

Tourette research highlights from 2025

Kevin J. Black, M.D.*

Departments of Psychiatry, Neurology, Radiology and Neuroscience



WashU Medicine



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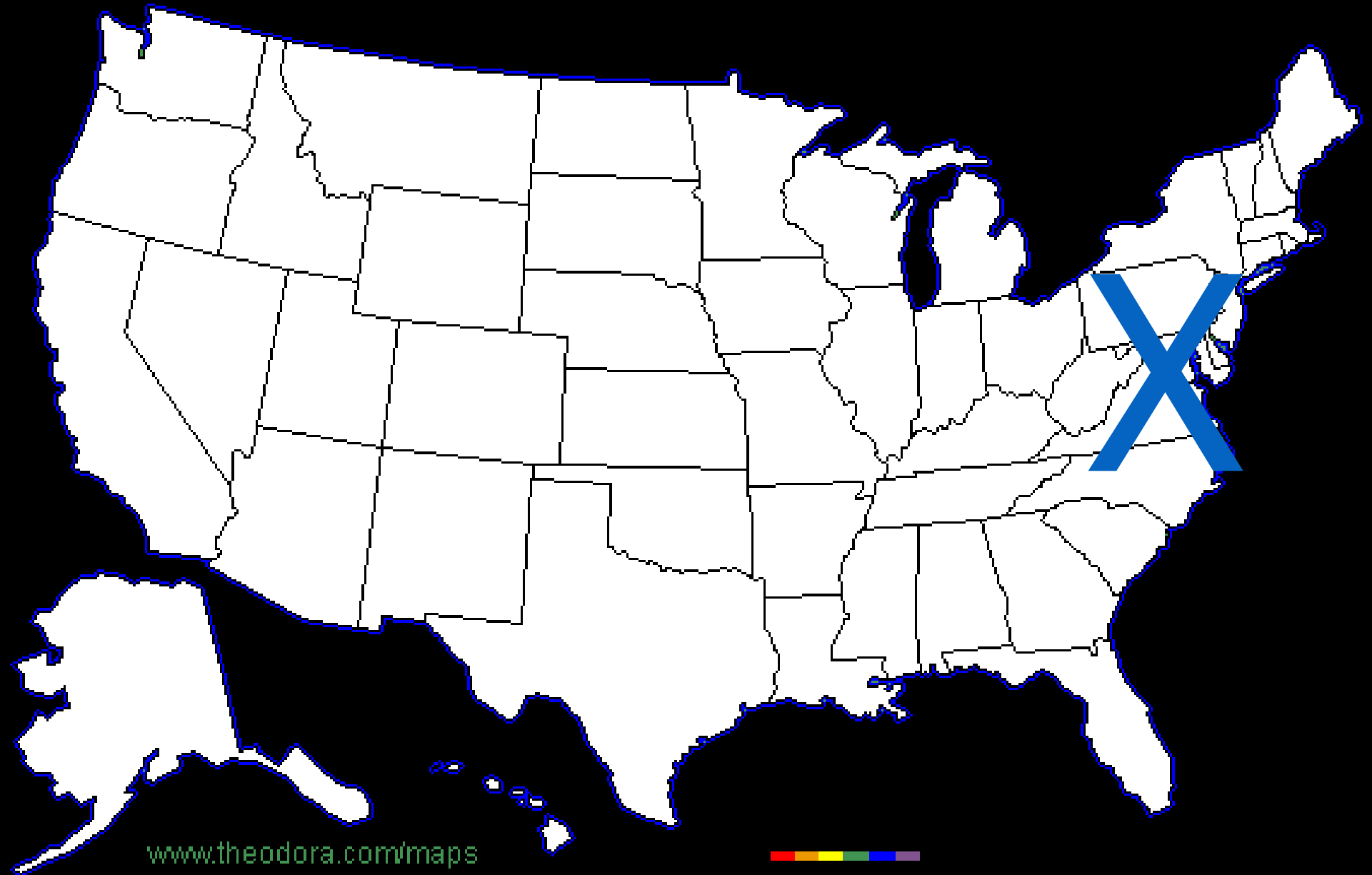
Cyril Atkinson-Clément, Nanette Mol Debes, Peristera Paschou, Natalia Szejko,
Cécile Delorme, Per Andrén, Virginie Czernecki, Simon Morand-Beaulieu,

Apostolia Topaloudi, Kirsten Müller-Vahl, ***Andreas Hartmann**



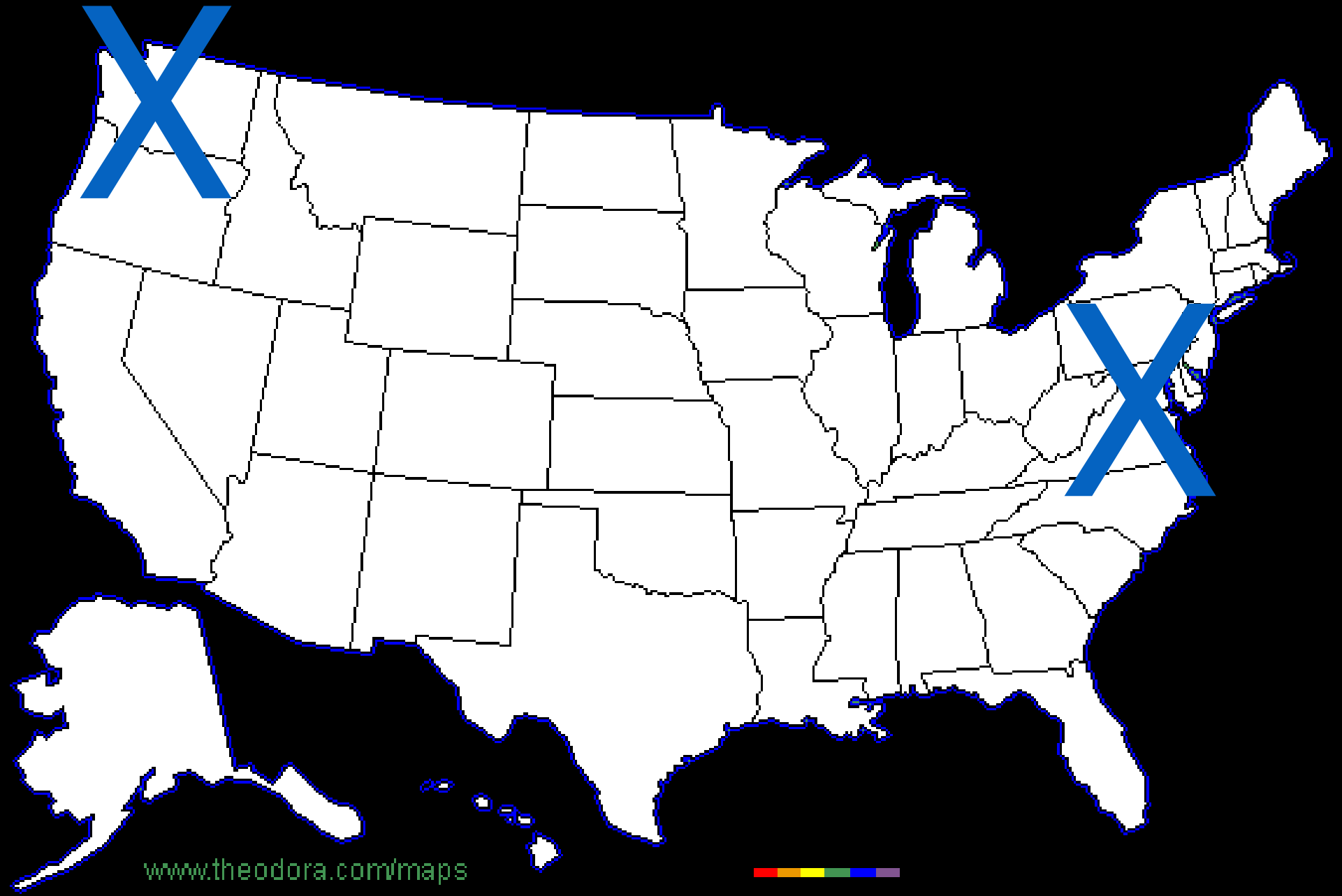
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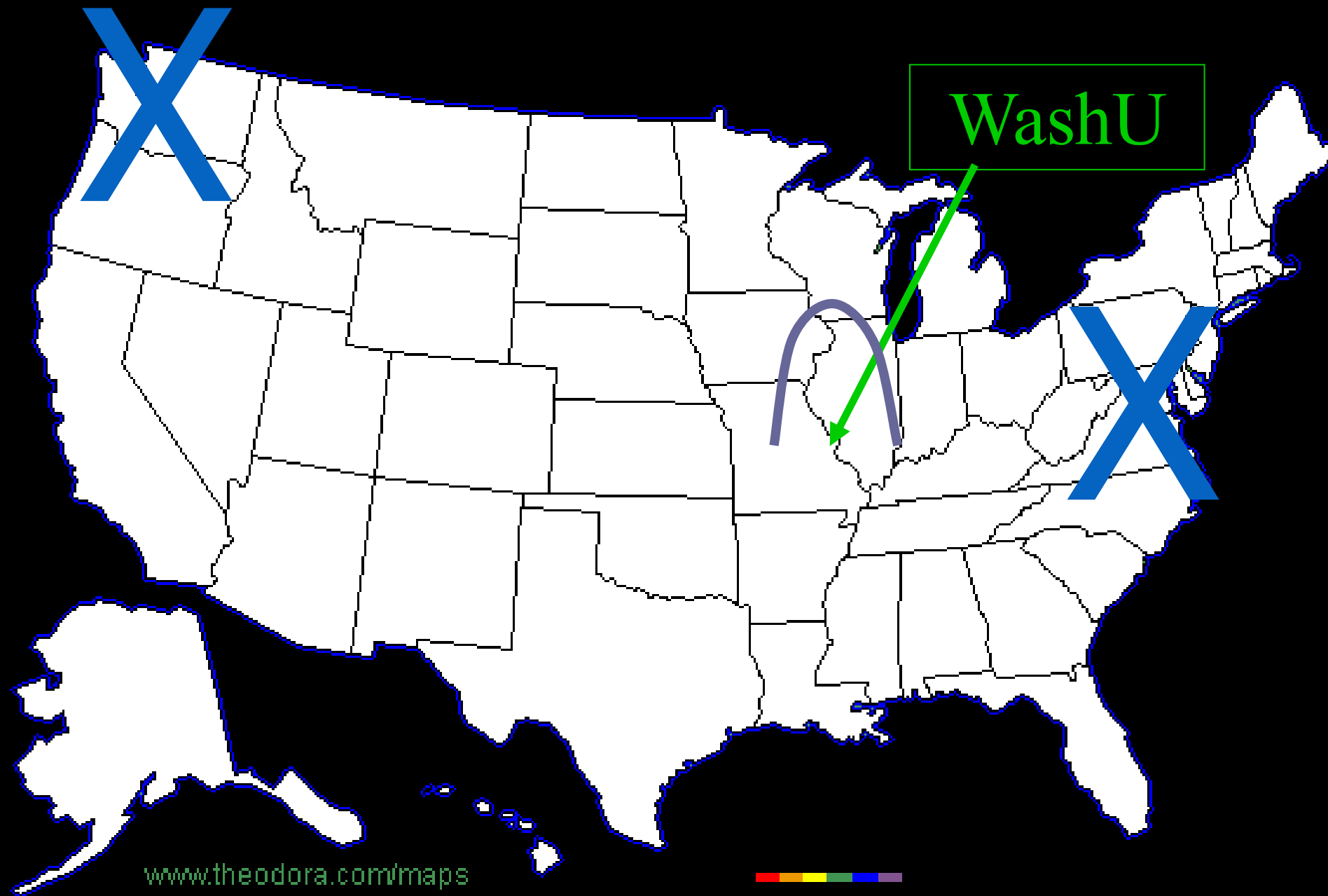
www.theodora.com/maps





