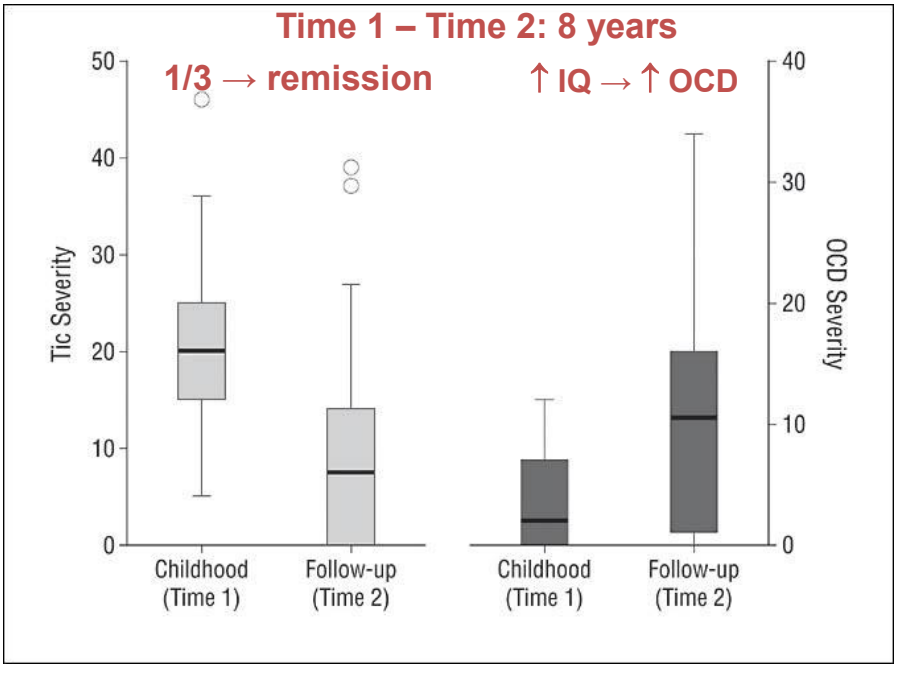
Structured interview at a mean age of 11.4 years and again at 19.0 years



Bloch et al. Arch Pediatr Adolesc Med 2006;160:65-69

118

Tic and OCD Severity at Initial Assessment in Childhood (time 1) and Follow-up in Early Adulthood (time 2)



Tic Severity (N = 46) measured by the Yale Global Tic Severity Scale (YGTSS), OCD (N = 19) by the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)

Bloch et al. Arch Pediatr Adolesc Med 2006;160:65-69

119

Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study.

Groth et al. J Am Acad Child Adolesc Psychiatry 2017;56:304-12

- **The prospective clinical cohort was recruited at the Danish National Tourette Clinic and data were collected at baseline (n = 314, age range 5-19 years) and at follow-up 6 years later (mean age 12.4 vs 18.5; n = 227).**
- **Tic severity declined yearly (0.8 points on the YGTSS) during adolescence; 17.7% of participants above age 16 years had no tics, whereas 59.5% had minimal or mild tics, and 22.8% had moderate or severe tics.**
- **At follow-up, 63.0% of participants had comorbidities or coexistent psychopathologies, whereas 37.0% had pure TS.**
- **Severity of tics, OCD, and ADHD were significantly associated with age and declined during adolescence, however, considerable comorbidities and coexisting psychopathologies persist throughout adolescence.**

120

Tourette Syndrome in Adults

Jankovic J, Gelineau-Kattner R, Davidson A. Mov Disord 2010;25:2171-5

- **We reviewed medical records of all new TS patients ≥19 y/o on initial evaluation referred to our Movement Disorders Clinic over the past 5 years and compared them with 100 TS patients ≤18 y/o**
- **The mean age of 43 adult TS patients was 58.8 ± 6.7 years**
- **Of the adult TS patients 35 (81.4%) had a history of tics with onset before age 18 (mean age at onset 8.5 ± 3.4 years); 8 (18.6%) reported first occurrence of tics after age 18 (mean age at onset 37.8 ± 13.2 years); only 2 (4.7%) patients reported tic onset after age 50**
- **Adult TS largely represents re-emergence or exacerbation of childhood-onset TS. During the course of TS, phonic and complex motor tics, self-injurious behaviors, and ADHD tend to improve, but facial, neck and trunk tics dominate the adult TS phenotype.**

Childhood psychiatric comorbidities and family history of psychiatric disorders were the strongest risk factors associated with tic disorder persistence into adulthood.

Mataix-Cols et al. Mov Disord 2023;38:1419-27

121

Epidemiology of Tourette Syndrome.

Yilmaz AY, Jankovic J. Brain Sci 2025;15:426

- **Based on a review of 48 studies, the prevalence of TS is estimated to be about 1% in children and adolescents and approximately 0.01% in adults.**
- **Male-to-female (M:F) ratio is about 4:1.**
- **Comorbid mental, behavioral, and developmental disorders are observed in over 80%; 33% learning disability.**
- **TS prevalence in the special education population is nearly twice that of the regular education population with prevalences of 1.5% and 0.8%, respectively.**

129

What Causes Tourette Syndrome?

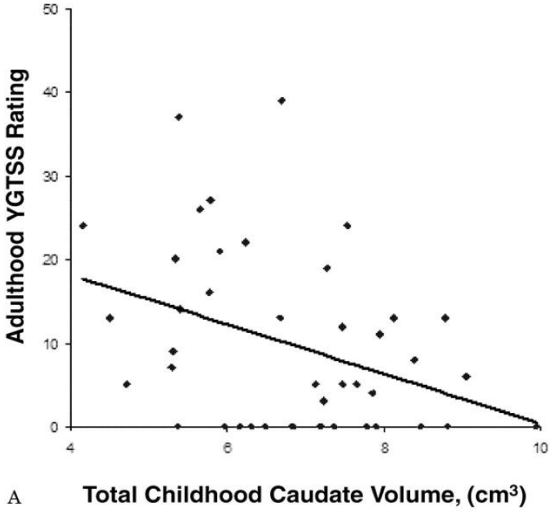
- Brain autopsies – rare and not revealing
- Structural neuroimaging
- Functional neuroimaging
  - PET
  - FDG
  - Neurotransmitters
  - Functional MRI
- Neurophysiology
- Genetics
- Secondary tics

135

Neuroimaging in Tourette Syndrome

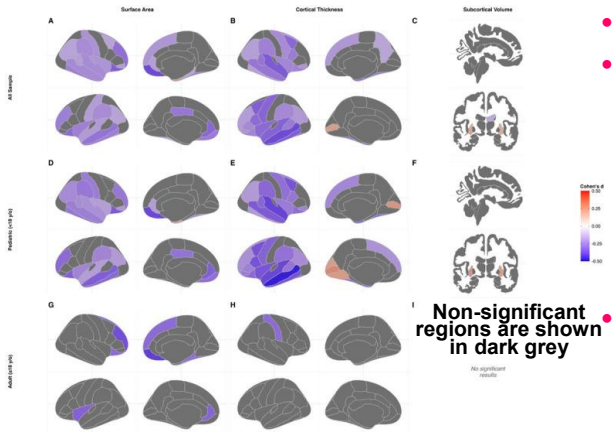
A prospective, longitudinal, study of 43 TS children, who had MRI before age 14 and again about 7.5 years later showed that caudate volumes correlate significantly and inversely with the severity of tics and OCD in early adulthood.

Bloch et al. Neurology 2005;65:1253



139

Brain maps illustrating effect sizes of structural differences between individuals with TS and healthy controls (ENIGMA-TS consortium)



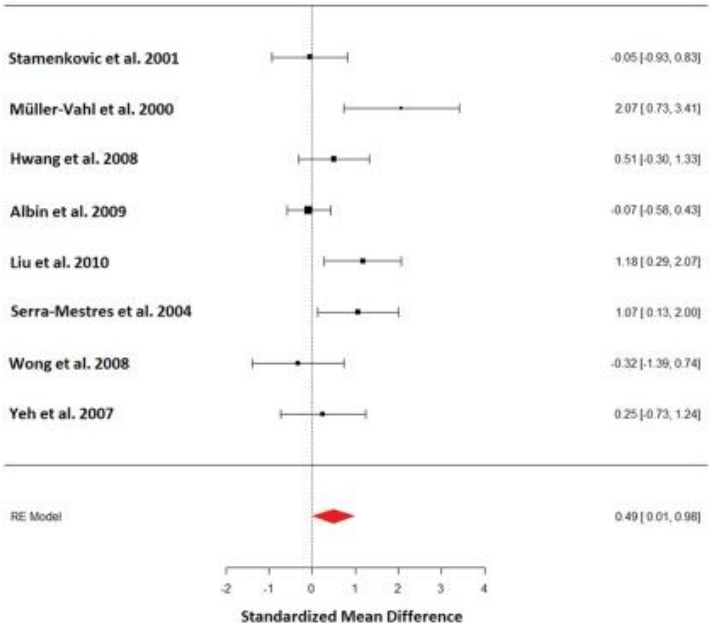
- N = 1,648
- The results reinforce the central role of CSTC circuitry in TS while also indicating involvement of additional frontal and paralimbic regions such as the insula, anterior cingulate, and orbitofrontal cortex.
- In contrast to cortical thinning in sensory-motor areas, several regions in occipital cortex showed increased thickness relative to controls, reflecting heightened sensitivity to visual stimuli, potential triggers for tic expression.
- In adults, the effects were more focal and restricted to frontal regions.

TS reflects not simply a motor disorder, but a disorder of inhibitory control and urge regulation involving frontal–striatal networks.

Jin et al. medRxiv 2026

140

Dopamine transporter (DAT) studies in TS:
Small but significant effect of high DAT availability



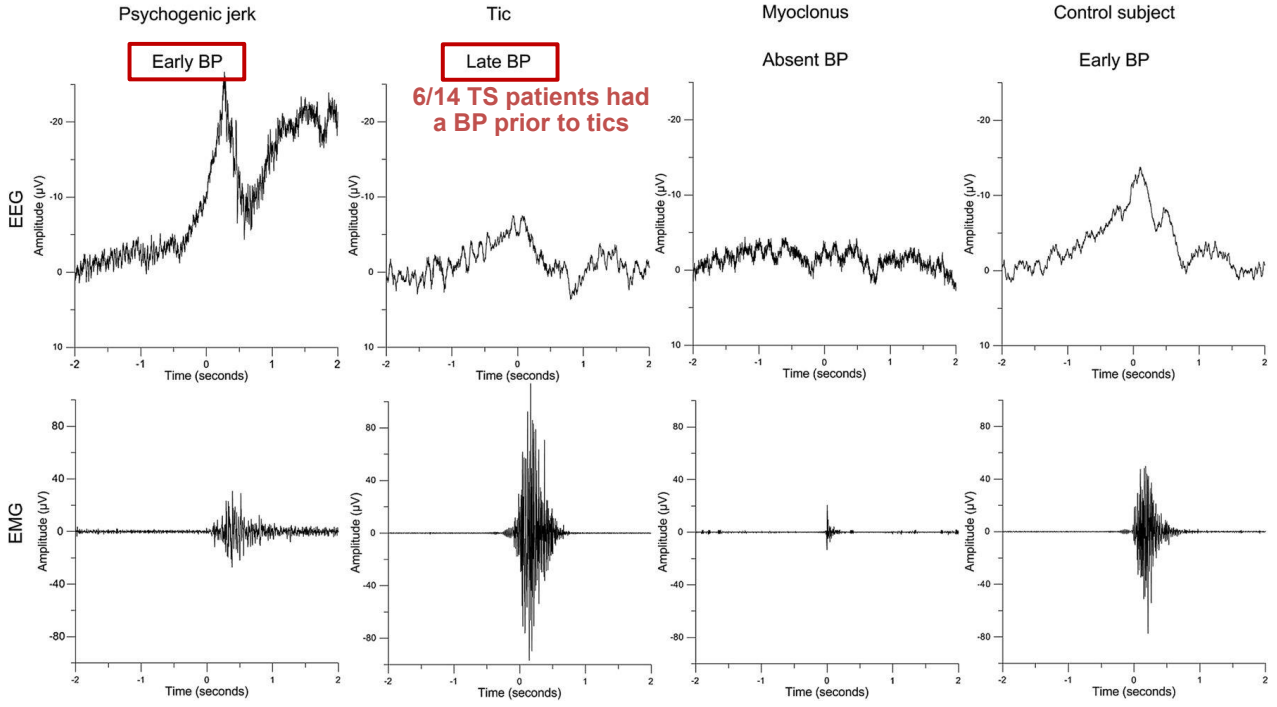
Slightly higher DAT binding in adult TS patients suggests dopaminergic hyperinnervation or presynaptic hyperactivity.

