Tourette syndrome research highlights from 2024

Andreas Hartmann

Kevin J. Black

May 14, 2024

We summarize a few research reports from 2024 relevant to Tourette syndrome that the authors consider most important or interesting. This working draft aims towards submitting this content for publication around the beginning of 2025 in the yearly Tourette Syndrome Research Highlights [series on **F1000Research**](https://f1000research.com/collections/tics). **The authors welcome article suggestions and thoughtful feedback from readers**, who can add a comment by clicking on the rectangular comment box icon just to the left of the LOG IN link at the top of this page. For private comments you can reach us by email (andreas {dot} hartmann {at} aphp {dot} fr, or kevin {at} wustl {dot} edu).

*Copyright © 2024, the authors.*

# Introduction

This article is meant to disseminate scientific progress on Gilles de la Tourette Syndrome (GTS) that appeared in the year 2024, summarizing research reports the authors judged important or interesting.

# Methods

We searched PubMed using the search strategy [(“Tic Disorders”[MeSH] OR Tourette) NOT ((Tourette[AU] OR Tourette[COIS]) NOT (“Tic Disorders”[MeSH] OR Tourette [tiab])) AND 2024[PDAT] NOT 1800:2023[PDAT]](https://pubmed.ncbi.nlm.nih.gov/?term=%28%22Tic+Disorders%22%5BMeSH%5D+OR+Tourette%29+NOT+%28%28Tourette%5BAU%5D+OR+Tourette%5BCOIS%5D%29+NOT+%28%22Tic+Disorders%22%5BMeSH%5D+OR+Tourette+%5Btiab%5D%29%29+AND+2024%5BPDAT%5D+NOT+1800%3A2023%5BPDAT%5D). On 24 Jan 2024 this search returned 14 citations. On the same date, a search of PubMed Central for [(“tic disorders”[mesh] OR tourette\*[ti] OR tourette\*[ab] OR Tourette\*[kwd] OR tourettism[tw]) AND 2024[dp] NOT 1800:2023[dp]](https://www.ncbi.nlm.nih.gov/pmc/?term=(%22tic+disorders%22%5Bmesh%5D+OR+tourette*%5Bti%5D+OR+tourette*%5Bab%5D+OR+Tourette*%5Bkwd%5D+OR+tourettism%5Btw%5D)+AND+2024%5Bdp%5D+NOT+1800%3A2023%5Bdp%5D) returned 7 citations. All these citations are available in [this NLM article collection](https://www.ncbi.nlm.nih.gov/sites/myncbi/kevin.black.1/collections/63702628/public/). Colleagues also recommended articles, and we attended selected medical conferences. We selected material for this review subjectively, guided by our judgment of possible future impact on the field.

# Results

## Phenomenology and natural history

### Definition and phenomenology

An analysis of a large TS genetics database examined possible sex differences in people with a persistent tic disorder (Dy-Hollins et al. 2024). Girls were diagnosed later and less often, but symptoms started only slightly later (0.5-1.0 years) and were of similar severity. OCD was more common in females and ADHD was more common in males. The Montreal group examined possible sex differences in 66 children age 7-14 with tics, 19 of whom were girls (doi 10.3390/jcm13092477). They found no differences in tic symptoms, but substantial differences in psychological style, comorbidity and impairment.

Sleep in TS (Keenan et al. 2024).

### Assessment and quantification of tics

Important work: “Automatic identification of facial tics using selfie-video” (Loewenstern et al. 2024).

### Prognosis and natural history

### Sensory phenomena and premonitory urge

### Comorbidities

<https://doi.org/10.1136/bmj-2023-077564>

Medication treatment for ADHD saves lives (Li et al. 2024).

### Functional tic-like behaviors

What features are most and least common in functional tic-like behaviors (FTLB) vs primary tic disorder? (Nilles et al. 2024). Specificity of some features of ESSTS criteria assessed vs. a registry of people with a primary tic disorder (Nilles et al. 2024).

## Etiology

### Genetics and epigenetics

In autism, genetic effects on several early neurodevelopmental traits are better explained indirectly by their effect on cognitive ability and educational attainment (Hegemann et al. 2024).

GWAS identifies 30 loci associated with OCD {DOI 10.1101/2024.03.13.24304161}.

### Environmental risk factors

“The Challenge of Examining Social Determinants of Health in People Living with Tourette Syndrome” (Dy-Hollins et al. 2023).

### Post-mortem studies

“[W]e performed single cell transcriptomic and chromatin accessibility analyses of the caudate nucleus from 6 adult TS and 6 control post-mortem brains. … interneurons were decreased by roughly 50% in TS brains, while no difference was observed for other cell types. … Differential gene expression analysis suggested that mitochondrial function, and specifically oxidative metabolism, in MSN and synaptic function in interneurons are both impaired in TS subjects, while microglia display strong activation of immune response pathways.” (Wang et al. 2024)

## Pathophysiology

### Electrophysiology

### Neuroimaging studies

Interesting fMRI study design looking at brain activity related to situations that trigger tics and tic imagery (Zapparoli et al. 2024).