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WashU

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Disclosures

- Sources of research support:
 - National Institutes of Health
 - Tourette Association of America
 - Zhitty Genesis Medicine
 - **Emalex** Biosciences, Inc.
- Consulting relationships
 - none
- Speaker's bureaus, Stock equity
 - none
- Off-label meds/devices ... almost all

I'm going to leave out some important work

- Telling you about your own work :/
- Skipping reviews, null results, and other important work
- I don't understand some areas as well as others
- And ... this year I'm trying to cover fewer papers
- So ... I may miss your important paper 😞
- **But: See f1000research.com for >100 papers**
doi 10.12688/f1000research.179831.1





Phenomenology and natural history



Phenomenology and natural history

Definition and phenomenology



Tic registry: adult

- Calgary and Paris **Adult** Tic Registry, N=227
- M:F = 1.8:1
- No significant sex differences in tic severity or tic phenomenology
- GAD in 50%, ADHD in 36%



Tic registry child: TS = chronic tics?

- Calgary and Paris **Pediatric** Tic Registry, N=341
- 90% TS **vs.** 7% PMTD, 2% PVTD
- No differences in sex ratio, tic severity or impairment
- TS earlier onset
- TS more psychiatric comorbidity, esp. ADHD, OCD
 - > probably the same illness

10.1007/s00787-025-02732-7



Simple and complex tics

- Consecutive patients with TS
- 24% had complex phonic tics
- Patients with simple **vs.** complex tics:
 - **No significant differences** in sex ratio, age at onset, age at presentation, or comorbid ADHD or OCD
 - Complex tics were associated with **trunk tics**, complex motor tics, copropraxia, a wider variety of phonic tics, and greater tic severity
- Authors conclude complex phonic tics mark a more severe and widely distributed presentation but likely on a continuum with other patients



Phenomenology and natural history

Tic assessment and nosology

Counting tics



Human tic detection

Human rating of video clips needs [training by?] experienced clinicians and is very time consuming.

AI tic detection

- Loewenstern et al, selfie video, smartphone app
 - 95% accuracy in training set



Phenomenology and natural history

Screening tools



Screening tools

- A-TAC (Autism–Tics, ADHD and other Comorbidities) screening tool
 - Swedish study
 - Compared to comprehensive clinical assessments in N = 263 children
 - High accuracy for most diagnoses
 - Over 40% of children screened positive for >1 neurodevelopmental disorder
- Psychiatric screening tools in adults with TS
 - From Canada
 - N=36, GAD-7, PHQ-9, PHQ-2, ASRS v1.1, and OCI vs. structured dx interview
 - Higher cutoff thresholds needed in TS than in the general population
 - ASRS best > GAD-7, OCI > PHQ-9, PHQ-2.



Phenomenology and natural history

Population samples



National survey of TS (and other dxs)

- 2021 National Survey of Children’s Health (NSCH) (U.S.A.)
- N = 79,236 children aged 3–17
- *“Has a doctor or other healthcare provider ever told you that this child has Tourette Syndrome?”*
- Defined thus, the prevalence of TS was 0.3%
- More common in adolescents, males, prematurity, low birth weight
- More comorbidity than in non-TS:
 - ADHD in 49%, ASD in 21%, anxiety in 60%, depression in 25%
 - Ratios to same in non-TS: 4.8, 6.6, 5.3, 5.0

10.3390/jcm14051485

Males & females



- TAA International Consortium for Genetics, N = 2403:
- ♀ later onset (if TS; earlier if CTD), later dx, longer time to dx, lower tic severity; diagnosed half as often
- TAAICG: mean onset difference 0.5-1.0 years, diagnosis 1.6 years, time to dx 1 year, tic severity 1.3 points on TTS.
- Calgary & Paris: no significant differences in tic severity or phenomenology

10.1212/WNL.0000000000210249

10.1111/ene.70252



Phenomenology and natural history

Prognosis



Mortality in TS

- Tic disorders, N = 50,018, national data from Taiwan
- N= 200,072 matched controls
- Statistics adjusted for demographics, clinical characteristics, psychiatric comorbidities
- People with tics were ...
 - More likely to die from unnatural causes
 - More likely to die by suicide

10.1111/sltb.70023



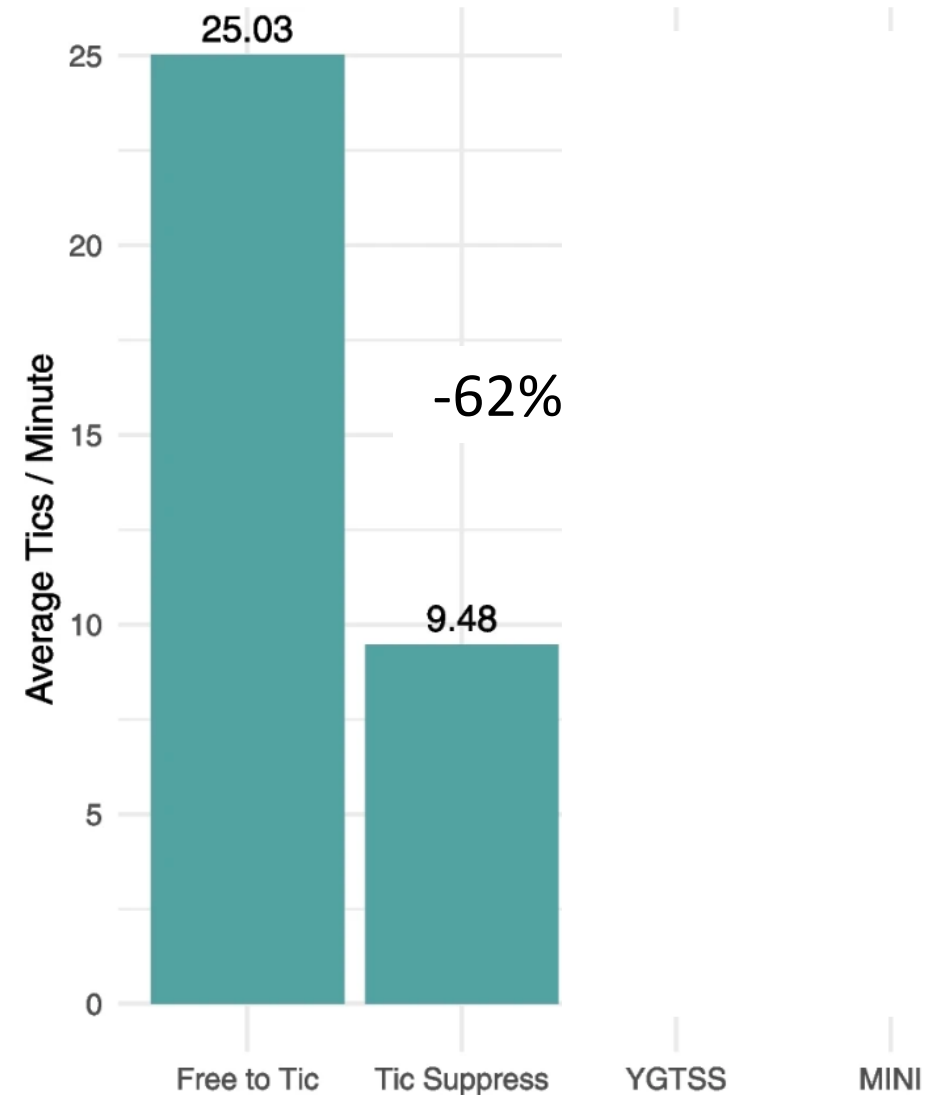
Phenomenology and natural history

Transient environmental
effects on tic severity

"Social automatic tic suppression"