Hienert et al. Transl Psychiatry 2018;8:143

145

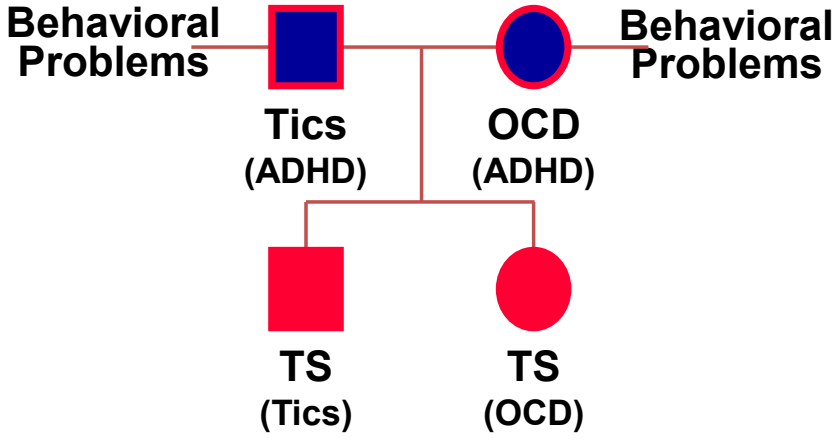
The bereitschaftspotential in jerky movement disorders.

van der Salm et al. J Neurol Neurosurg Psychiatry 2012;83:1162-7



150

Genetics of Tourette Syndrome



Bilineal Transmission

Assortative mating ("like marry like")

Hanna et al. Neurology 1999;53:813-818

People with psychiatric disorders have a higher probability of marrying those who also have psychiatric disorders. The co-occurrence of disorders between parents and their offspring show consistent trends with spousal correlations. This can impact interpretation of genetic correlations based on GWAS.

Fan et al. Nat Hum Behav 2025;9:2539-47

173

Heritability of Tourette Syndrome

- **Genetic variants explain 77.0-92.4% of the heritability of tic disorders. There is a 15-fold increased risk in full siblings compared to that of the general population**
  Mataix-Cols et al. JAMA Psychiatry 2015;72:787-93
- **TS appears to be highly polygenic (genetic risk arises from a cumulative burden of hundreds of small effects size variants)**

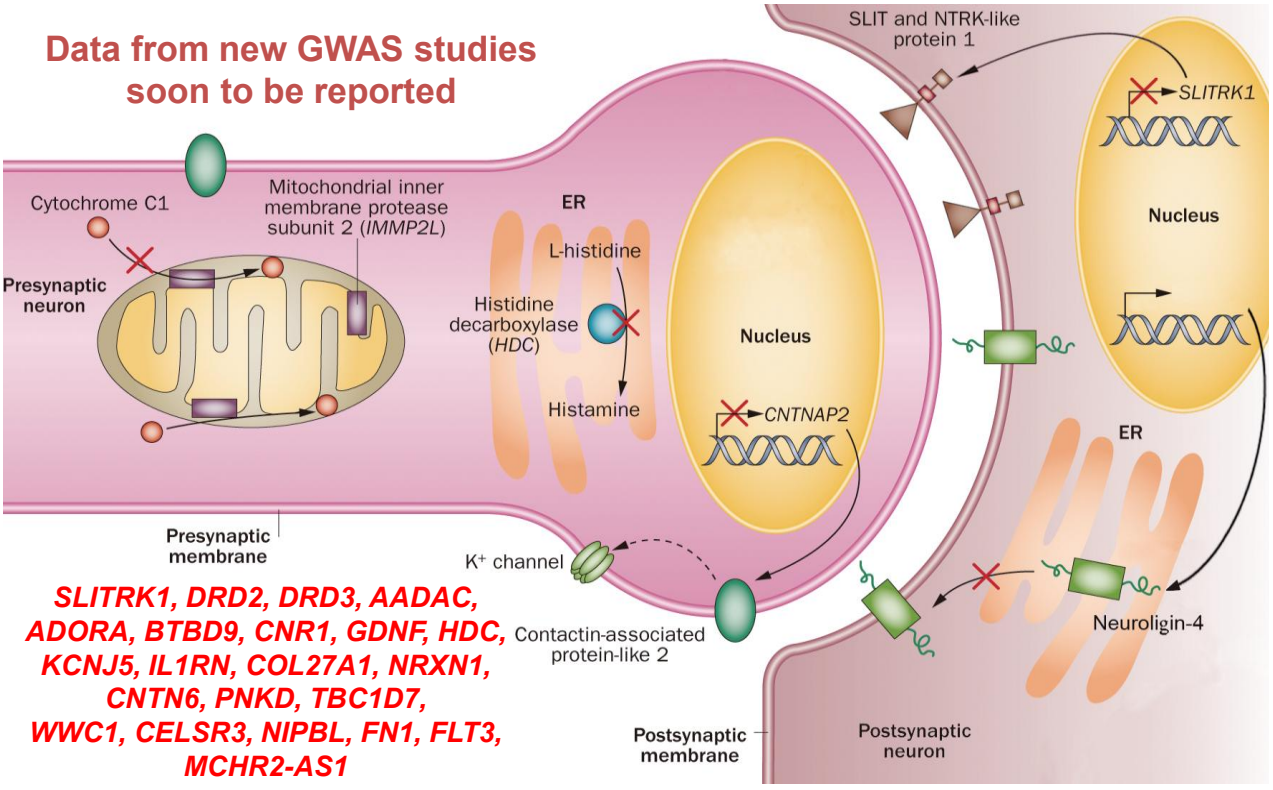
Risk of developing TS

- **Nobody in the family has tics: 1-2%**
- **A family member has tics: 10-17%**
- **A non-identical twin has TS: 23%**
- **An identical twin has TS: 77%**

182

Neuronal location and possible function of the gene products associated with Tourette syndrome

Data from new GWAS studies soon to be reported



SLITRK1, DRD2, DRD3, AADAC, ADORA, BTBD9, CNR1, GDNF, HDC, KCNJ5, IL1RN, COL27A1, NRXN1, CNTN6, PNKD, TBC1D7, WWC1, CELSR3, NIPBL, FN1, FLT3, MCHR2-AS1

Deng H, Gao K, Le W, Jankovic J. Nature Reviews 2012;8:203-13 - Updated

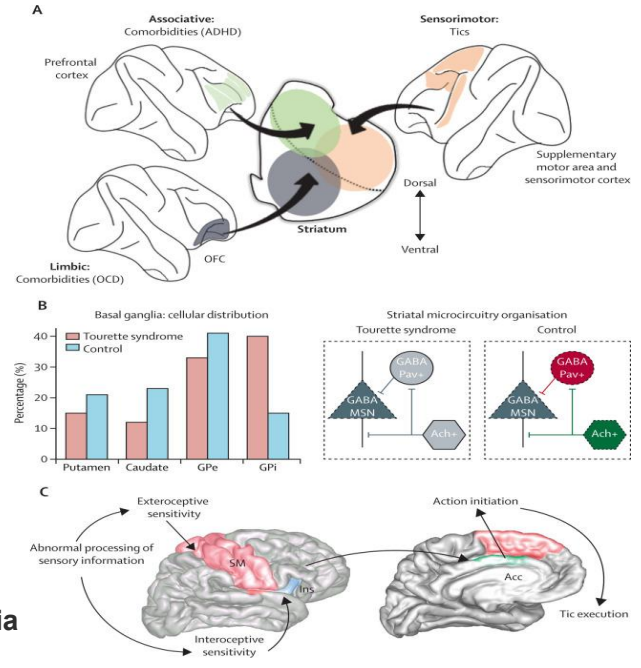
189

Pathophysiology of Tourette syndrome

- **Polygenic disorder**
- **Altered neurotransmitters**
  - ⬆ **Dopamine (striatum)**
  - ⬇ **GABA (SMA)**
  - ⬆ **Glutamate (cortex)**

  … and related modulators (acetylcholine, histamine)

  → disinhibition
- **Cortico–striato–thalamo–cortical and other network disorder**



Abnormal interoceptive (insular cortex; blue) and exteroceptive processing (sensorimotor cortex; pink) ➡ premonitory urges (insular cortex) ➡ action initiation (via anterior cingulate cortex; green) ➡ tic execution (via cortico-basal ganglia sensorimotor network)

Johnson et al. Lancet Neurol 2023;22:147-58

192

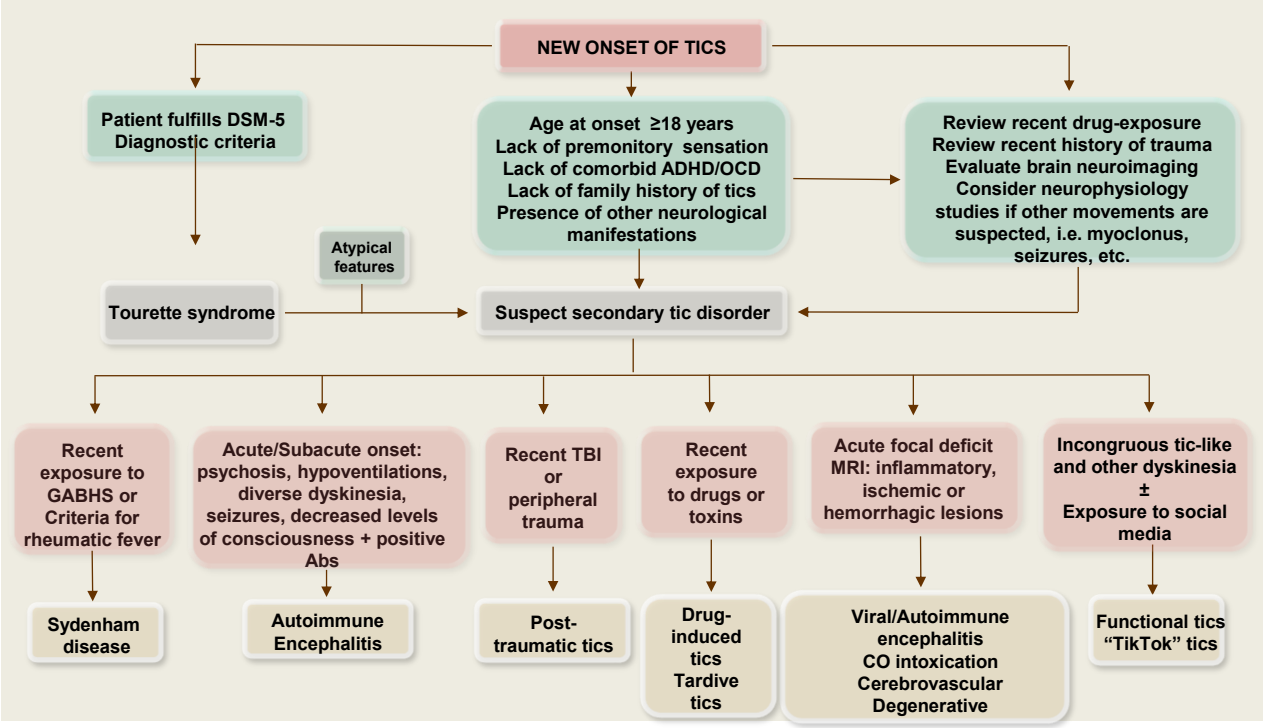
Secondary Tics

- **Genetic: HD, neuroacanthocytosis, autistic disorders, neurocutaneous syndromes, *SLC20A2*-Associated Primary Familial Brain Calcification**
- **Drugs: DRBD (antipsychotics, antiemetics), amphetamines, cocaine, levodopa, anticonvulsants**
- **Infectious/Immunologic: Encephalitis, C-J disease, Sydenham's chorea, autoimmune disorders, PANDAS (?), COVID-19 (?)**
- **Toxins: Carbon monoxide**
- **Other: Static encephalopathy, stroke, brain tumor, trauma (central and peripheral), functional (psychogenic)**

Baizabal-Carvallo JF, Alonso-Juarez M, Jankovic J.
J Neural Transm 2023;130:931-6

193

Secondary Tics



Baizabal-Carvallo and Jankovic. Handbook of Clinical Neurology, Elsevier, 2025

194



203

The Clinical Features of Psychogenic Movement Disorders resembling Tics and Stereotypies.

Baizabal-Carvallo JF, Jankovic J. JNNP 2014;85:573-5

- 9 patients, 5 females, with psychogenic tics diagnosed over a 3-year period.
- Mean age at onset: 29.7 years (range: 16-66).
- Psychogenic movement disorders resembling tics/stereotypies were observed in 4.9% of 184 patients first evaluated at BCM PDCMDC.
- Lack of premonitory sensations, incapable to (even) transiently suppress the movements, and frequent coexistence of other functional movement disorders and pseudoseizures were common.
- Compared to 273 patients with Tourette syndrome, those with psychogenic tics were older: 36 vs. 18 years, ($P = 0.014$) at presentation and more frequently female: 55.6% vs. 21.5%, ($P = 0.030$).
- No patient with functional tics reported childhood or family history of a tic disorder (or occurrence of tics during sleep).
- Conclusions: Movements resembling tics/stereotypies can be observed in a small proportion of patients with psychogenic movement disorders. Clinical features can help to differentiate them from organic movement disorders.