“Functional connectivity of the nucleus accumbens predicts clinical course in treated and non-responder adult ADHD” (Zaher et al. 4AD).

### Animal models

“Phonic Tics in a Rat Model of Tourette Syndrome Enable Research on Symptom-Based DBS” (Sagalajev et al. 6AD). [Note: preprint appeared in 2023]

### Other

## Treatment

(Wang et al. 2024) summarize the pill placebo response rate in tic disorders. They find a pooled effect size of −0.79, and note that 44% of study participants reported adverse events on placebo. These results are important for designing future treatment studies in TS.

### Psychological interventions

Tic suppression-based treatments for tics have been criticized (mostly by those who do not do behavior therapy) as likely to provoke tic substitution or to be too difficult. The group that performed the first large CBIT trial in children 11 years ago followed up with those participants, now adults, to ask about such experiences then or since (Barber et al. 2024). The great majority of study participants recalled no such negative experiences, and importantly those who did were no more likely to have been in the CBIT arm vs. the control therapy arm. This study adds to substantial prior data showing that such negative experiences are rare, and hopefully can put to rest these concerns.

(Mohamed et al. 2024) provide a meta-analysis of differential reinforcement of other (DRO) as a treatment of tics. Here, DRO refers to rewarding someone every time a defined duration passes with no tics. In 8 studies totaling 79 participants, DRO decreased tic frequency by an average of 10.25 tics per minute (p  < 0.00001). An important caveat is that the available primary studies focus only on immediate results, i.e. decrease of tic frequency for a period several minutes long while DRO rewards are given consistently. Nevertheless, the authors note that DRO’s potential ease of dissemination and use provide justification for real-world treatment studies. We note that an open software web implementation of DRO is available gratis (Black and Black 2017).

Rotstein and colleagues from Tel Aviv developed a gamified adaptation of exposure and response prevention (DRO) that provides immediate rewards for tic suppression, and tested it in a crossover trial with 35 children with tics (Rotstein et al. 2024). Compared to non-contingent, end-of-session reward, immediately rewarded tic suppression resulted in substantially increased tic suppression during treatment sessions. Clinically, tic ratings improved 26% during treatment and 43% at 3 months after treatment. This approach adds reward variety and a much more engaging format to TicTrainer (Black and Black 2017), and seems very likely to prove clinically useful.

### Pharmacological studies

The Phase 2b T-GOLD study of valbenazine for youth with Tourette syndrome did not meet its primary endpoint (BNN Correspondents 2024). Secondary analyses are planned to determine whether a subgroup of patients responded well.

A mechanistic study of vitamin D3 in a rodent model of tics (Li et al. 2024).

### Neurosurgery

“Responsive” DBS for TS (Okun et al. 2024).

## Tics, family and society

(Isaacs et al. 2024) completed a focus group to summarize thoughts of adults with TS on priorities for research and on the development of a registry.

In the past decade, the first authors of over half of Tourette-related publications were women (Mahajan et al. 2024).

## Additional sources

# Conclusions

# Competing interests

AH is a consultant for Noema Pharma. PA has received royalties from the Tourette OCD Alberta Network. CD is a consultant for Medtronic. KJB participated in a clinical trial sponsored by Emalex Biosciences; he received research support from Zhittya Genesis Medicine and from NIH (R01MH118217, UL1TR002345, R01MH126213, R21NS133875, R01MH127187 ).

NMD has no conflicts of interest. VC has no conflict of interest. KU participated in a clinical trial sponsored by Emalex Biosciences. PP has no conflict of interest. AT has no conflict of interest. CAC has no conflict of interest.

NSZ participated in clinical trial supported by Emalex and Nuvelution. She received scientific grants from the Polish Neurological Society, European Stroke Organisation, Polish Ministry of Health, Polish Foundation of Science, Tourette Association of America, American Academy  of Neurology and American  Brain Foundation. She received speaker honoraria from Biogen.

PP was supported by EMTICS (Grant No. 278367), TS-EUROTRAIN (Grant No. 316978), the National Institute of Neurological Disorders and Stroke (Grant No. R01NS105746), U.S. National Science Foundation (Grant Nos. 2006929 and 1715202), and the National Institute of Mental Health (Grant No. R01MH126213).

KMV has received financial or material research support from EU (FP7-HEALTH-2011 No. 278367, FP7-PEOPLE-2012-ITN No. 316978), DFG: GZ MU 1527/3-1 and GZ MU 1527/3-2, BMBF: 01KG1421, National Institute of Mental Health (NIMH), Tourette Gesellschaft Deutschland e.V., Else-Kröner-Fresenius-Stiftung, GW pharmaceuticals, Almirall, Abide Therapeutics, Emalex Biosciences, Inc., Noema Pharma, CannaXan, and Therapix Biosiences.