- Not surprising:
 - "Please hold back your tics":
↓ tics

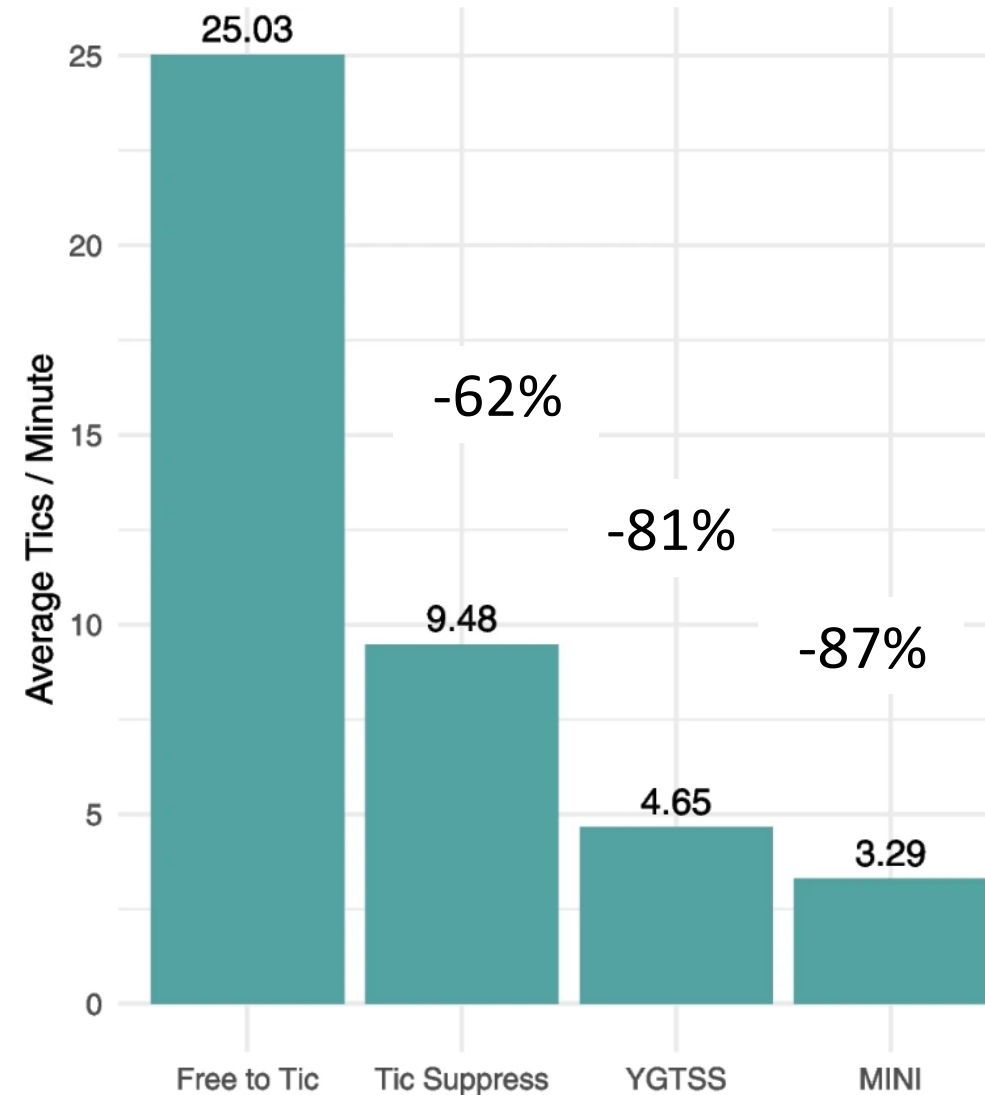


10.1007/s00787-025-02818-2

"Social automatic tic suppression"



- Not surprising:
 - "Please hold back your tics":
↓ tics



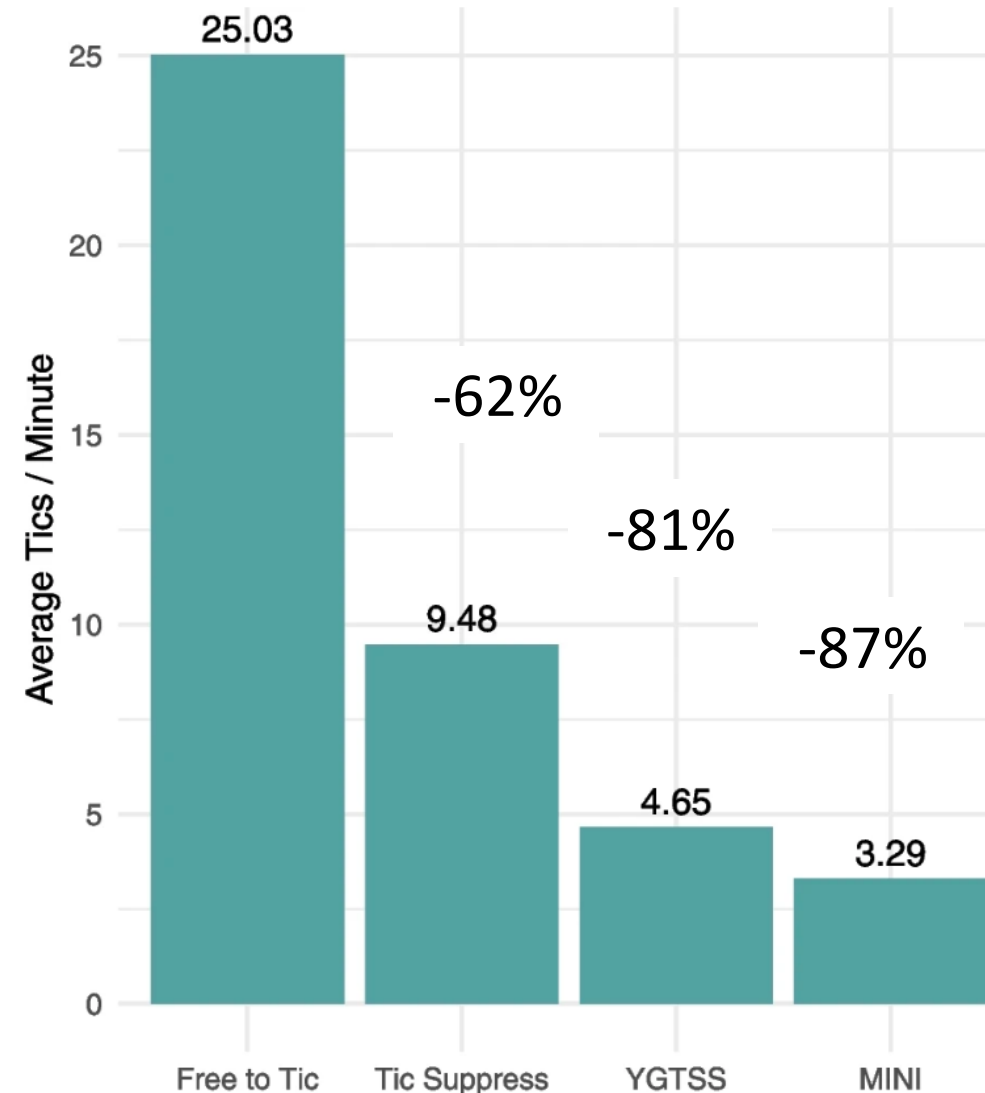
10.1007/s00787-025-02818-2



"Social automatic tic suppression"

- Not surprising:
 - "Please hold back your tics":
↓ tics
 - Looking at patient: ↓ tics
 - Talking about tics: ?↑ tics
- Unknown:
 - quantification
 - which effect is largest?

10.1007/s00787-025-02818-2





Phenomenology and natural history

Symptoms other than tics

Tics can hurt



- 76 adults with TS
 - 74% reported tic-related pain
 - Almost all in >1 body part
 - Highest domain score: affective
 - Only 18% who sought medical care for pain said it helped
- Insurance databases, USA
 - Age 6-64, tic disorder, 2016-2023
 - 27,262 commercial, 19,980 Medicaid
 - 22% had any chronic pain diagnosis
 - From 1.1 to 7.5 times more than people without tic diagnosis
 - Headache, especially migraine, especially prominent