204

Increased Incidence of Functional (Psychogenic) Movement Disorders in Children and Adults Amid the COVID-19 Pandemic

A Cross-sectional Study

Mariam Hull, MD, Mered Parnes, MD, and Joseph Jankovic, MD

Neurology: Clinical Practice October 2021 vol. 11 no. 5 e686-e690 doi:10.1212/CPJ.0000000000001082

Correspondence
Dr. Hull
mariam.hull@bcm.edu

Movement Disorders
CLINICAL PRACTICE
2021;8:1248-52

CASE SERIES

Tics and TikTok: Functional Tics Spread Through Social Media

*Mariam Hull, MD** and *Mered Parnes, MD*

"TikTok Tics" = teenage girls exhibiting tics after they watched TikTok person with millions of followers, named "This Trippy Hippie"
(https://www.youtube.com/watch?v=zJhAJ-1-hGA;
https://www.tiktok.com/@thistrippyhippie/video/6808229929579187461?lang=en)

212

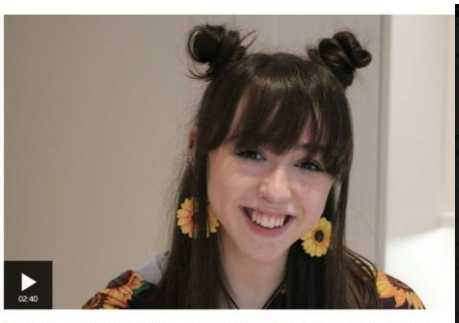
Rapid-onset Functional Tic-like Behaviors

- **Recently, perhaps exacerbated by the COVID-19 pandemic, there has been a surge of this behavior, affecting chiefly adolescent girls**
- **Sudden onset and rapidly evolving (hours-days) simple and complex motor and phonic tic-like behavior, sometimes self-injurious behaviors manifested by large amplitude arm repetitive movement, hitting and throwing objects, screaming and coprolalic utterances and gestures (sexual, offensive, derogatory)**
- **Touching and hitting chest, head, thighs; clapping, whistling, clicking; pointing, sign language; hitting other people (parents)**
- **Often severely disabling – unable to go to school or work**
- **Typically start de novo, but 10-15% had prior history of mild tics**
- **Prior anxiety, depression, and other behavioral abnormalities in ≤90%; physical and mental trauma (predisposition)**
- **Age at onset 12-25 years**
- **Almost exclusively females except in Germany (only 38% -** Paulus et al. Mov Disord 2021;36:2932-5**)**

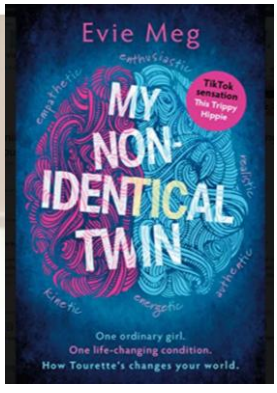
214

trippy hippie





TikTok star Evie-Meg Field on life with Tourette's syndrome



Twitch Streamer With Tourette's Sweet Anita Goes Viral



220

Functional Neurological Disorders Society (FNDS)

http://www.fndsociety.org/

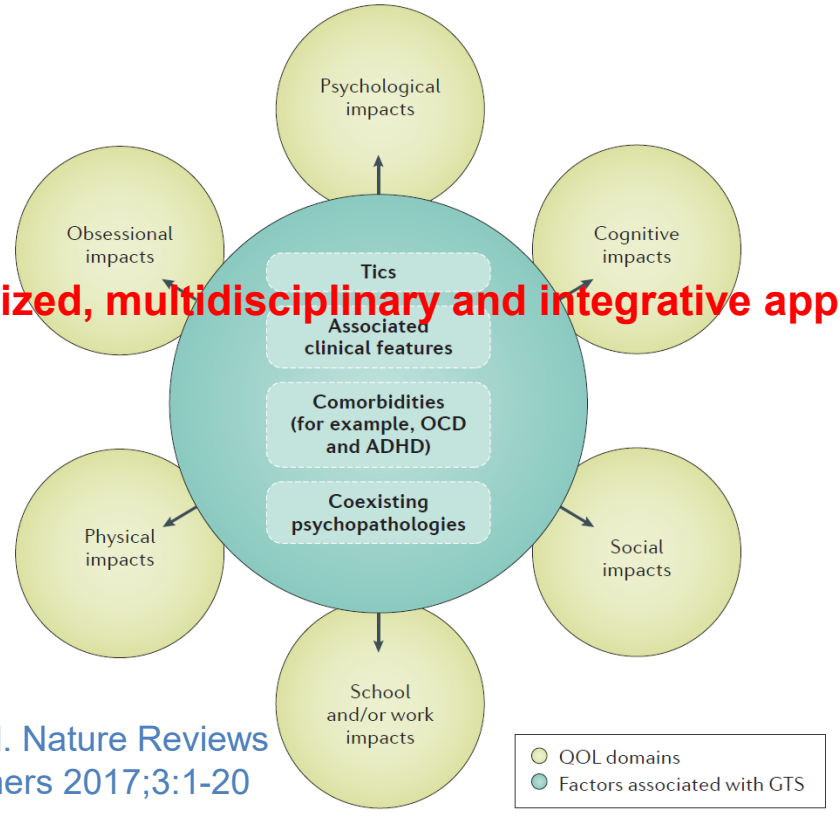


267

Behavioral, Pharmacological, and Surgical Treatment of Tourette Syndrome

278

Quality of Life Domains Affected in Tourette Syndrome



Individualized, multidisciplinary and integrative approach

Robertson et al. Nature Reviews Disease Primers 2017;3:1-20

279

Clinical Assessments of Tourette Syndrome

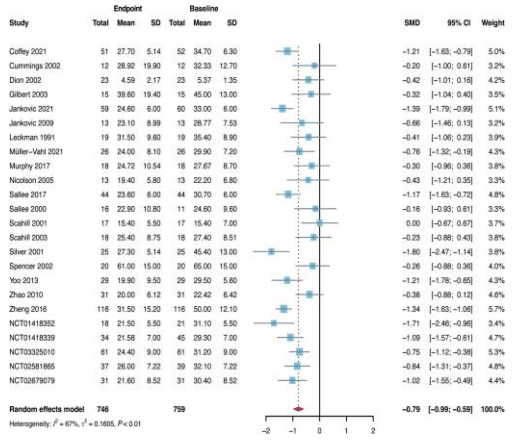
- Yale Global Tic Severity Scale (YGTSS) – Total Tic Severity (TTS)
- TS-Clinical Global Impression (TS-CGI)
- TS-Patient Global Impression of Severity (TS-PGIS)
- TS-Patient Global Impression of Change (TS-PGIC)
- TS-Patient Global Impression of Impact (TS-PGII)
- Premonitory Urge for Tics Scale (PUTS)
- Tic-free interval
- Rush Video-based Tic Rating Scale (RVTRS)
- The Motor or Vocal Inventory of Tics (MOVeIT) symptom screener;
- The Description of Tic Symptoms (DoTS) brief diagnostic tool
- Gilles de la Tourette Syndrome – Quality of Life Scale (GTS-QOL)
- Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; CY-BOCS)
- Conners' Adult Attention Deficit Hyperactivity Disorder Rating Scale (CAARS)
- Children's Depression Inventory 2 (CDI-2)
- Beck Depression Inventory (BDI)
- Children's Columbia Suicide Severity Rating Scale (C-SSRS)
- Barratt Impulsiveness Scale (BIS)
- Hamilton Anxiety Scale (HAM-A)
- Mini International Neuropsychiatric Interview For Children and Adolescents (MINI–KID)
- Brief Psychiatric Rating Scale (BPRS)

280

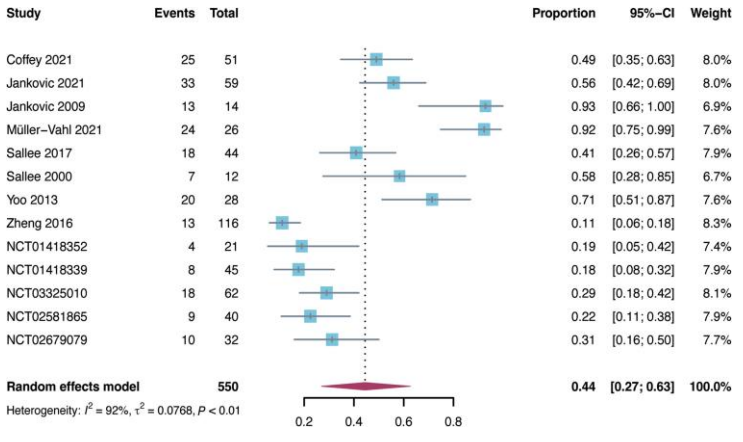
Placebo and Nocebo Responses in Pharmacological Trials of Tic Disorders: A Meta-Analysis.

Wang et al. Mov Disord 2024;39:585-95

Placebo response



Nocebo response



Meta-analysis of 24 trials involving 2,222 participants found -11 point "improvement" on the YGTSS-Total Score and 44% experienced AEs while taking inert pills.

Conclusion: There were considerable placebo and nocebo responses in the tic disorder clinical trials. These results are of great relevance for the design of future trials and for clinical practice in TD.

289

Treatment of Tics

Behavioral Therapy
- Comprehensive Behavioral Intervention for Tics (CBIT), Habit Reversal Therapy (HRT), and Exposure Response Prevention (ERP)

Alpha agonists
- Clonidine
- Guanfacine

Dopamine Receptor Blockers
- Fluphenazine
- Risperidone
- Aripiprazole*
- Pimozide*
- Haloperidol*

Dopamine Depletors (VMAT2 inhibitors)
- Tetrabenazine, Deutetrabenazine, Valbenazine

Antiepileptics
- Topiramate

Botulinum Toxin

Deep Brain Stimulation
- Thalamus
- Globus Pallidus Interna

Experimental Therapeutics

* FDA approved

300

Long-term efficacy and safety of fluphenazine in patients with Tourette syndrome

Wijemanne S, Wu LJC, Jankovic J. Mov Disord 2014;29:126-30

- A retrospective chart review of patients 268 patients with TS treated with fluphenazine over a 26-year period
- Response rating 1 through 5 (1 = marked reduction in tics, 5 = worsening of tics)
- Mean age at start of fluphenazine was 15.8 ± 10.7 years (range 4.1-70.2) and it was the first line agent used in 187 (70%) patients
- Fluphenazine was continued for mean duration of 2.6 ± 3.2 years (range: 0.01-16.8 years) and the mean daily dose at the end of treatment was 3.2 ± 2.3 mg per day (range: 0.5-12 mg)
- 80.5% showed marked to moderate improvement (response rating 1 and 2) and none had worsening of symptoms
- 51 (19.0%) patients discontinued fluphenazine due to side effects and 28 (10.4%) discontinued treatment due to lack of efficacy
- The most common adverse effects were drowsiness (26.1%), weight gain (11.6%), akathisia (8.5%), acute dystonic reaction (7.0%) and depression (6.3%). There were no cases of tardive dyskinesia.

302

Randomized, Double-Blind, Placebo-Controlled Trial Demonstrates the Efficacy and Safety of Oral Aripiprazole for the Treatment of Tourette's Disorder in Children and Adolescents.