10.3389/fpsyg.2025.1537088

10.1002/mdc3.70151

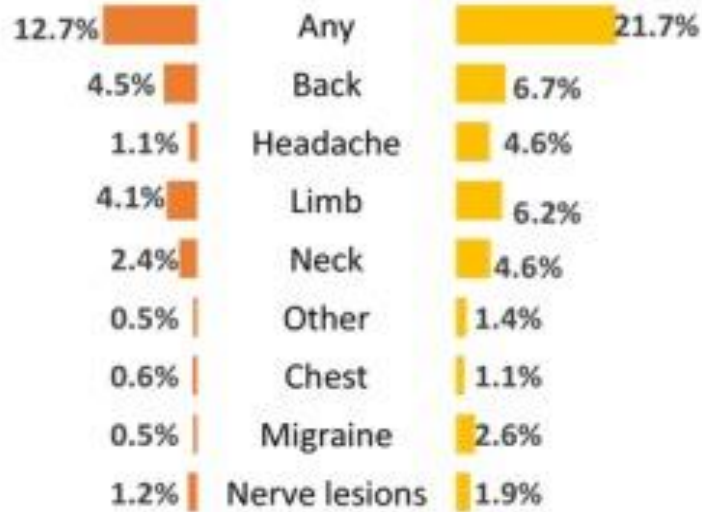


Commercial Database

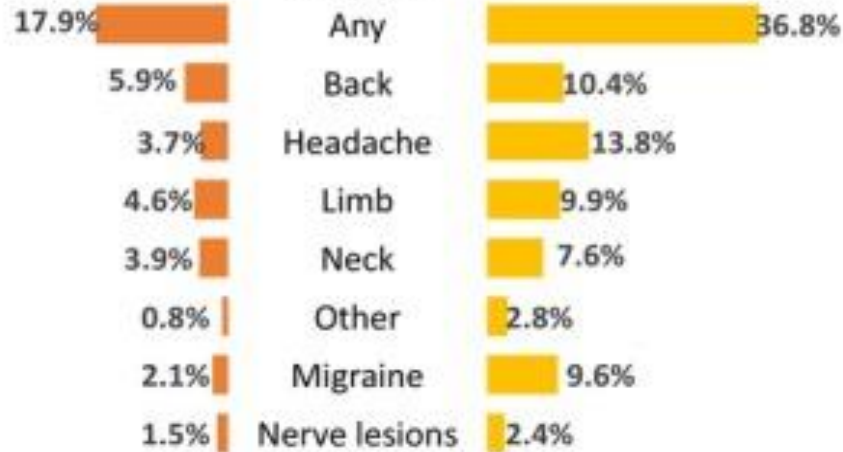
Enrollees without tic disorders

Enrollees with tic disorders

Males



Females

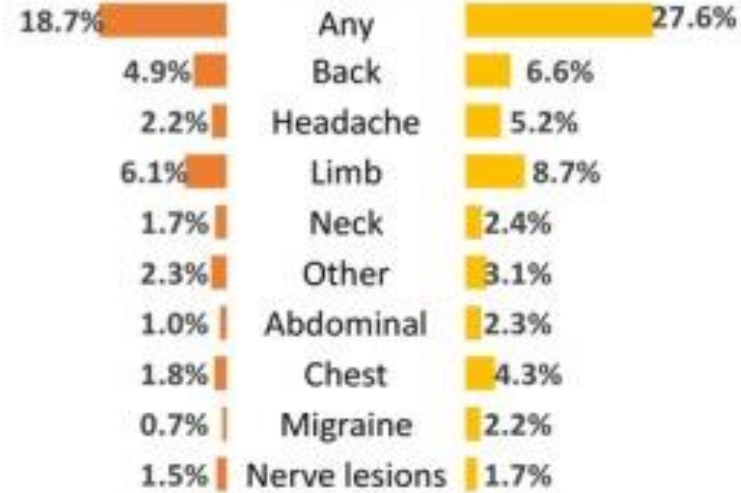


Medicaid Database

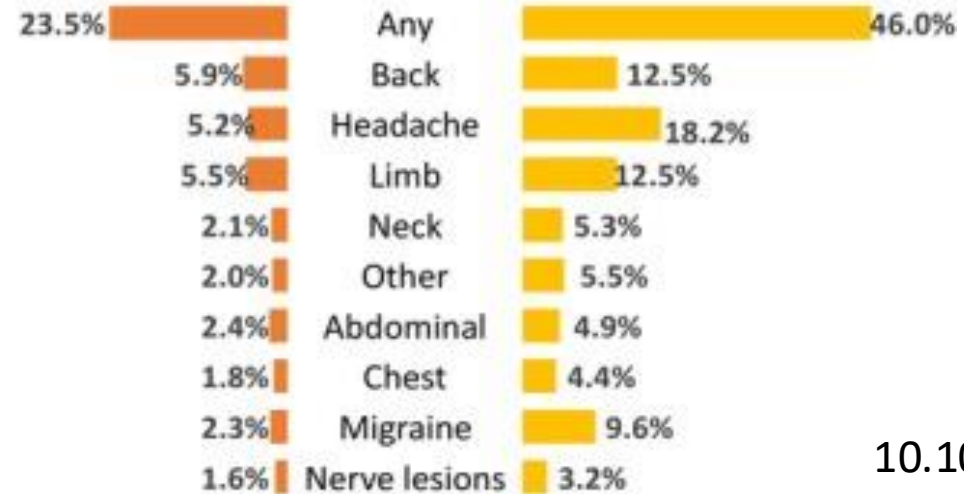
Enrollees without tic disorders

Enrollees with tic disorders

Males

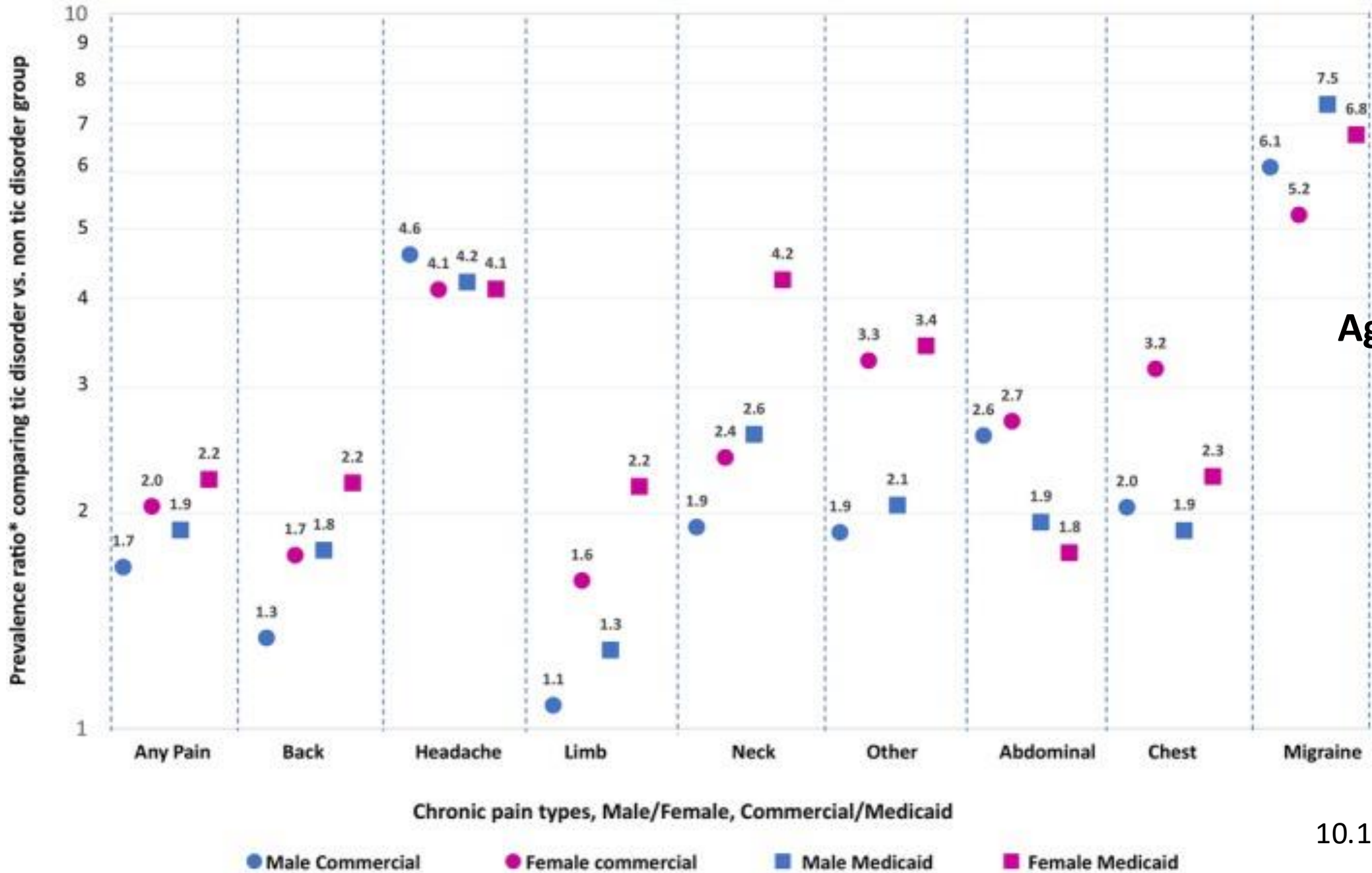


Females



Ages 18-34

10.1002/mdc3.70151



Ages 6-17

10.1002/mdc3.70151



Sensory hypersensitivity

- 40 patients age 6-17 with chronic tic disorders
- Total scores on Sensory Profile questionnaires were associated with:
 - Severity of tics
 - Severity of premonitory urges
- Sensory avoidance was associated with:
 - Severity of OCD
 - Severity of anxiety
- Sensory sensitivity was associated with:
 - Severity of OCD
 - Severity of anxiety

10.1177/08830738251351806



Phenomenology and natural history

Functional tic-like symptoms

FTLB



Outcome

- 43 teens at 2.6 years
 - 2/3 improving or recovered
- 30 pts **social media FTLB**, 2.2 yrs
 - Most improved or remitted
 - Predicted recovery: younger, male, fewer comorbidities, no depression, early diagnosis, ending 2° gain
 - Medication, psychotherapy:
no meaningful effect on recovery

TS + FTLB

- 63 patients TS + later FTLB by ESSTS criteria, vs. 63 TS only
- FTLB associated with:
 - Complex vocal tics, including
 - Coprolalia
 - Self-injurious behaviors
 - Tic attacks
 - Other functional neurological symptoms