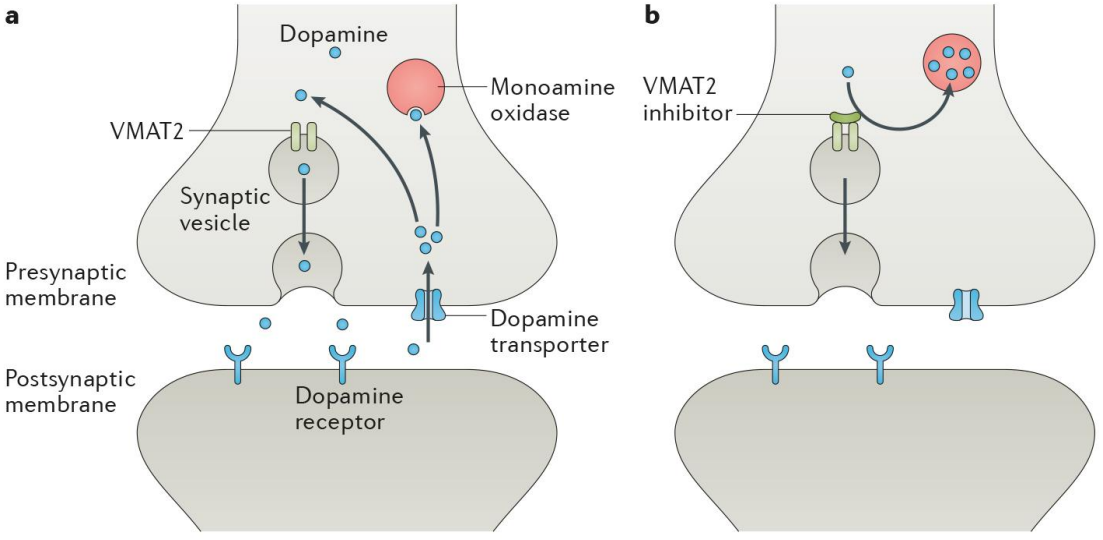
Sallee et al. J Child Adolesc Psychopharmacol 2017;27:771-81

- **Phase 3, randomized, double-blind, placebo-controlled trial which enrolled 133 patients.**
- **At week 8, the treatment difference in YGTSS-TTS vs placebo was -6.3 (p=0.0020) and -9.9 (<0.0001), respectively.**
- **Furthermore, 69% (29/42) of patients in the low-dose (5-10 mg/day) and 74% (26/35) of patients in the high-dose (10-20 mg/day) aripiprazole groups indicated that they were much or very much improved.**
- **The most common adverse events were sedation and fatigue.**

Peña MS, Yaltho TC, Jankovic J. Tardive dyskinesia and other movement disorders secondary to aripiprazole. Mov Disord 2011;26:147-52

305

Mechanism of action of VMAT2 inhibitors



Vesicular membrane transporter type 2 (VMAT2) mediates loading of dopamine into synaptic vesicles for release. Breakdown of dopamine is mediated by monoamine oxidase.

VMAT2 inhibitors block transport of dopamine into synaptic vesicles, reducing dopamine release and depleting dopamine levels through its breakdown by monoamine oxidase.

VMAT2 inhibitors do not cause tardive dyskinesia

Jankovic. Nature Reviews Neurology 2017;13:76-8

308

Tics before and after tetrabenazine

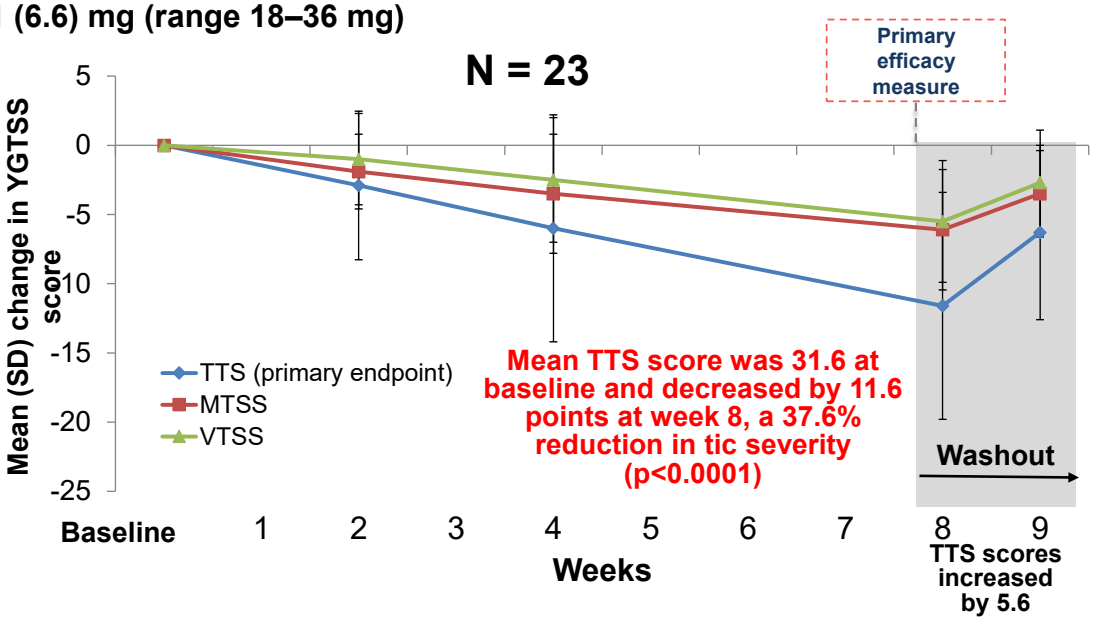


310

Deutetrabenazine in Tics associated with Tourette Syndrome.

Jankovic J, Jimenez-Shahed J, Budman C, Coffey B, Murphy T, Shprecher D, Stamler D. Tremor Other Hyperkinet Mov 2016;6:422

At Week 8, all three YGTSS measures were significantly reduced compared with baseline (P<0.0001) and the mean (SD) daily deutetrabenazine dose was 32.1 (6.6) mg (range 18–36 mg)



TTS = Total Tic Severity score

BDI and CY-BOCS also improved

316

JAMA Network Open. Jankovic et al. JAMA Netw Open 2021;4:e2128204

Original Investigation | Neurology

Safety and Efficacy of Flexible-Dose Deutetrabenazine in Children and Adolescents With Tourette Syndrome
A Randomized Clinical Trial

ARTISTS1

Joseph Jankovic, MD; Barbara Coffey, MD, MS; Daniel O. Claassen, MD; Joohi Jimenez-Shahed, MD; Barry J. Gertz, MD, PhD; Elizabeth A. Garofalo, MD; David A. Stamler, MD; Maria Wieman, MPH; Juha-Matti Savola, MD, PhD; Mark Forrest Gordon, MD; Jessica Alexander, PhD; Hadas Barkay, PhD; Eran Harary, MD

JAMA Network Open. Coffey et al. JAMA Netw Open 2021;4:e2129397

Original Investigation | Neurology

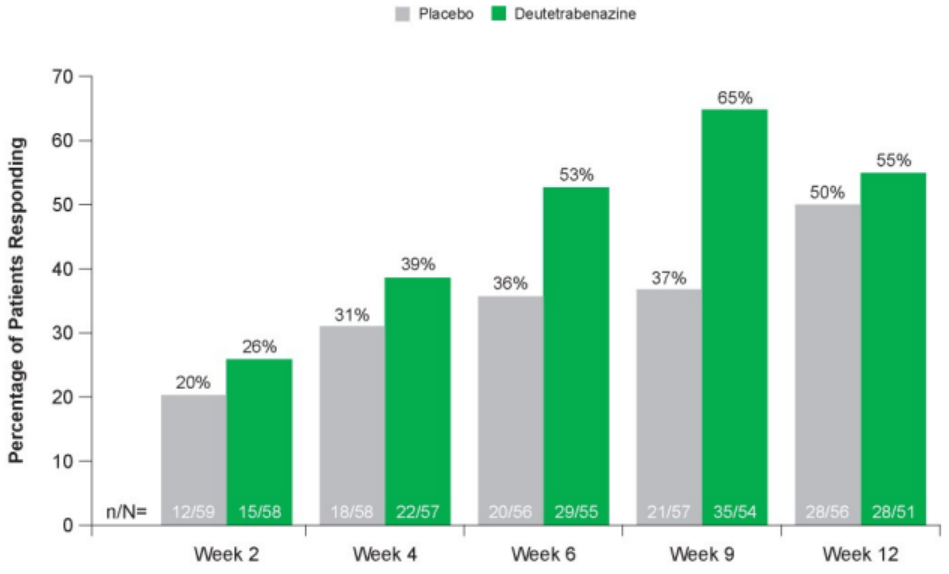
Efficacy and Safety of Fixed-Dose Deutetrabenazine in Children and Adolescents for Tics Associated With Tourette Syndrome
A Randomized Clinical Trial

ARTISTS2

Barbara Coffey, MD, MS; Joseph Jankovic, MD; Daniel O. Claassen, MD; Joohi Jimenez-Shahed, MD; Barry J. Gertz, MD, PhD; Elizabeth A. Garofalo, MD; David A. Stamler, MD; Maria Wieman, MPH; Juha-Matti Savola, MD, PhD; Mark Forrest Gordon, MD; Jessica K. Alexander, PhD; Hadas Barkay, PhD; Eran Harary, MD

322

Proportion of Patients With 25% or Greater Reduction From Baseline in YGTSS-TTS



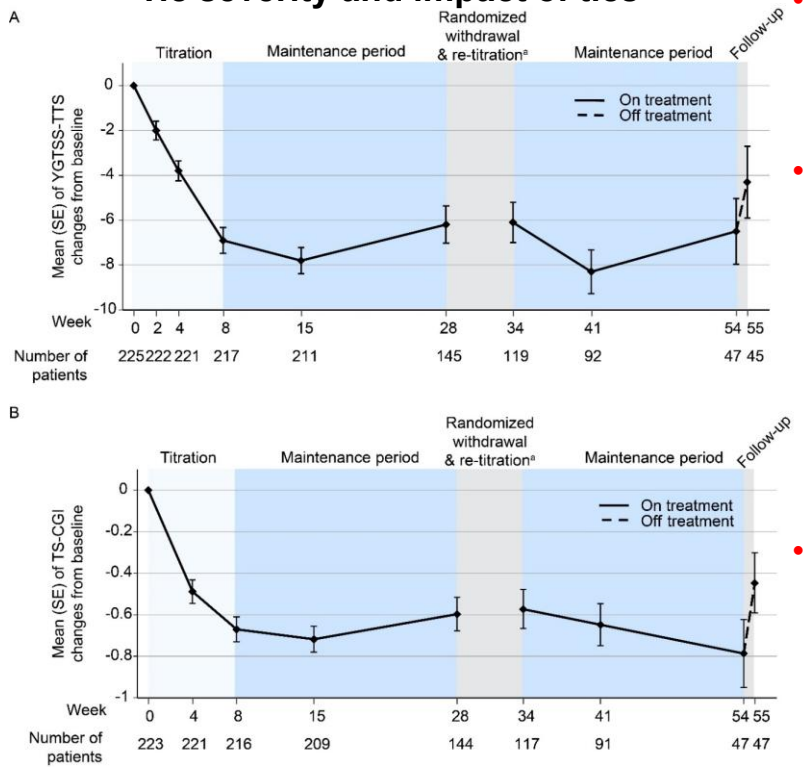
YGTSS-TTS, Yale Global Tic Severity Scale-Total Tic Score.

Jankovic et al. JAMA Netw Open 2021;4:e2128204

326

Long-term safety and efficacy of deutetrabenazine in TS

Tic severity and impact of tics



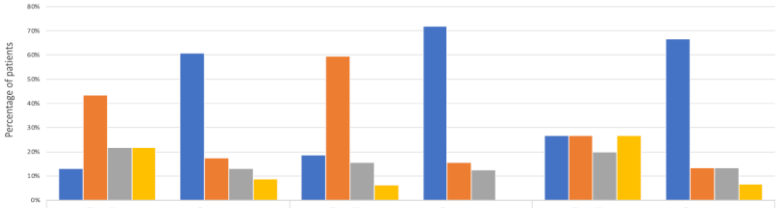
- **OLE study of ARTISTS 1 and ARTISTS 2 with a two-week 2:1 randomized withdrawal period.**
- **There was a reduction in tics and improvement in quality of life and other secondary measures through the end of treatment, followed by a numeric increase (worsening) at follow-up 1 week after treatment.**
- **Deutetrabenazine was well tolerated in this pediatric population, with low rates of adverse events.**

Jankovic et al. Mov Disord Clin Pract 2023;10:1388-98

340

Real-World Experience With VMAT2 Inhibitors

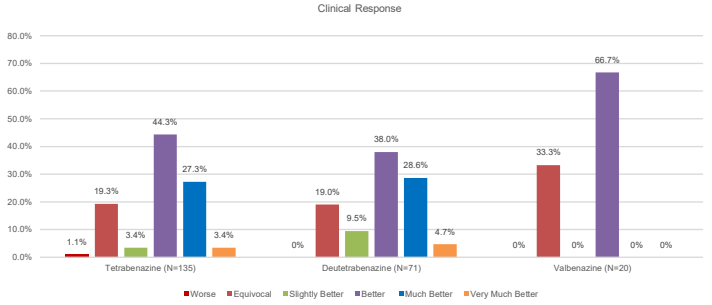
Hyperkinetic disorders N = 135



	Baseline	On treatment	Baseline	On treatment	Baseline	On treatment
	TBZ (n=23)		DTBZ (n=32)		VBZ (n=15)	
1 Normal or mildly ill	13.0	60.9	18.8	71.9	26.7	66.7
2 Moderately ill	43.5	17.4	59.4	15.6	26.7	13.3
3 Markedly ill	21.7	13.0	15.6	12.5	20.0	13.3
4 Severely ill	21.7	8.7	6.3	0.0	26.7	6.7

Niemann N, Jankovic J. Clin Neuropharmacol 2019;42:37-41

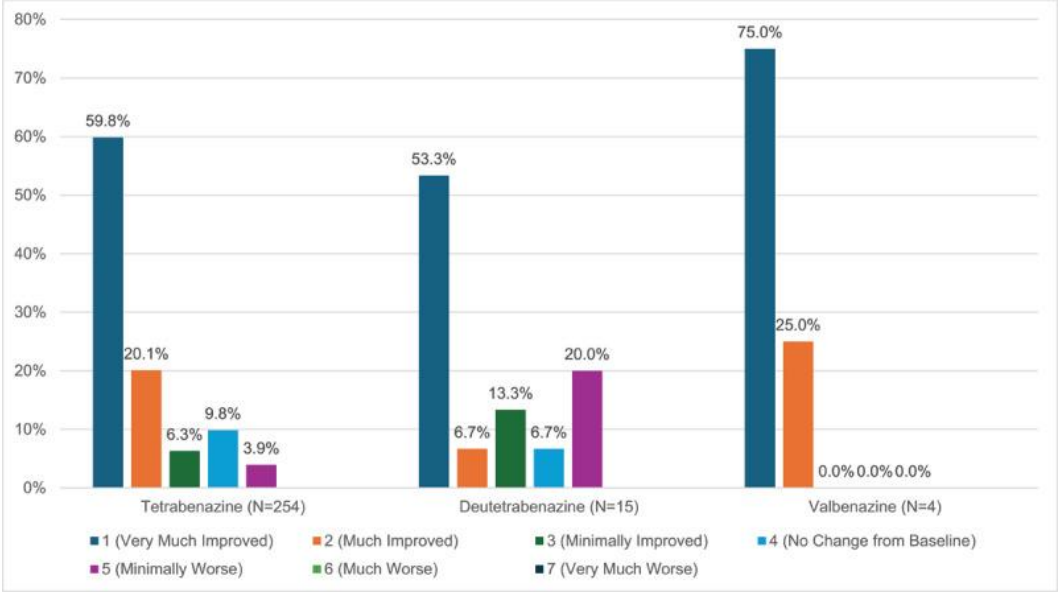
Tourette syndrome N = 165



Makhoul K, Jankovic J. J Neurol 2023;270:4518-22

352

Percentage of patients undergoing treatment with VMAT2 inhibitor with resultant Clinical Global Impression-Improvement.

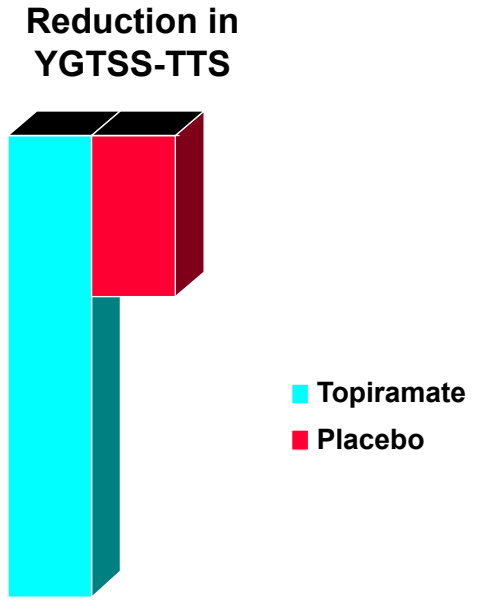


359

A Randomized, Double-Blind, Placebo-Controlled Study of Topiramate in the Treatment of Tourette Syndrome

Jankovic et al. J Neurol Neurosug Psychiatry 2010;81:70-3

- N = 29 (26 males)
- Mean age 16.5 ± 9.89 years
- The Total Tic Score (TTS), the primary endpoint, improved by 14.29 ± 10.47 points from baseline to visit 5 (day 70) compared to 5.00 ± 9.88 point change in the placebo group (p = 0.0259)
- There were also improvements in the other components of the YGTSS and various secondary measures
- No differences were observed in the frequency of adverse events between the two treatment groups



361

Ecopipam for Tourette Syndrome: A Randomized Trial.

Gilbert et al. Pediatrics 2023;151:e2022059574

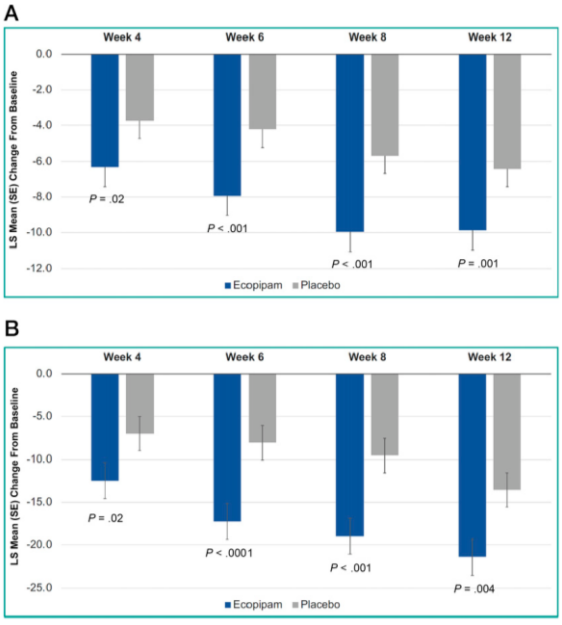
- **Multicenter, randomized, double-blind, placebo-controlled, phase 2b trial of ecopipam, dopamine 1 receptor antagonist.**
- **153 subjects aged ≥6 to <18 years with a baseline Yale Global Tic Severity Score Total Tic Score of ≥20 were randomly assigned 1:1 to ecopipam (n = 76) or placebo (n = 77). The primary endpoint was mean change over 12 weeks in the Yale Global Tic Severity Score Total Tic Score.**
- **Total tic scores were significantly reduced from baseline to 12 weeks in the ecopipam group compared with placebo (P = 0.01). Improvement in Clinical Global Impression of Tourette Syndrome Severity was also greater in the ecopipam group (P = 0.03).**
- **Headache (15.8%), insomnia (14.5%), fatigue (7.9%), and somnolence (7.9%) were the most common adverse events. More weight gain was seen in subjects assigned to placebo.**

387

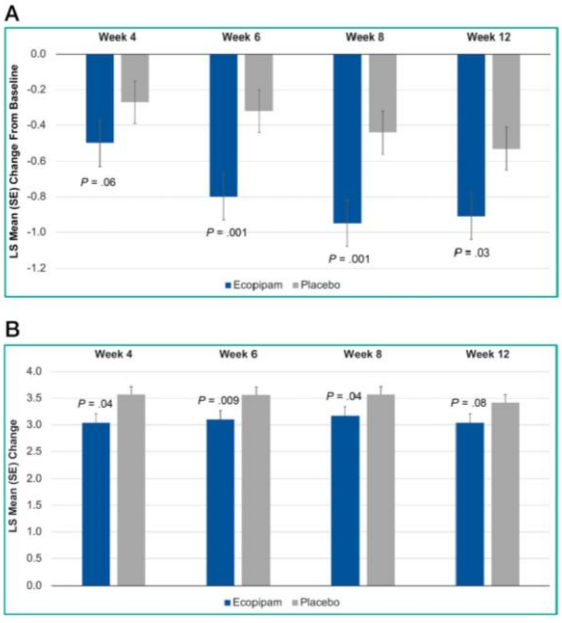
Ecopipam for Tourette Syndrome: A Randomized Trial.

Gilbert et al. Pediatrics 2023;151:e2022059574

(A) YGTSS-TTS and (B) YGTSS-GS LS mean change from baseline



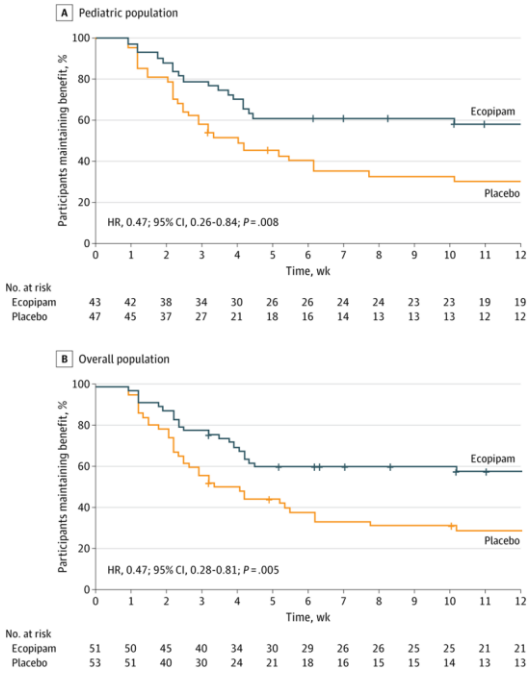
(A) CGI-TS-S LS and (B) CGI-TS-I LS mean change from baseline



N = 153 subjects randomized; 16 (10.5%) discontinued prematurely

388

Efficacy and Safety of Ecopipam for Tourette Syndrome:
Phase 3, double-blind, placebo-controlled, randomized withdrawal study
Kaplan-Meier Curves for Time to Relapse in the Pediatric Population (A) and Overall Population (B) From Randomization (Week 12)



- **216 patients with TS (77.3% pediatric; 67.6% male) enrolled in open-label withdrawal of ecopipam trial.**
- **Ecopipam significantly reduced the relapse risk vs placebo in the pediatric population (P = .008; n = 90), but this trend was not significant in adults.**
- **The most frequently reported adverse events with ecopipam were somnolence, anxiety, headache, and insomnia.**

Gilbert et al. JAMA Neurol 2026;83:645-53

390

REVIEW

The Therapeutic Potential of Cannabinoids for Movement Disorders

Benzi Kluger, MD, MS,[1†*] Piera Triolo, BS,[1†] Wallace Jones, BS,[1†] and Joseph Jankovic, MD[2†]

[1]*Movement Disorders Center, Department of Neurology, University of Colorado School of Medicine, Aurora, Colorado, USA*
[2]*Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA*

Mov Disord 2015;30:313-27

ABSTRACT: There is growing interest in the therapeutic potential of marijuana (cannabis) and cannabinoid-based chemicals within the medical community and, particularly, for neurological conditions. This interest is driven both by changes in the legal status of cannabis in many areas and increasing research into the roles of endocannabinoids within the central nervous system and their potential as symptomatic and/or neuroprotective therapies. We review basic science as well as preclinical and clinical studies on the therapeutic potential of cannabinoids specifically as it relates to movement disorders. The pharmacology of cannabis is complex, with over 60 neuroactive chemicals identified to date. The endocannabinoid system modulates neurotransmission involved in motor function, particularly within the basal ganglia. Preclinical research in animal models of several movement disorders have shown variable evidence for symptomatic benefits, but more consistently suggest potential neuroprotective effects in several animal models of Parkinson's (PD) and Huntington's disease (HD). Clinical observations and clinical trials of cannabinoid-based therapies suggests a possible benefit of cannabinoids for tics and probably no benefit for tremor in multiple sclerosis or dyskinesias or motor symptoms in PD. Data are insufficient to draw conclusions regarding HD, dystonia, or ataxia and nonexistent for myoclonus or RLS. Despite the widespread publicity about the medical benefits of cannabinoids, further preclinical and clinical research is needed to better characterize the pharmacological, physiological, and therapeutic effects of this class of drugs in movement disorders. © 2015 International Parkinson and Movement Disorder Society.

Key Words: cannabinoids; cannabis; movement disorders; Parkinson's disease; Huntington's disease

Tetrahydrocannabinol and cannabidiol in Tourette syndrome.