10.1136/archdischild-2024-327408

10.1002/mdc3.70384

10.3390/brainsci15050435

Etiology



Etiology

Genetics

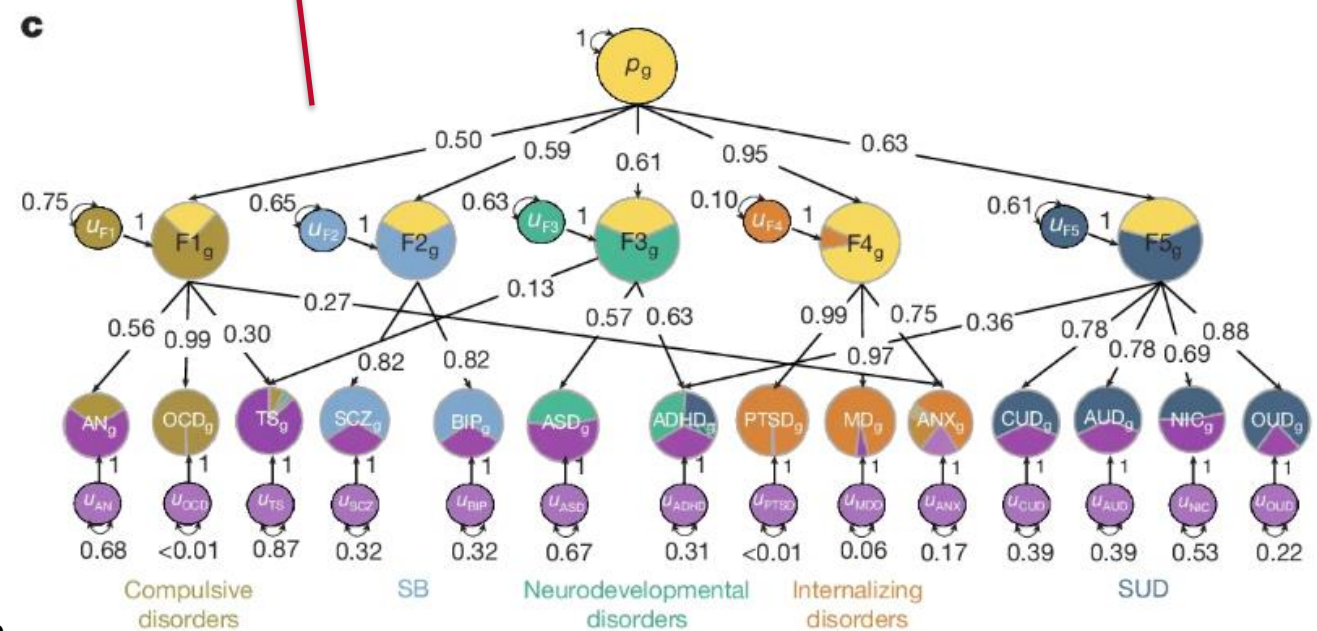
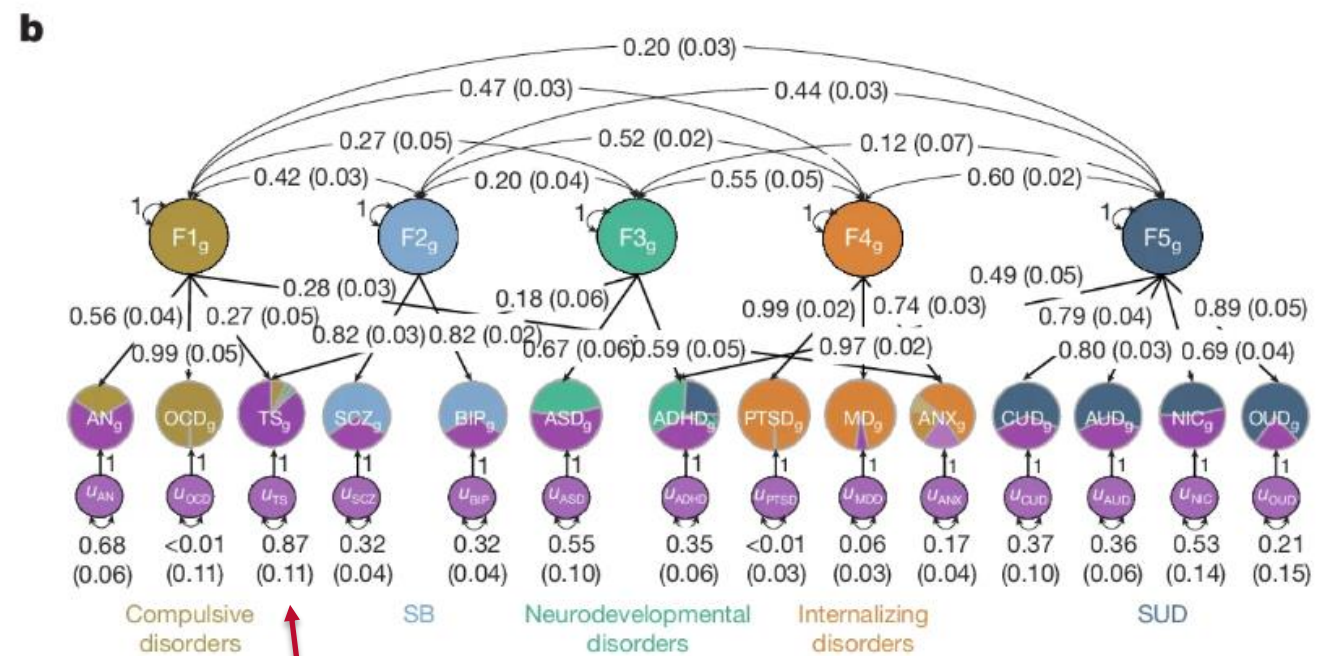
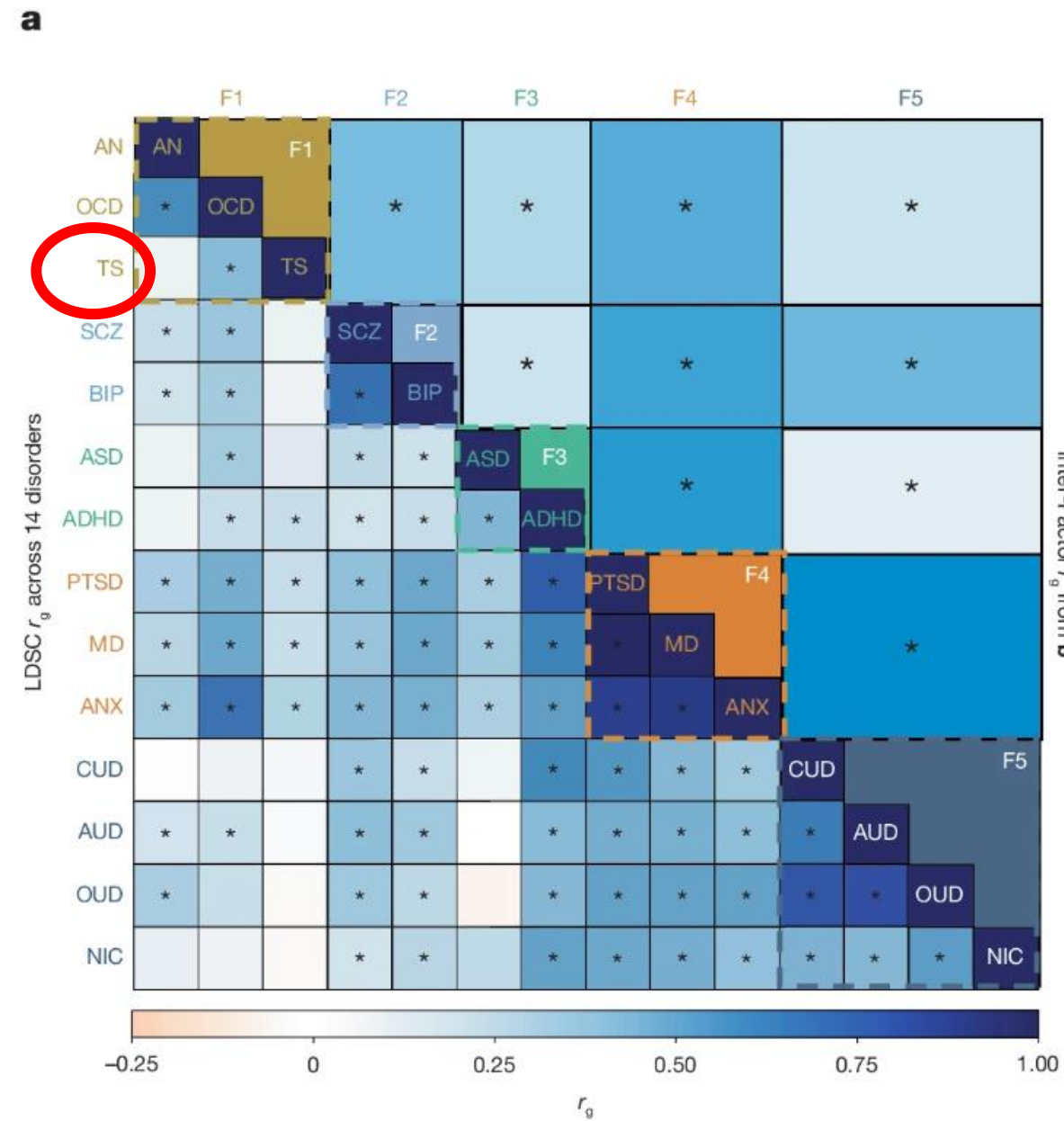




14 psychiatric disorders, DNA from > 1,000,000

- Cross-disorder psychiatric genomics analysis
- 5 latent factors captured the majority of shared genetic variance
- TS loaded mostly on the Compulsive Disorders factor with OCD and anorexia nervosa
- Less strongly on the ASD + ADHD factor
- TS showed the most genetically distinct profile of all 14 disorders, with 87% of its genetic variance left unexplained by the five factors

10.1038/s41586-025-09820-3



10.1038/s41586-025-09820-3



Etiology

Environmental

Maternal autoimmune disease



- Taiwan national database
- 76,411 children whose mothers had an autoimmune disease and 1,211,936 children without maternal autoimmune disease exposure
- Higher risk of tics and Tourette's disorder: adjusted hazard ratio (aHR): 1.22; 95% CI, 1.15–1.29.
 - rheumatoid arthritis (aHR: 1.46), lupus (aHR: 1.57), Sjögren's syndrome (aHR: 1.28), ankylosing spondylitis (aHR: 1.49), Graves' disease (aHR: 1.26), Hashimoto's thyroiditis (aHR: 1.59), and type I diabetes (aHR: 1.68)
- Also other illnesses
 - urinary tract infections, diabetes mellitus, hyperlipidemia, anemia, a sleep disorder, endometriosis, and depression

10.3389/fped.2025.1440366

Pathophysiology





Pathophysiology

Autopsy studies



6 TS, 6 control brains

- Caudate/putamen postmortem specimens
- Interneurons (only) were decreased by ~50% in TS brains
- Single-cell RNA transcripts:
 - mitochondrial oxidative metabolism in medium spiny neurons decreased in TS
 - synaptic adhesion and function in interneurons decreased in TS
 - immune response in microglia increased in TS

10.1016/j.biopsych.2024.12.022



Pathophysiology

Animal models

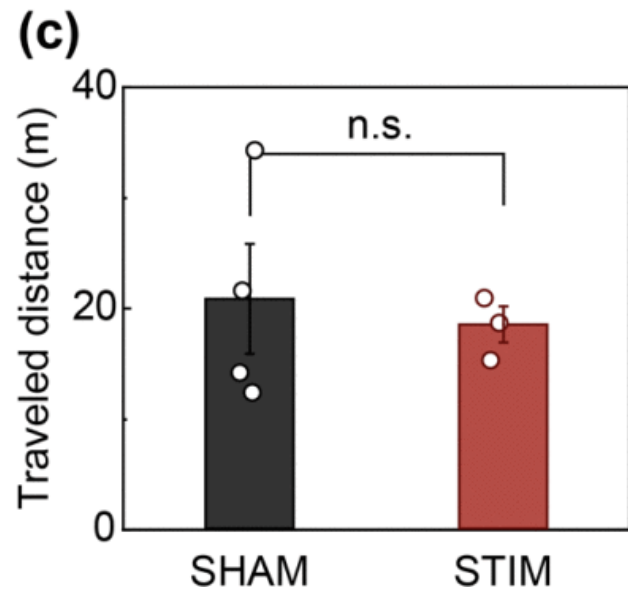
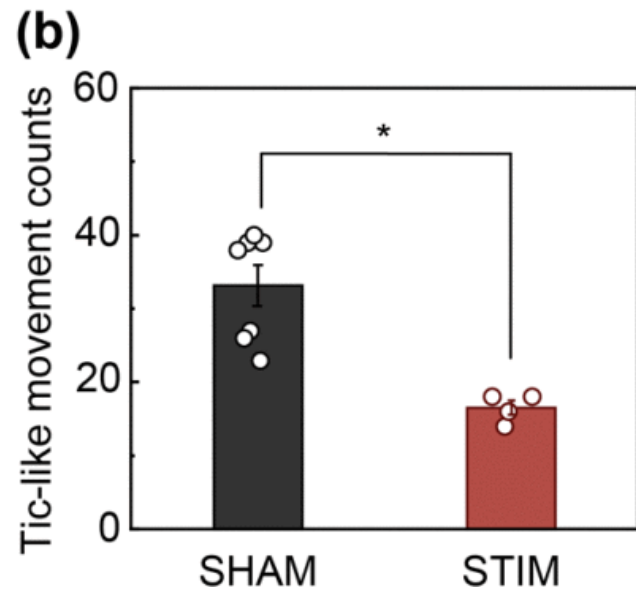
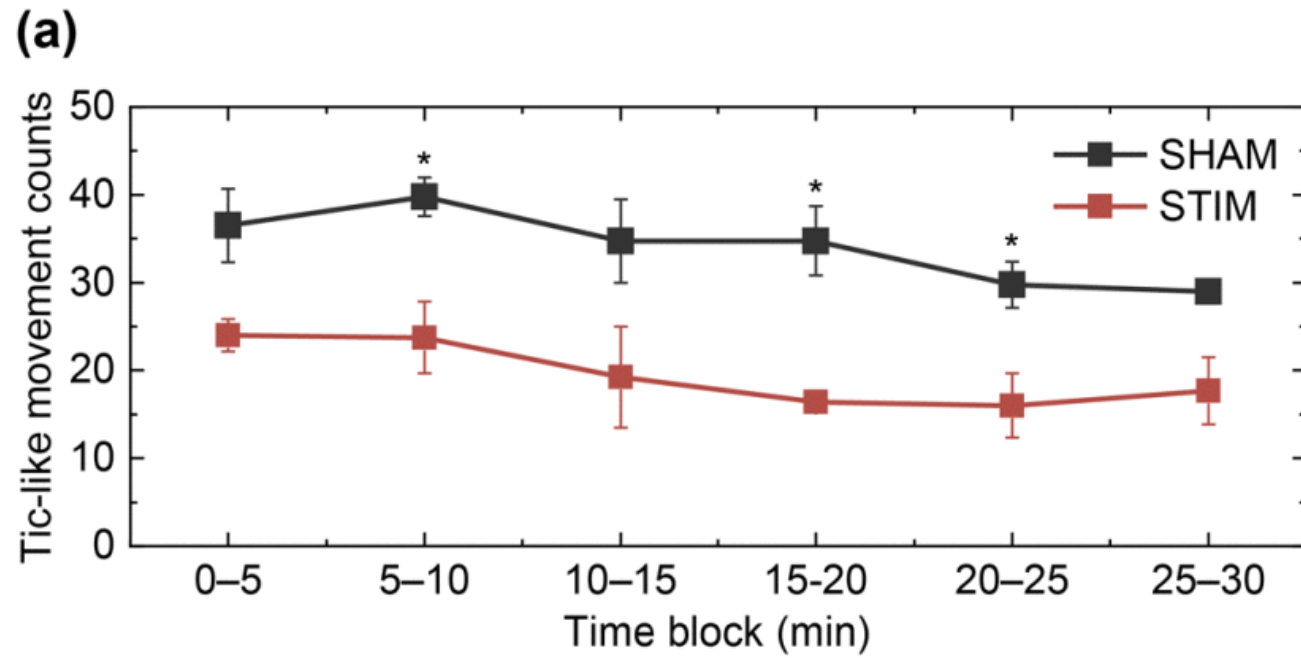