Mosley et al. NEJM Evid 2023

https://evidence.nejm.org/doi/full/10.1056/EVIDoa2300012

- **In this double-blind, crossover trial, participants with severe Tourette syndrome were randomly assigned to a 6-week treatment period with escalating doses of an oral oil containing 5 mg/ml of THC and 5 mg/ml of CBD, followed by a 6-week course of placebo, or vice versa, separated by a 4-week washout period.**
- **22 participants (8 female) were enrolled.**
- **Reduction in total tic score (at week 6 relative to baseline) as measured by the YGTSS was 8.9 (±7.6) in the active group and 2.5 (±8.5) in the placebo group (P=0.008).**
- **Outcomes were correlated with plasma levels of cannabinoid metabolites.**
- **The most common adverse effect in the active treatment period was cognitive difficulties (n=8).**
- **CONCLUSION: In severe Tourette syndrome, treatment with THC and CBD reduced tics and may reduce impairment due to tics, anxiety, and obsessive-compulsive disorder.**

407

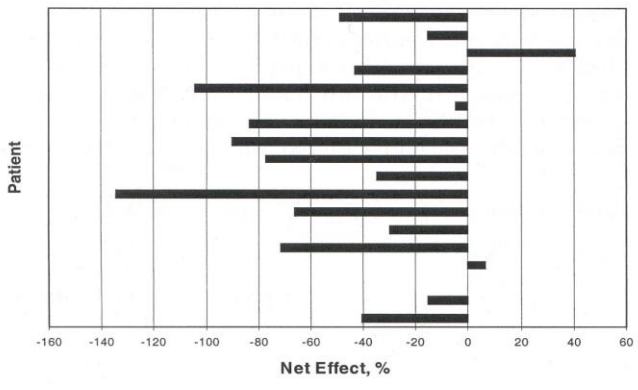
Botulinum Toxin for Motor Tics

Marras et al. Neurology 2001;56:605-10

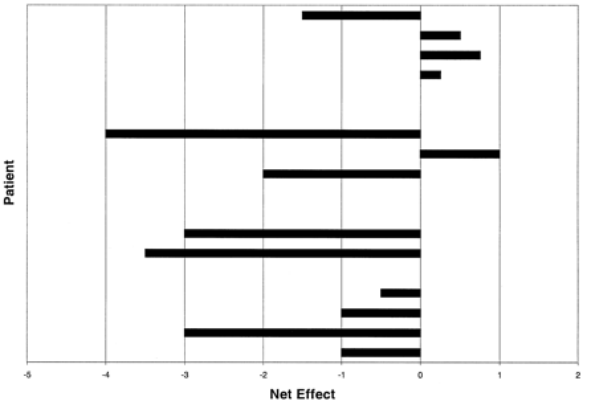
18 patients completed the study

39% ↓ in tics/min with BTX vs 6% ↑ with placebo (*P* = 0.004)
0.46 ↓ in urge score with BTX vs 0.49 ↑ with placebo (*P* = 0.02)

Median Net Effect (at 2 weeks): –37% (p< 0.004)



tics/min



urge scores

442

Summary of Studies on Botulinum Toxin in Motor and Phonic Tics

References	Type of Study	Type of Participants	Types of Intervention	Types of Outcome Measures	Conclusion
Jankovic[42]	Pilot study Open label	Cases: n = 10 (motor tics, all males)	BTX A	(1) Intensity and frequency of tics (2) PMUs	BTX injections (inj) appear to be safe and effective treatment for patients with focal dystonic tics. The treatment ameliorates not only involuntary movements but also the premonitory sensory component associated with some tics
Salloway et al[48]	Case report	One male (phonic)	BTX A	(1) Speech: loudness (UPDRS severity rating scale and 7-point scale) (2) Tic severity score and frequency (3) Premonitory tension	BTX led to a moderate reduction in the loudness of the tics, decrease in tic severity and frequency, may decrease the premonitory symptoms of tension and discomfort
Scott et al[49]	Case report	One male (phonic)	BTX A	Corpolalia and premonitory surge	BTX resulted in marked improvement in coprolalia as well as marked reduction in the premonitory urges associated with the vocal tics and coprolalia
Trimble et al[43]	Case report	One male (phonic)	BTX A	Corpolalia loudness intensity	Response to BTX was considerable, and affected not only the coprolalia, but also aided the general pattern of his symptoms, improved psychological state secondary to the relief of the coprolalia with its attendant psychosocial distress
Kwak et al[43]	Clinical trial	Cases: n = 35 (motor tics, 30 male, 5 female)	BTX A	(1) Clinical rating scale (0–4) (2) Patients' impressions of overall efficacy (3) Degree of benefit with premonitory sensations	BTX A improved the motor component of tics in all patients and also provided relief of premonitory sensations in 84% of the patients
Marras et al[41]	Randomized double-blinded controlled clinical trial	Cases: n = 18 (simple motor tics)	BTX	Primary: the number of treated tics per minute on a videotape segment Secondary: number of untreated tics per minute, the Shapiro Tourette Syndrome Severity Scale score, a numerical assessment of the urge to perform the treated tic and the patient's global impression of change	BTX reduced treated tic frequency (39% reduction; $P = 0.0007$) and the urge associated with the treated tic ($P = 0.02$). Despite these changes, patients did not report an overall benefit from the treatment
Porta et al[45]	Clinical trial Open label	Cases: n = 30 (only phonic tics)	BTX A	(1) Global impression of changes by physician and patient (2) PMU (3) Impact on quality of life	BTX A is an effective and safe treatment for phonic tics associated with Tourette syndrome (93% improved with 50% tic free, PMU dropped from 53% to 20%)
Srirompotong et al[47]	Case report	One male (ear wiggling tics)	BTX A	Disappearance of tics	There was complete disappearance of ear wiggling tics with BTX inj
Vincent[51]	Case series	Two cases with laryngeal tics (1 female, 1 male)	BTX A	(1) Clinical rating scale (2) Premonitory surge	Successful treatment with low-dose BTX type A to reduce the symptoms of laryngeal tics, premonitory surge leading to improved quality of life
Aguirregomozcorta et al[46]	Case report	One male (cervical dystonic tics)	BTX A	Resolution of cervical tics	Complete resolution of cervical dystonic tics with BTX in case of Tourette syndrome was seen
Rath et al[44]	Observational study	Cases: n = 30 (simple motor tics)	Not known	(1) Efficacy (rated on a 4-level scale) and duration of effect (2) Latency of response, changes of PMU and possible side effects	BTX A appears a safe and effective treatment for simple motor tics and retains its efficacy after long-term treatment. BTX may also induce permanent remission of the treated tics

Pandey S, Dash D. Neurologist 2019;24:93-108

Malignant Tourette Syndrome

Cheung MC, Shahed J, Jankovic J. Mov Disord 2007;22:1743-50

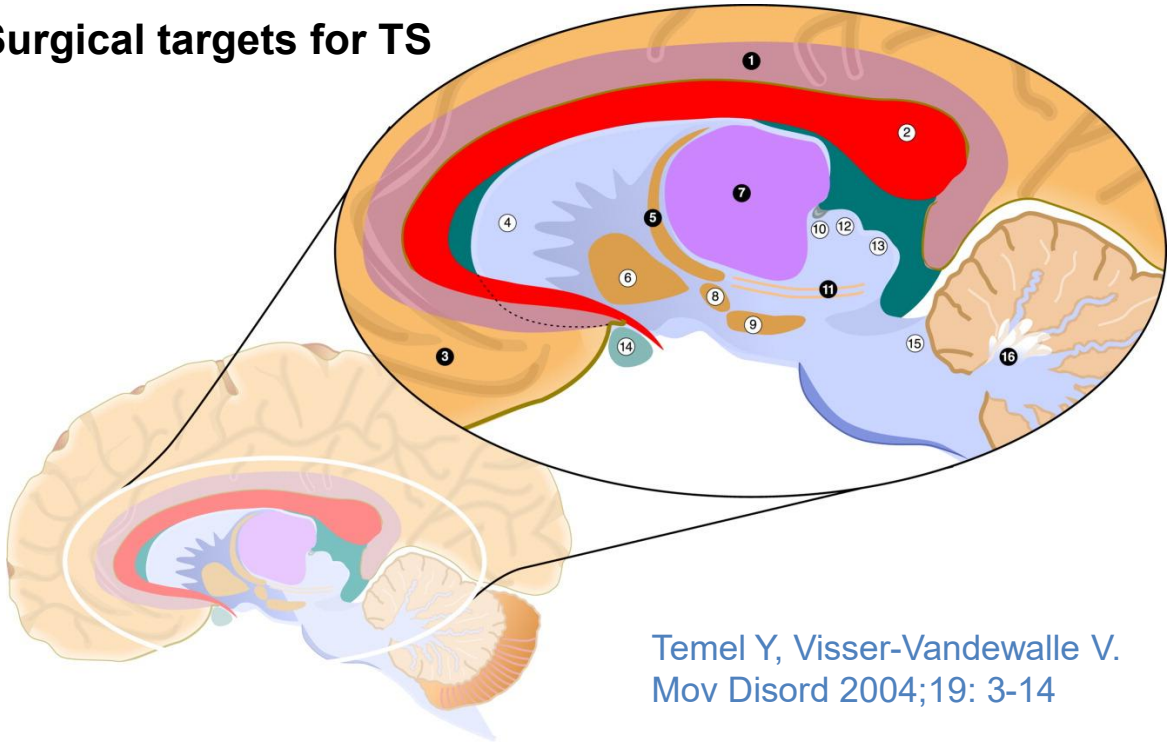
"In one patient with a 'whiplash' tic causing compressive cervical myelopathy, we were able to reverse the neurological deficit with botulinum toxin injections into the cervical muscles. This treatment modality can be particularly effective and even life-saving in patients with tics manifested by severe, repetitive, neck extension, the so called 'whiplash tics'. Such tics, if left untreated could results in secondary compressive myelopathy and quadriparesis."



Krauss JK, Jankovic J. Severe motor tics causing cervical myelopathy in Tourette's syndrome. Mov Disord 1996;11:563-6
Baizabal-Carvallo JF, Cavanna AE, Jankovic J. Tics emergencies and malignant tourette syndrome: Assessment and management. Neurosci Biobehav Rev 2024;159:105609

450

Surgical targets for TS

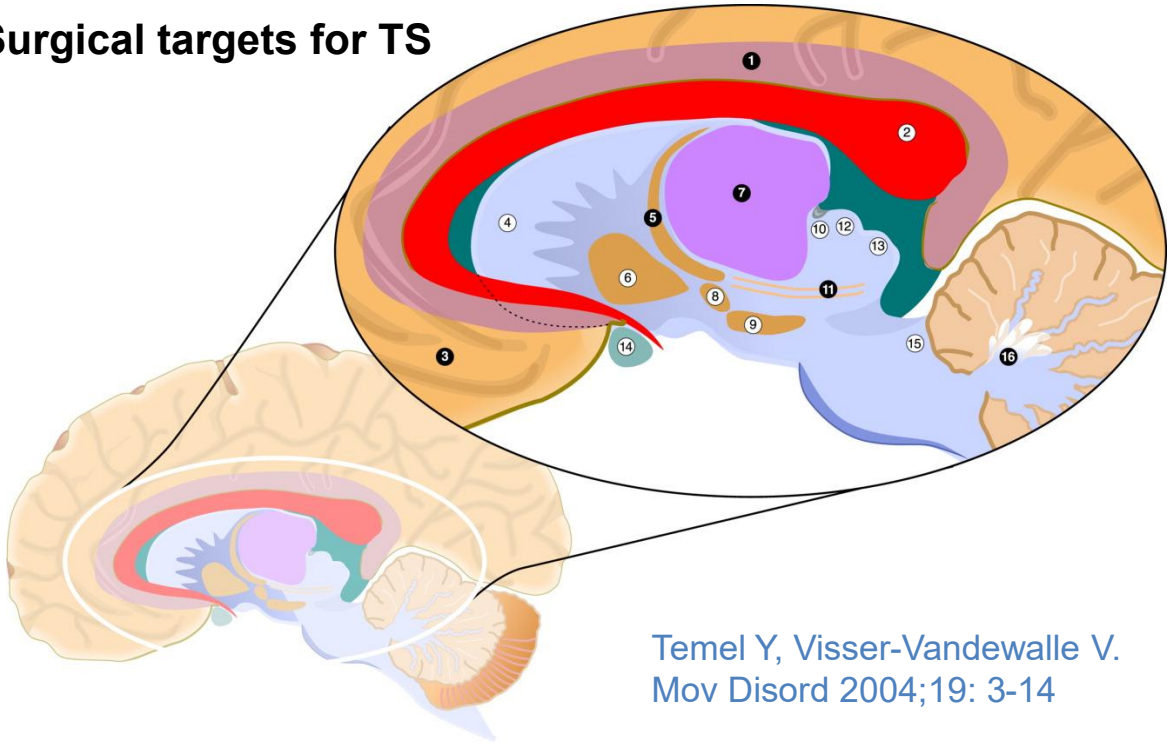


Temel Y, Visser-Vandewalle V.
Mov Disord 2004;19: 3-14

1. cingulate cortex, 2. corpus callosum, 3. frontal lobe, 4. caudate-putamen, 5. zona incerta, 6. globus pallidus, 7. thalamus, 8. subthalamic nu, 9. substantia nigra, 10. posterior commissure, 11. H fields of Forel, 12. superior colliculus,13. inferior colliculus, 14. optic chiasm, 15. superior cerebellar peduncle, 16. dentate nucleus