Treating mice

- GABA-A receptor antagonist bicuculline injected into anterior dorsal striatum of mice
- "a robust increase in tic-like movements such as head-body twitches"
- LIFU to M2 (premotor cortex), or sham treatment 1 cm off head



10.1109/tnsre.2025.3629724



10.1109/tnsre.2025.3629724



Pathophysiology

Electrophysiology



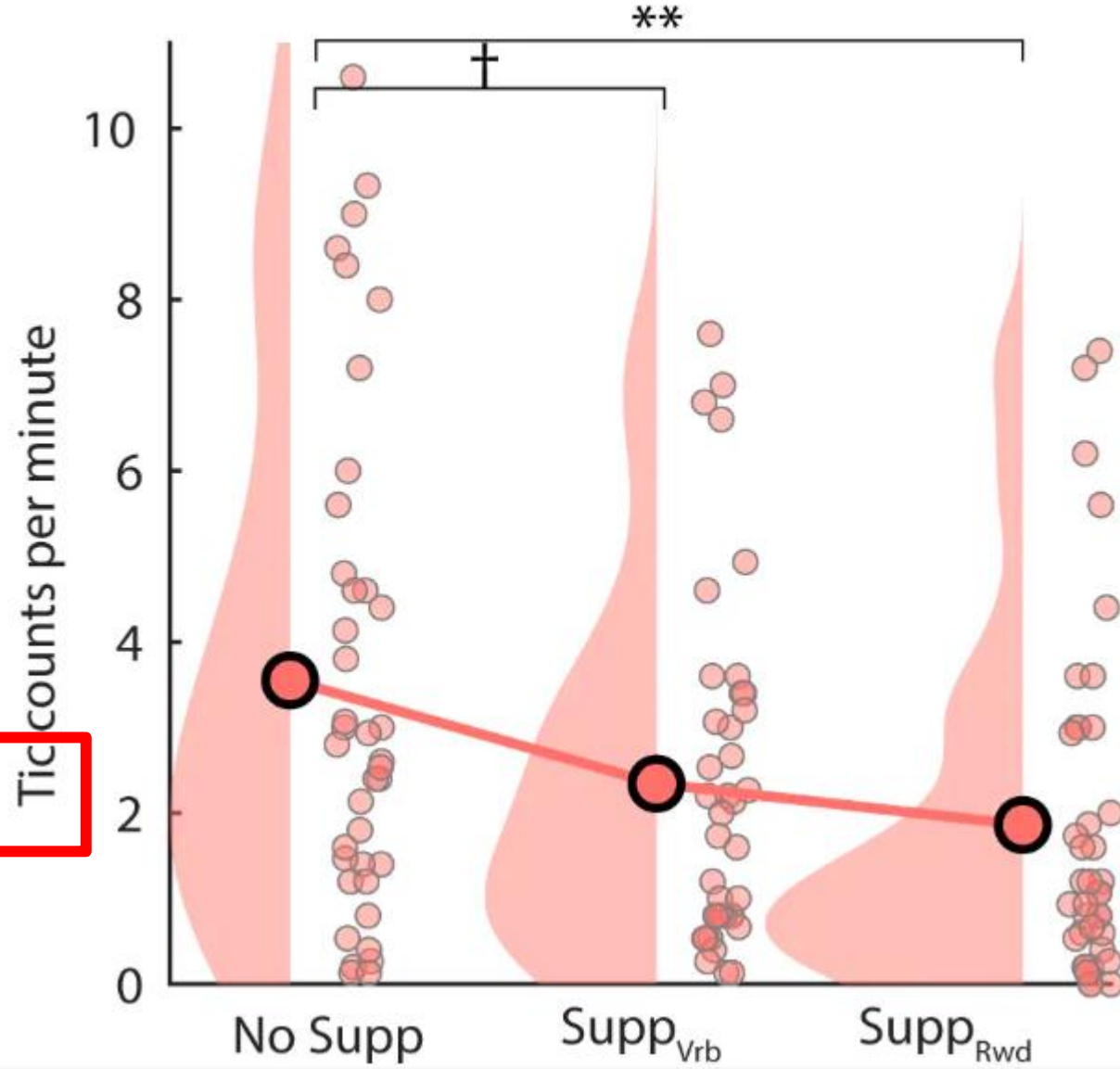
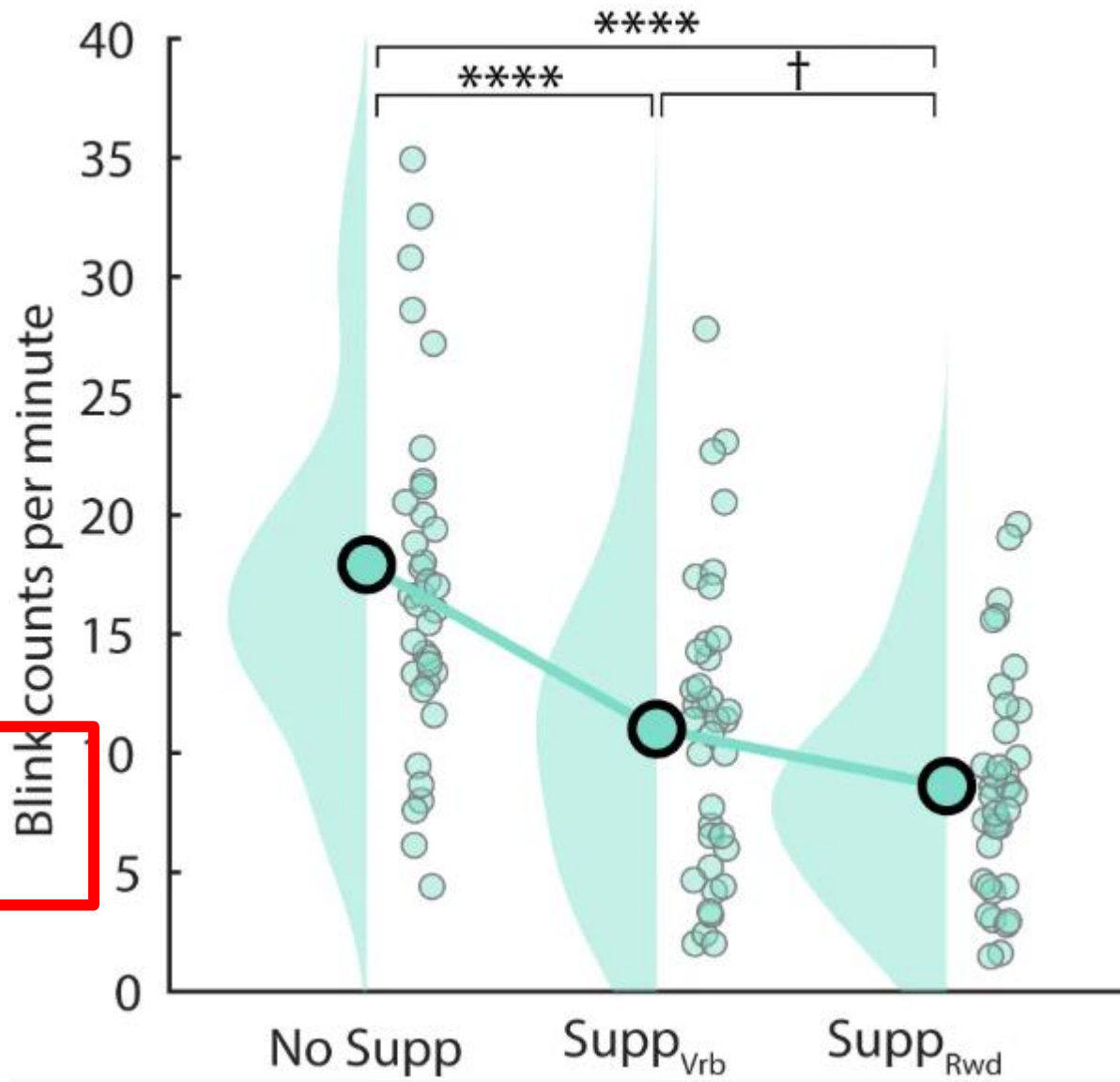
EEG when not ticcing or blinking

- Event-related EEG in 39 children with CTD and 37 without
- "Better tic suppression was associated with increased EEG power, a similar pattern observed among controls during blink suppression."
- "EEG power in sensorimotor regions is a neural marker of tic suppression performance in children with CTD."