454

Surgical targets for TS



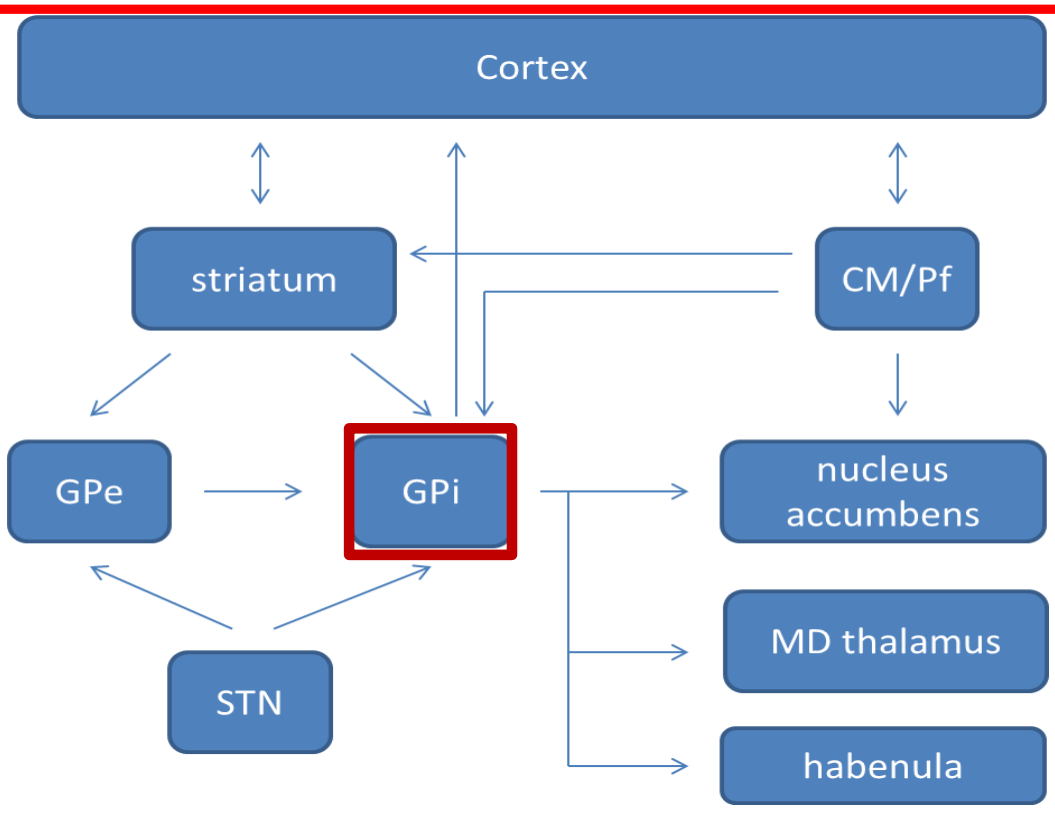
Temel Y, Visser-Vandewalle V.
Mov Disord 2004;19: 3-14

1. cingulate cortex, 2. corpus callosum, 3. frontal lobe, 4. caudate-putamen, 5. zona incerta, 6. globus pallidus, 7. thalamus, 8. subthalamic nu, 9. substantia nigra, 10. posterior commissure, 11. H fields of Forel, 12. superior colliculus,13. inferior colliculus, 14. optic chiasm, 15. superior cerebellar peduncle, 16. dentate nucleus

455

Deep Brain Stimulation for TS – Target Selection

Viswanathan A, Jimenez-Shahed J, Baizabal-Carvallo F. Jankovic J.
Stereotact Funct Neurosurg 2012;90:213-24



457

The International Tourette Syndrome Deep Brain Stimulation Public Registry and Database

Martinez-Ramirez et al. JAMA Neurol 2018;75:353-9

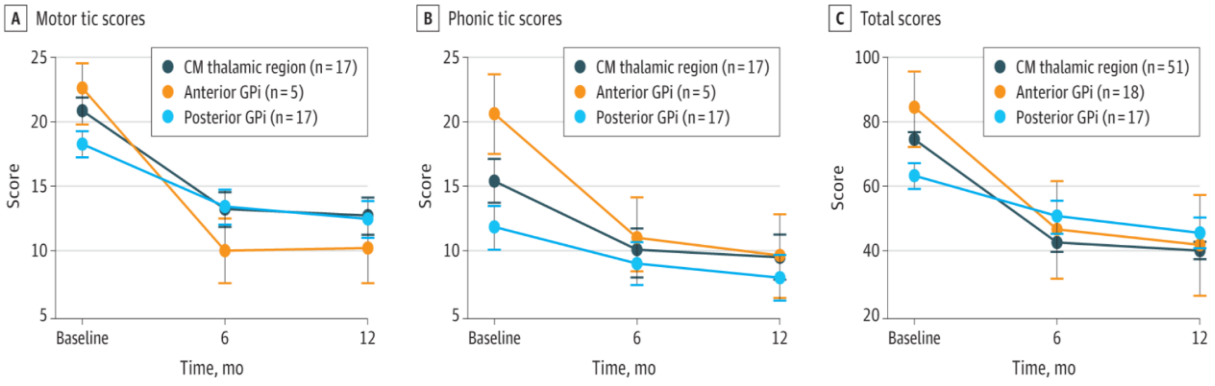
- **185 patients (78% male; mean age at surgery, 29.1 years, range 13-58) with medically refractory TS who underwent DBS implantation from 2012-2016 at 31 institutions in 10 countries**
- **Implanted targets: centromedian thalamic region (57%), anterior globus pallidus internus (25%), posterior globus pallidus internus (15%), and the anterior limb of the internal capsule (3%).**
- **OCD present in 64% of patients and 22% had a history of self-injurious behavior.**
- **The YGTSS mean total score improved from 75.0 at baseline to 41.2 at 1 year after DBS implantation (p<.001); the motor and phonic tic subscores also improved significantly (both p<.001).**
- **The overall AE event rate was 35.4%, with intracranial hemorrhage occurring in 1.2% of patients, infection in 2.5%, and lead explantation in 1%; the most common stimulation-induced side effects were dysarthria (6.3%) and paresthesia (8.2%).**
- **Multiple brain targets resulted in similar suppression of tics.**

461

The International Tourette Syndrome Deep Brain Stimulation Public Registry and Database

Martinez-Ramirez et al. JAMA Neurol 2018;75:353-9

Yale Global Tic Severity Scale (YGTSS) Scores by Time and Brain Target

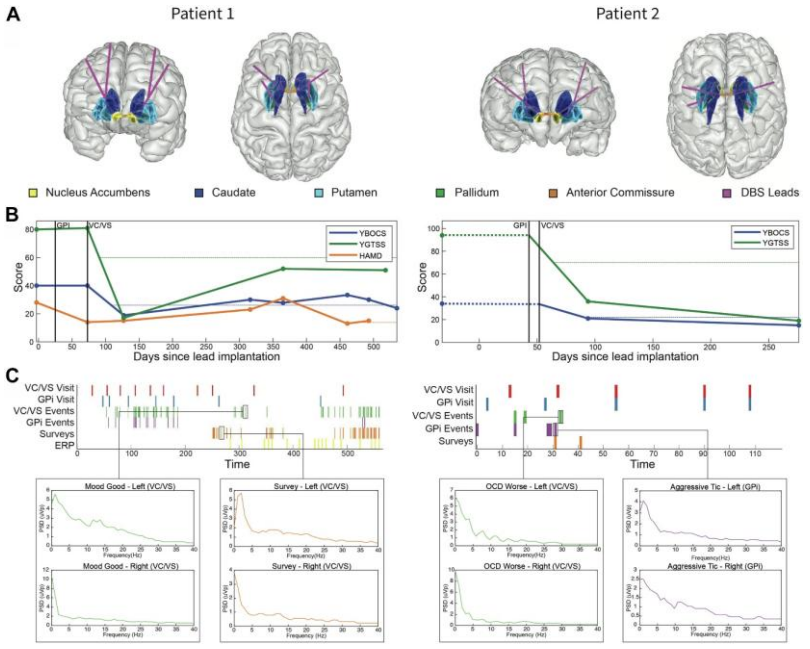


CM = centromedian; GPi = globus pallidus internus

462

Dual-Target Deep Brain Stimulation for Obsessive-Compulsive Disorder and Tourette Syndrome.

Najera et al. Biol Psychiatry 2023;93:e53-e55



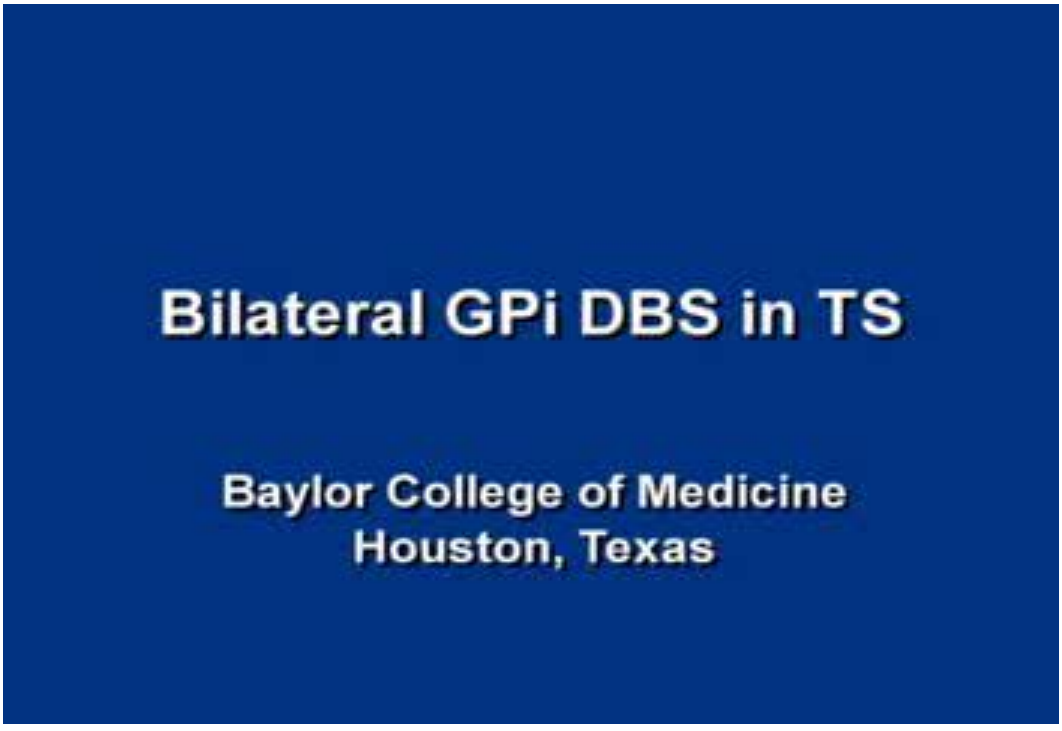
Targets: bilateral ventral capsule/ventral striatum (VC/VS) for OCD and posteroventral (motor) GPi for TS.
Each patient received 2 IPGs (Percept PC; Medtronic), 1 for each pair of leads

(A) Multi-Modality Visualization Tool reconstructions of patient brains showing frontal and superior views of cortical surfaces, labeled subcortical structures and DBS leads. (B) Clinical scores indicating favorable outcomes over time (C) Timeline indicating patient programming visits and use of event markers

475

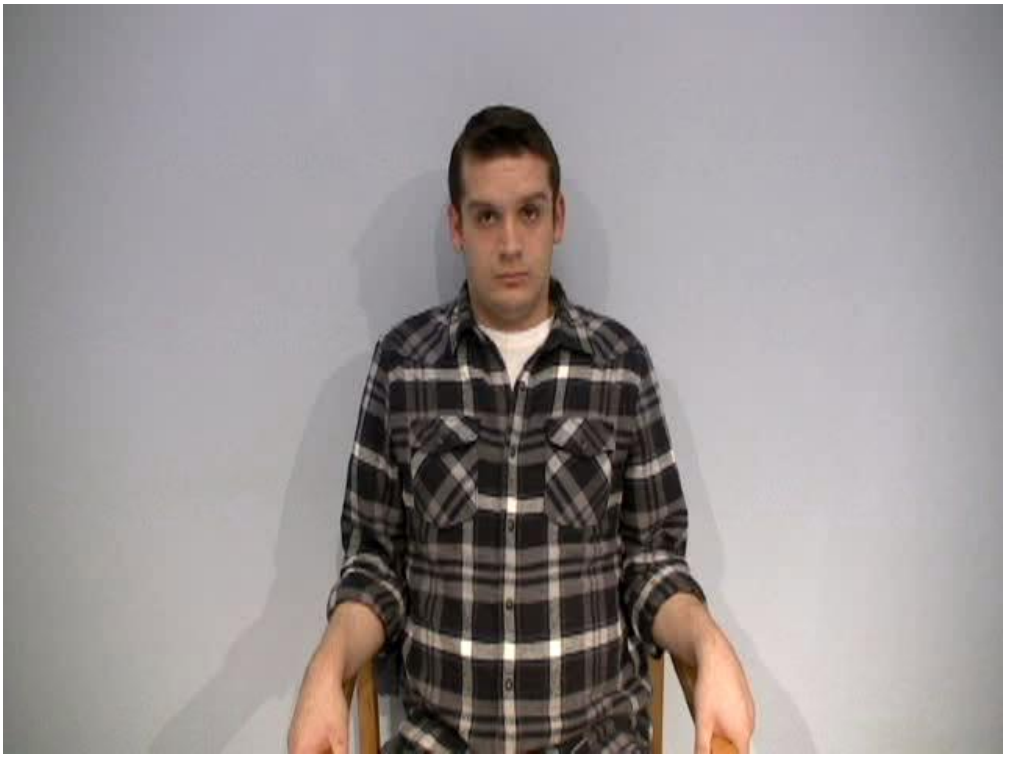
Bilateral GPi DBS in TS

Baylor College of Medicine

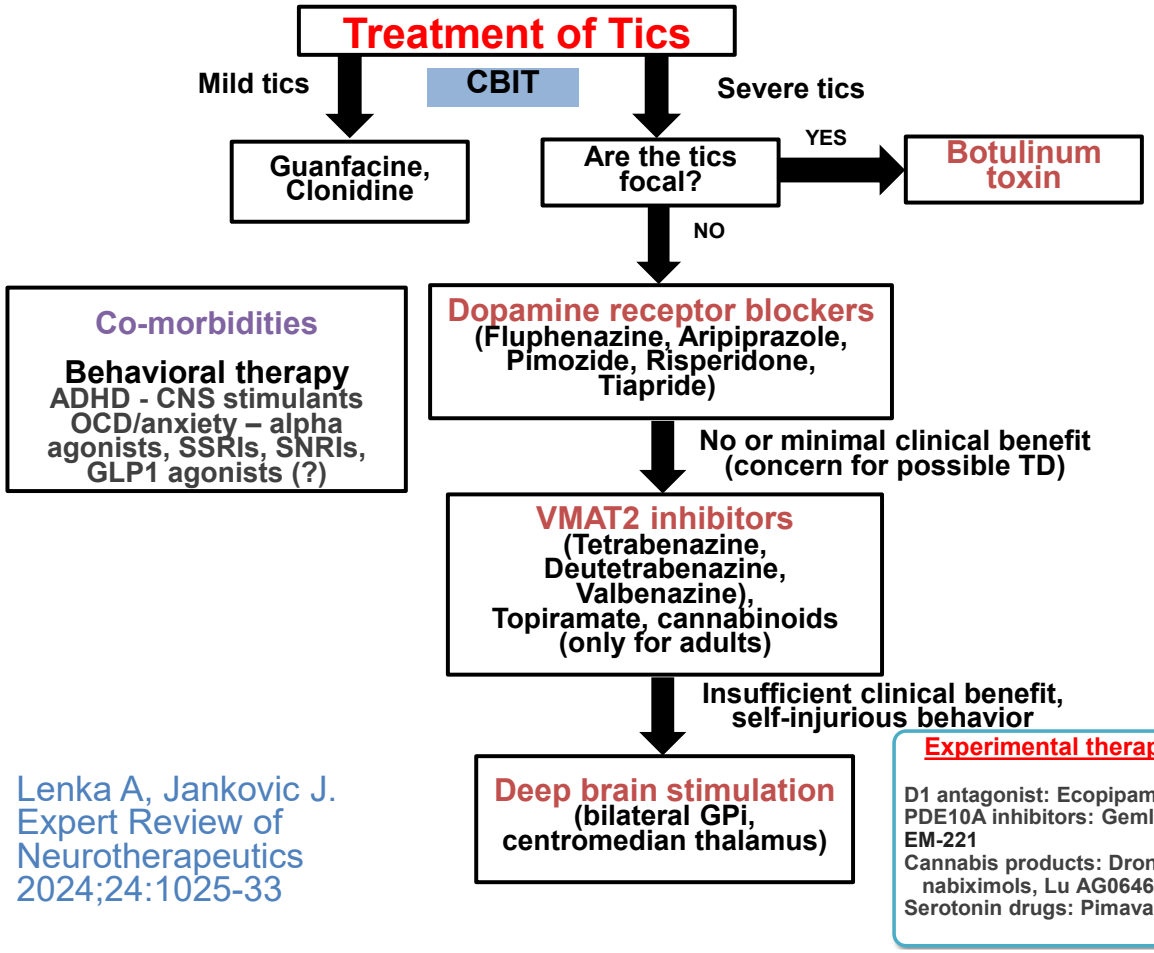


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5 years after GPi DBS implantation



487



Lenka A, Jankovic J. Expert Review of Neurotherapeutics 2024;24:1025-33

519

Mozart's movements and behaviour: a case of Tourette's syndrome?

Aidin Ashoori, Joseph Jankovic

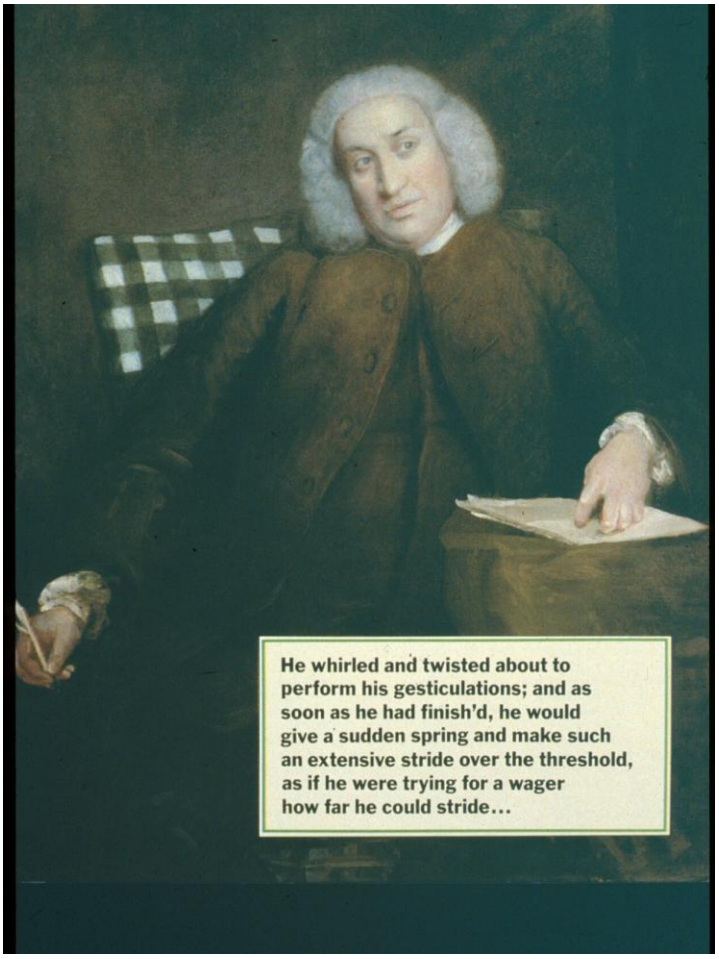
J Neurol Neurosurg Psychiatry 2007;**78**:1171–1175. doi: 10.1136/jnnp.2007.114520

In this review, we intend to explore the often asked question: ''Did Mozart have Tourette's syndrome?'' Although there are numerous reports attributing Mozart's peculiar personality and behaviour to a spectrum of neurobehavioural disorders such as Tourette's syndrome, autistic disorder, Asperger's syndrome, attention deficit hyperactivity disorder, obsessive–compulsive disorder and paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection, the evidence for any of these disorders is lacking. Whether Mozart's behaviour was nothing more than a reflection of his unique personality or a more complex neurological disorder, aggravated later in life by enormous demands by his father and society, his behaviour has been the subject of many biographies. It will also remain unknown to what extent his accomplishments and failures were shaped by his childhood experiences, pressured lifestyle, and his innate genius and extraordinary talent. Lessons from his life may have important implications for other gifted individuals and savants whose special attributes may lead them to succeed or, on the other hand, suppress their emotional growth and make them more vulnerable to stress and failure.

The 250th anniversary of the birth of one of the greatest musical geniuses of all times, Wolfgang Amadeus Mozart (1756–1791), provides an opportunity not only to reflect on his immeasurable contributions to the world of classical music, but also to examine him as a man of exceptional creative power. Mozart's biographical accounts often comment on his peculiar behaviour which has been interpreted by some as a manifestation of an underlying neurobehavioural disorder, such as Tourette syndrome (TS). Once considered a rare psychiatric syndrome.[7 8] Various structural and functional imaging studies of brains of musicians have found that in contrast with non-musicians, the musicians' brains tend to have increased gray matter in Broca's area and in certain portions of the auditory cortex, such as the Heschl's gyrus and planum temporale.[9 10] Studies of developmental and acquired disorders of musical listening and interpretation have shown that brain plasticity is involved in musical perceptions and integration with cognitive and emotional responses,[11] and that music could have both evocative and suppressive effects on some patients with movement disorders such as TS and parkinsonism.[12]

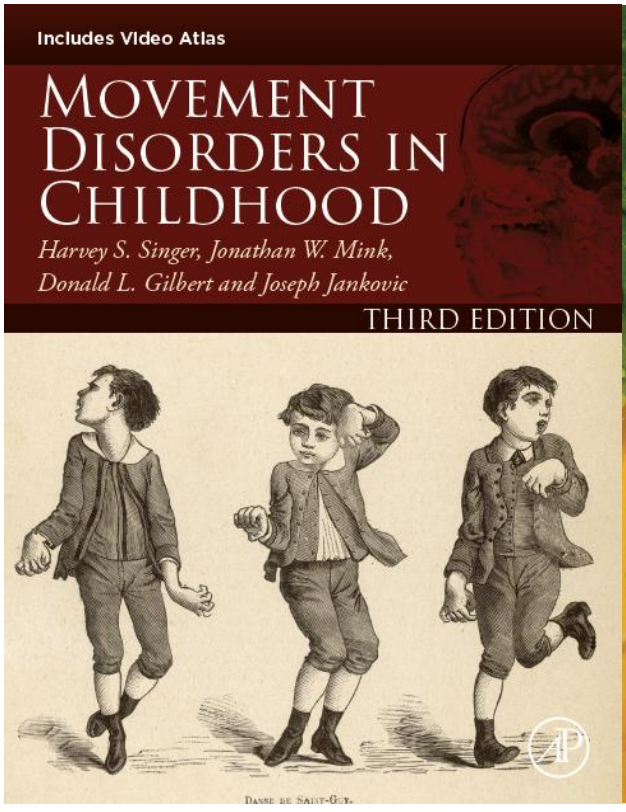
Although many individuals with unique talents have been carefully studied, no unified theory has emerged to explain the neurological basis of such exceptional creative or interpretive abilities, as demonstrated by some people with autism or some savant artists. It is beyond the scope of this review to discuss the neurobiology of savant and the reader is referred to other sources,[13 14] but the brain mechanisms giving rise to savant-like features may be relevant to the understanding of the neurobiology of a genius mind, such as that of Mozart. Whether savant is more frequently observed in patients with TS or whether some savant cases manifest features of TS, such as tics and OCD, has not been systematically studied.

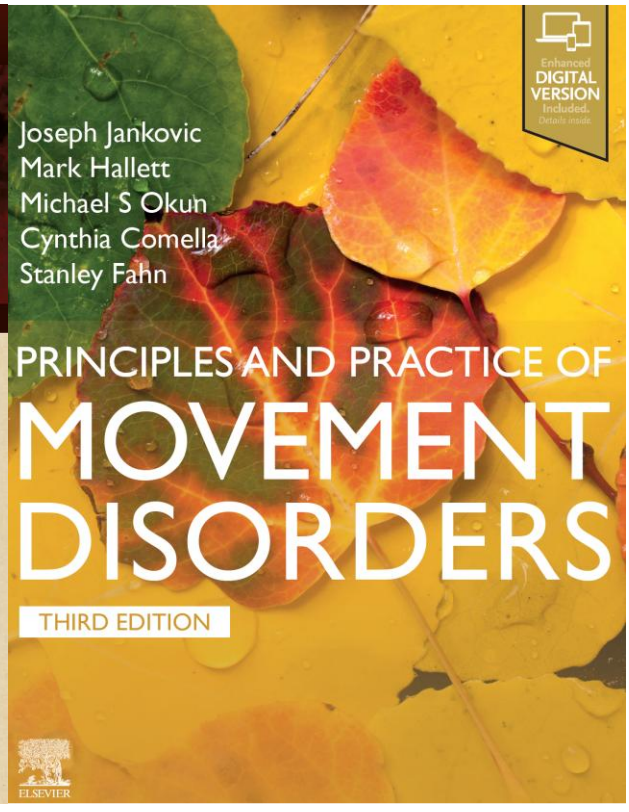
Insanity and exceptional musical talent have often been thought to be linked, but the mechanism of this relationship is unknown.[15] As an example, David Helfgott, a prodigious pianist featured in the movie ''Shine,'' has been thought to suffer from a mild form of schizophrenia with positive symptoms. He grunts, mutters, sings, talks to himself very loudly and exhibits other tic-like mannerisms as he plays.[16] Creativity has often been associated with bipolar disorder and some composers, artists, authors and



Dr. Samuel Johnson

538


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Harvey S. Singer, Jonathan W. Mink, Donald L. Gilbert and Joseph Jankovic
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542

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555

THANKS



556