10.3389/fpsy.2025.1580636

Typically developing Children (n = 37)

Children with Chronic Tic Disorder (n = 39)



10.3389/fpsy.2025.1580636



Pathophysiology

Neuroimaging

Iron in TS



25 adults with TS, 40 without

- 7T MRI iron measures & D1R receptor binding in a subgroup
- ↓ **iron** in substantia nigra, subthalamic nucleus, red nucleus and pallidum

50 children with TS, 50 without

- 3T MRI quantitative susceptibility mapping (QSM)
- ↓ iron in right anterior cingulum
- ↑ **iron** in L & R putamen
- L putamen QSM values correlated negatively with tic severity



Iron in TS

25 adults with TS, 40 without

- 7T MRI iron measures
& D1R receptor binding in a subgroup
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50 children with TS, 50 without

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Iron in TS

20 adults with TS, 20 without

- **D1R receptor binding** in dorsal striatum
- ↓D1R binding in dorsal striatum
- ... and that correlated with tic severity

10.1093/braincomms/fcaf104



Glymphatic system in TS

- Huang et al: children with TS showed increased perivascular space volume and reduced DTI index, suggesting impaired glymphatic clearance
- Wang et al: children with TS showed reduced glymphatic system function, as measured by the analysis along the perivascular space (ALPS) index
 - Lower glymphatic activity was strongly associated with greater tic severity and poorer quality of life

Follow-up on median nerve stimulation



- 15 healthy controls without tics
- 10 Hz median nerve stimulation ... rhythmic and arrhythmic
- 7T MRI to measure glutamate (Glu) and GABA concentrations in contralateral sensorimotor cortex
- Rhythmic and arrhythmic stimulation: similar response
- Trend for an initial increase in Glu ratio followed by a decrease over time, whereas GABA ratio decreased

10.1002/brb3.70250



Pathophysiology

Clinical studies



Tics after dopamine depletion

- 10 patients with a tic disorder who later developed Parkinson disease
- Parkinson disease has decreased nigrostriatal dopamine innervation, earliest in posterior putamen but eventually throughout the striatum
- Development of parkinsonian signs did not improve tics
- Treatment with dopaminomimetics did not worsen tics
- Same result as in a previous case series from Chicago
- ∴ Dopamine is not trivially “more bad, less good” for tics

10.1002/mdc3.70111

Treatment





Tx: what's a meaningful change

- Determined **minimal clinically important difference** on YGTSS-TTS and YGTSS-I,
- Compared to CGI-TS-S and CGI-TS-I
- Data from N = 133 children in ecopipam treatment trials
- Conclusion: a **25%** reduction in YGTSS corresponded best to clinical judgment of meaningful improvement



Treatment

Psychological interventions



Mindfulness for TS

- 135 children with TS or CTD randomized to
 - Standard care (clonidine or aripiprazole), or
 - Standard care + a mindfulness-based intervention
- 12-week mindfulness program: breathing exercises, body awareness, and structured movement with daily home practice
- Greater ↓ YGTSS TTS in intervention group
- Also more improvement in mindfulness, anxiety, quality of life

- Note: not matched for time and intensity of contact

10.1038/s41598-025-21088-1

Treatment

Medication



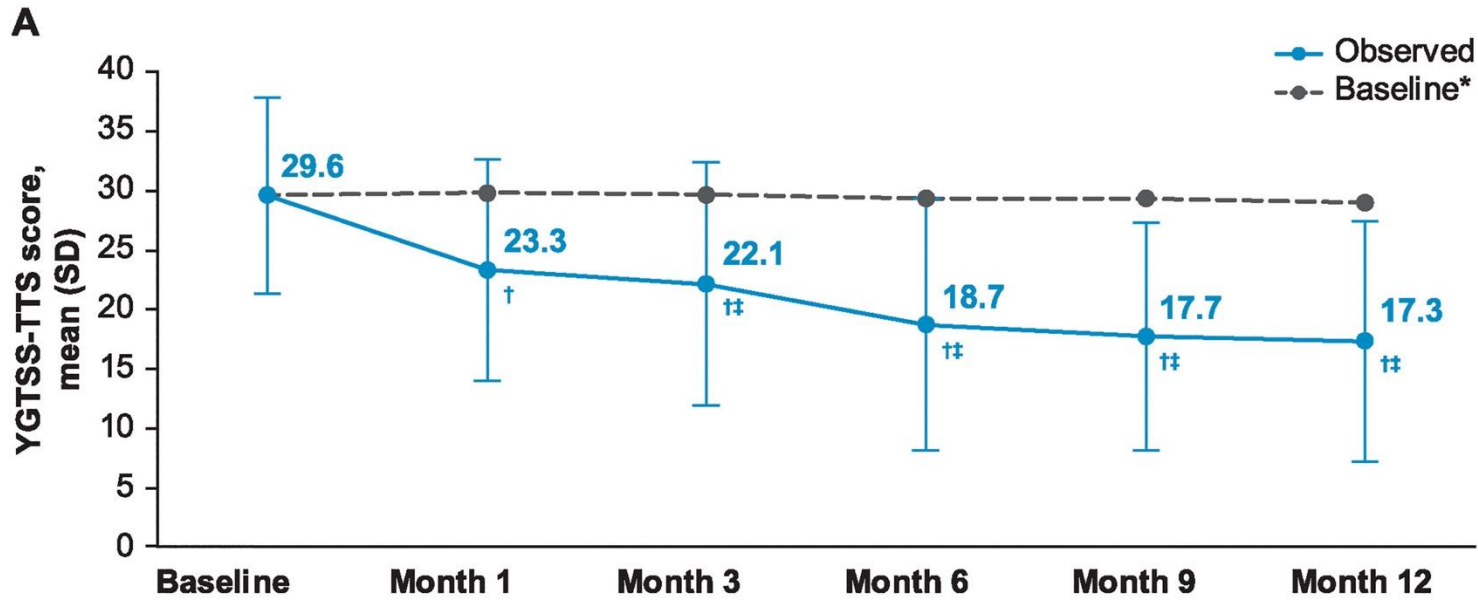
I couldn't pick just one



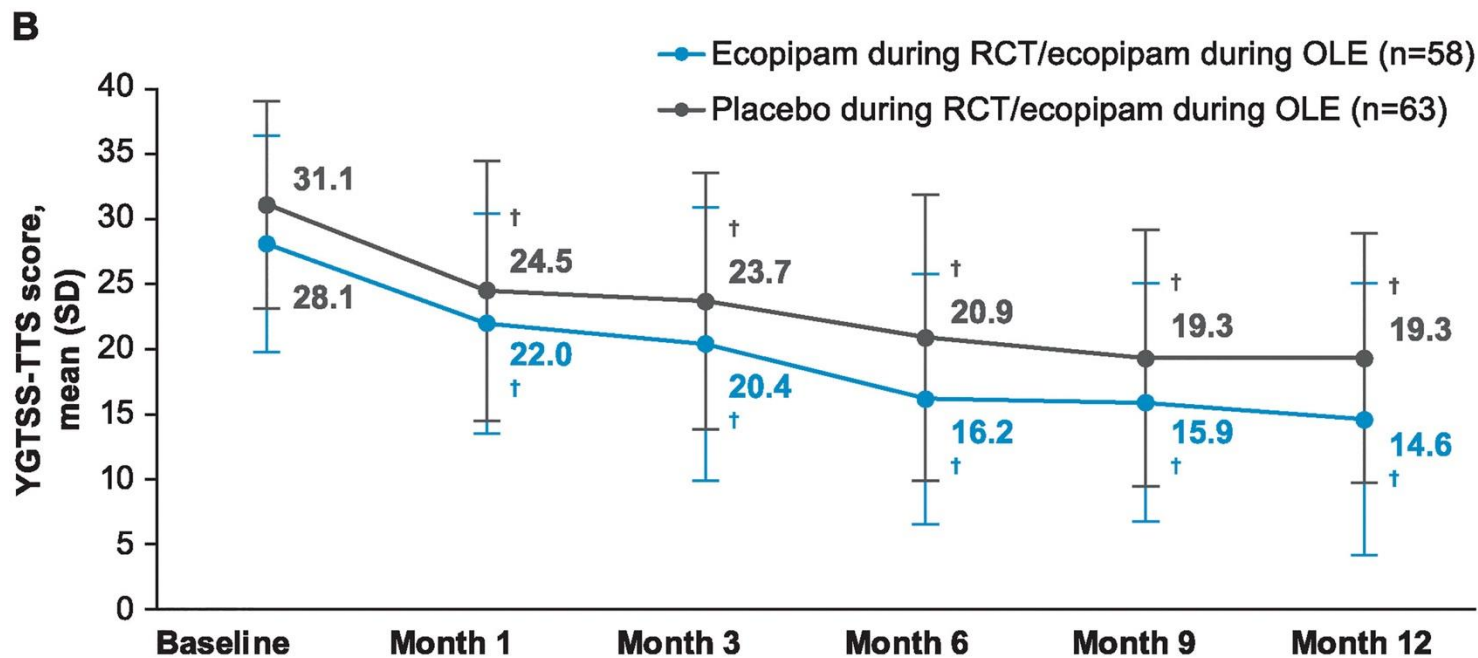
- Retrospective summary of N = 50 **pediatric** patients with motor tics treated with **botulinum toxin**
- 64% improved, 36% no change, 6% worsened symptoms
- 4% weakness
- 54% of dystonic tics improved, 73% of clonic tic improved
- Urge & OCD not predictive
- **Open**-label extension data with **ecopipam**, a D1R antagonist
- 121 → 80 children with TS
- (ESSTS 2025)
- No akathisia, dystonia, rigidity-bradykinesia, tremor, ...
- No weight gain

10.1177/08830738251360210

10.1002/mdc3.70091



bel extension data with
m, a D1R antagonist
30 children with TS
(2025)



chisia, dystonia, rigidity-
nesia, tremor, ...
ht gain

10.1002/mdc3.70091

Treatment

Neurosurgery





Listening to 4 DBS leads

- 6 patients with severe, treatment-resistant TS
- Each had 4 leads implanted targeting centromedian thalamus (CM) and anterior globus pallidus internus (aGPi)
- Tic generation was associated with increased low-frequency activity (<20 Hz) in both CM thalamus and aGPi
- Thalamic activity consistently preceded pallidal signals

Treatment

Other

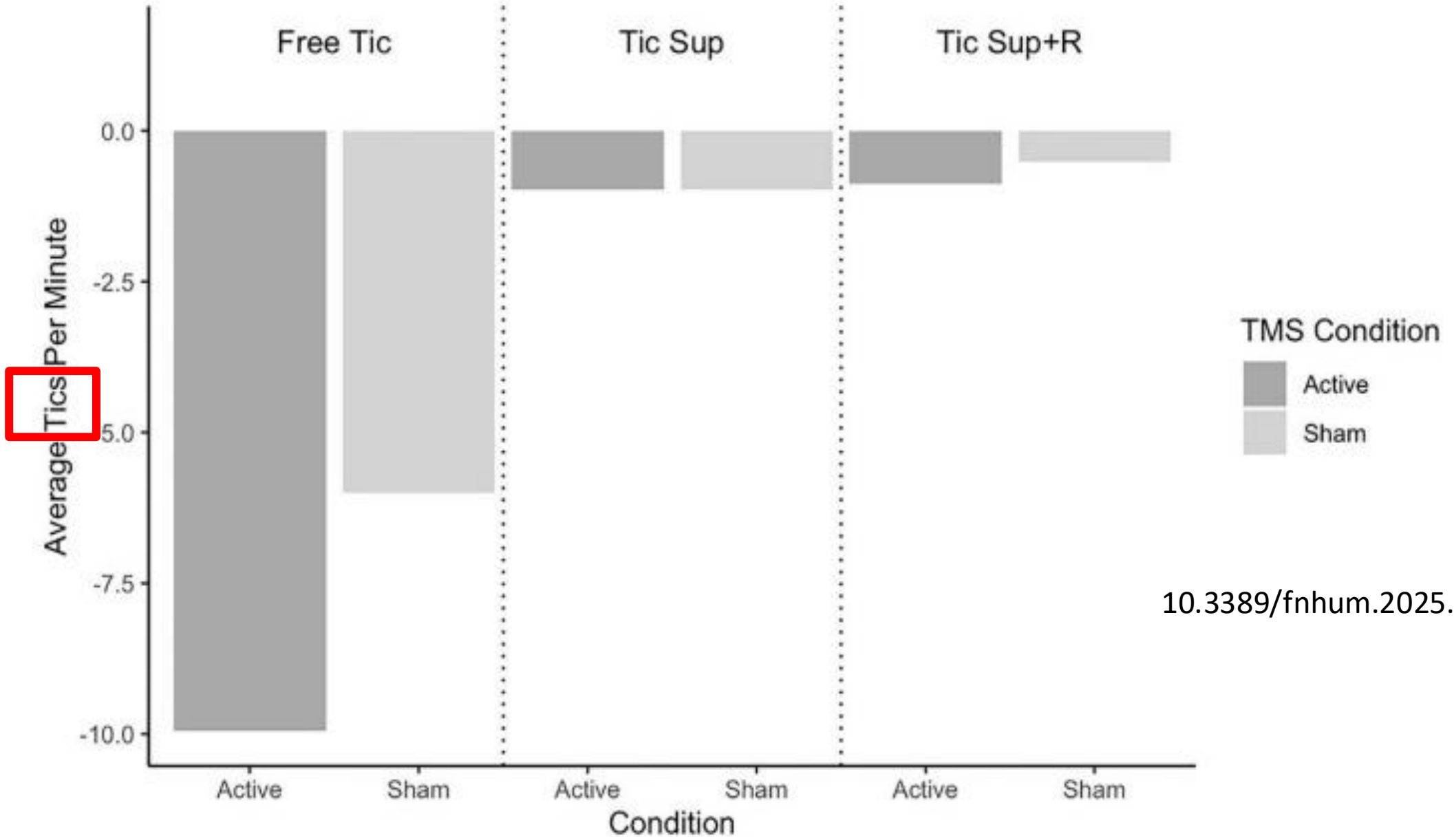




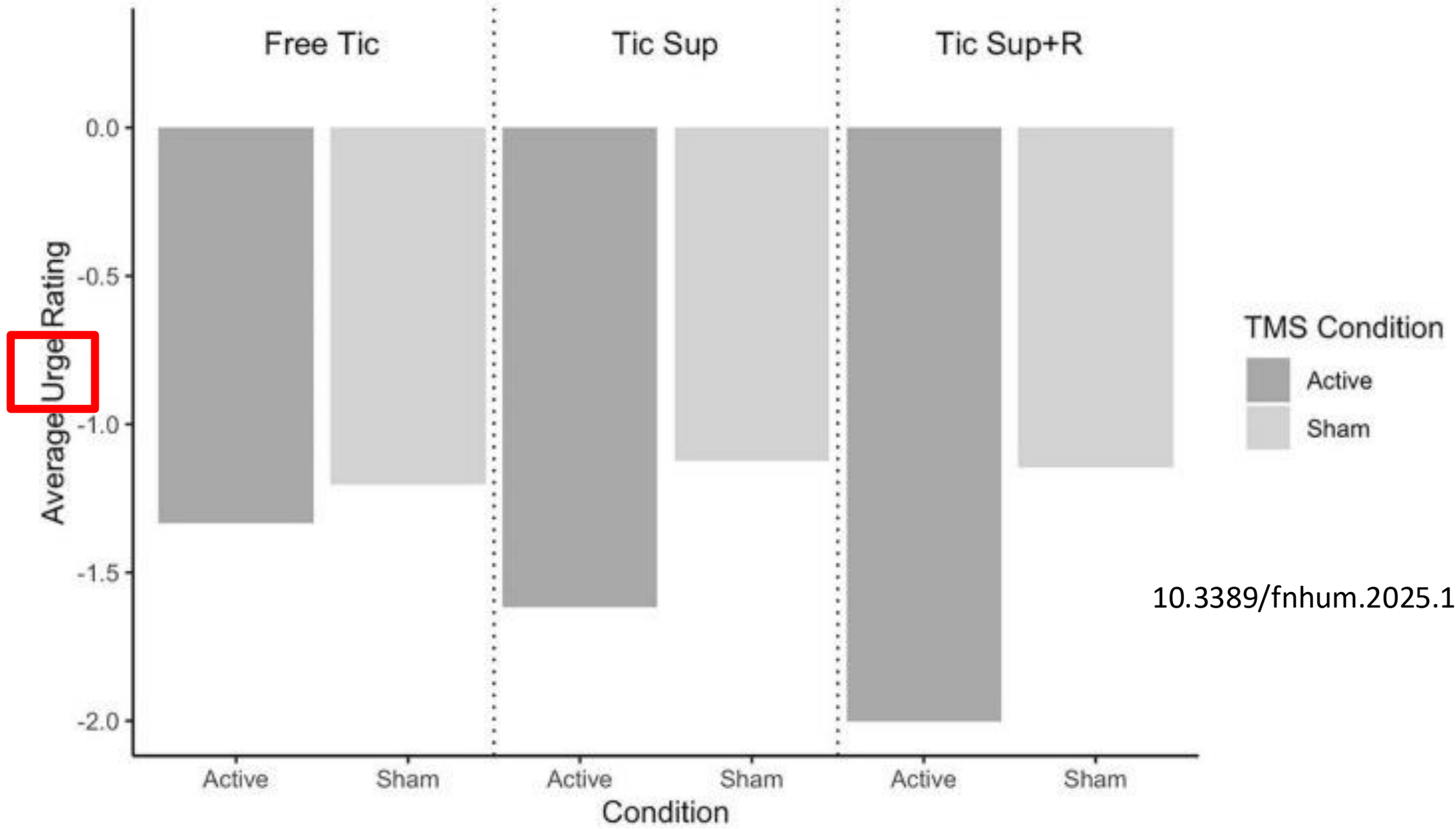
rTMS to SMA for tics and urges

- N=14 with TS, age 12-17
- Random allocation rTMS at 1 Hz (N=8) or sham (N=6)
- 3 conditions: tic at will, don't tic, don't tic and reward for not ticcing

10.3389/fnhum.2025.1720968



10.3389/fnhum.2025.1720968



10.3389/fnhum.2025.1720968

Tics, family and society



(see paper)



1. Survey of 174 patients, 160 caregivers, 89 health care professionals from 26 countries: Patients and caregivers favored the term “Tourette syndrome.” Healthcare professionals preferred “Tourette spectrum.”
2. It's hard to get good care: reports from Argentina/Chile (Canada), UK, France, USA

10.1002/mdc3.70110

Conclusions





Lot of good research is being done

- TS research is **bigger**: 16% more PubMed reports in 2025 vs. 2024
- TS research is **wider**, with more attention to comorbidity, functional symptoms, and patient-directed concerns such as pain.
- TS research is **more diverse**; our paper includes authors from Argentina, Australia, Brazil, Canada, Chile, China, Japan, Korea, and Taiwan, in addition to Europe and the United States.
- TS research is increasingly **deeper**, with larger studies and prospective registries.
- All of these characteristics indicate increasing likelihood in the near future of important, replicated, treatment-relevant research on TS.

Important new results expected in 2026



- Ecopipam phase III randomized withdrawal results just published
- ENIGMA-TS: >700 patients, >900 controls, preprint just out
- Genetics consortium
- The neurosteroid sepranolone (isoallopregnanolone)
- ... and ... unexpected new results may be amazing!

Please help!

To improve next year's talk, we warmly invite your cooperation:

Nominate important articles from 2026:





- Suggest a new publication of your own best work
- and/or one from someone else
- (email me or Andreas Hartmann)

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REVIEW

Tourette syndrome research highlights from 2025 [version 1; peer review: awaiting peer review]

✉ [Andreas Hartmann](#) ¹, [Cyril Atkinson-Clément](#)², [Nanette Mol Debes](#)³, [Peristera Paschou](#)⁴, [Natalia Szejko](#) ⁵, [Cécile Delorme](#)¹, [Per Andrén](#)⁶, [Virginie Czernecki](#)¹, [Simon Morand-Beaulieu](#)⁷, [Apostolia Topaloudi](#)⁴, [Kirsten Müller-Vahl](#) ⁵, [Kevin J. Black](#) ⁸

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This article is included in the [Tics](#) collection.

Abstract

This article is the annual update for the F1000Research Tics collection, in which we summarize research reports from 2025 on Tourette Syndrome (TS) and other tic disorders. The authors welcome article suggestions for future editions and thoughtful feedback from readers.

Kevin J. Black, M.D.
MSC 8134-70-2205
660 S. Euclid Ave.
St. Louis, MO 63110

blacklab.WUSTL.edu

+1 314-362-5041

kevin@WUSTL.edu