She has received consultant’s and other honoraria from Abide Therapeutics, adjupharm, Alexion, AMP Alternative Medical Products GmbH, Ingelheim International GmbH, Bionorica Ethics GmbH, CannaMedical Pharma GmbH, Canopy Grouth, Columbia Care, CTC Communications Corp., Demecan, Enua pharma, Ethypharm GmbH, Eurox Group, Global Praxis Group Limited, Hormosan Pharma GmbH, Lundbeck, MCI Germany, Neuraxpharm, Noema Pharma, Sanity Group, Stadapharm GmbH, Synendos Therapeutics AG, Syqe, Tilray, and Zambon.

She is an advisory/scientific board member for Alexion, Branchenverband Cannabiswirtschaft e.V. (BvCW), CannaMedical Pharma GmbH, Bionorica Ethics GmbH, CannaXan GmbH, Canopy Growth, Columbia Care, Ethypharm GmbH, Hormosan Pharma GmbH, IMC Germany, Leafly Deutschland GmbH, Neuraxpharm, Sanity Group, Stadapharm GmbH, Synendos Therapeutics AG, Syqe Medical Ltd., Therapix Biosciences Ltd., and Tilray.

She has received speaker’s fees from Agaplesion Frankfurter Diakonie Kliniken gemeinnützige GmbH, Almirall, Aphria Deutschland GmbH, Arbeitsgemeinschaft Cannabis als Medizin (ACM), Bedrocan, Branchenverband Cannabiswirtschaft e.V. (BvCW), Camurus, CEREBRO SPAIN BIDCO S.L, Cogitando GmbH, Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde (DGPPN), Diplomado Internacional de Endocannabinología (Programa Universitario de Investigación en Salud - PUIS, UNAM), Dresden International University (DIU), Emalex, Eurox Deutschland GmbH, Ever pharma GmbH, Georgia Medical Cannabis Project (GMCP), GROW, Hessische Landesstelle für Suchtfragen e.V. (HLS), LIO Pharmaceuticals GmbH, Medizinischer Dienst Westfalen Lippe, Meinhardt Congress GmbH, PR Berater, Spectrum Therapeutics GmbH, Swiss Alpinopharm, targoEvent GmbH, Takeda GmbH, Tilray, von Mende Marketing GmbH, and Wayland Group.

She has received royalties from Deutsches Ärzteblatt, Der Neurologie und Psychiater, Elsevier, Medizinisch Wissenschaftliche Verlagsgesellschaft Berlin, and Kohlhammer.

She served as a guest editor for Frontiers in Neurology on the research topic “The neurobiology and genetics of Gilles de la Tourette syndrome: new avenues through large-scale collaborative projects”, is an associate editor for “Cannabis and Cannabinoid Research”, an Editorial Board Member of “Medical Cannabis and Cannabinoids” and “MDPI-Reports” and a scientific board member for “Zeitschrift für Allgemeinmedizin”.

# Grant information

Supported in part by the National Institutes of Health (grants R01MH118217, UL1TR002345, R01MH126213, R21NS133875, R01MH127187). The authors confirm that the funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Supported in part by EMTICS (Grant No. 278367), TS-EUROTRAIN (Grant No. 316978), EU (FP7-HEALTH-2011 No. 278367, FP7-PEOPLE-2012-ITN No. 316978), DFG: GZ MU 1527/3-1 and GZ MU 1527/3-2, BMBF: 01KG1421, Tourette Gesellschaft Deutschland e.V., Else-Kröner-Fresenius-Stiftung, the National Institutes of Health (Grant Nos. R01NS105746, R01MH126213), and the U.S. National Science Foundation (Grant Nos. 2006929 and 1715202).

# Supplemental material

None.

# References

Barber KE, Pitts BX, Stiede JT, Espil FM, Woods DW, Specht MW, et al. Perceived Negative Effects of Tic Management Strategies in Adults With Tic Disorders. Behav Modif. 2024;:1454455241236446.

Black JK, Black KJ. Software for web-based tic suppression training. F1000Research [Internet]. 2017;6:2150. Available at: <http://dx.doi.org/10.12688/f1000research.13460.2>

Dy-Hollins ME, Carr SJ, Essa A, Osiecki L, Lackland DT, Voeks J, et al. The Challenge of Examining Social Determinants of Health in People Living with Tourette Syndrome (preprint). SSRN [Internet]. 2023; Available at: <http://dx.doi.org/10.2139/ssrn.4601966>

Dy-Hollins ME, Chibnik LB, Tracy N, Osiecki L, Budman CL, Cath DC, et al. Sex Differences in People with Tourette Syndrome and Persistent Motor or Vocal Tic Disorder in the Tourette Association of America International Consortium for Genetics Database (preprint). medRxiv [Internet]. January 2024; Available at: <http://dx.doi.org/10.1101/2024.01.07.24300816>

Hegemann L, Eilertsen E, Pettersen JH, Corfield EC, Cheesman R, Frach L, et al. Direct and Indirect Genetic Effects on Early Neurodevelopmental Traits (preprint). medRxiv [Internet]. January 2024; Available at: <http://dx.doi.org/10.1101/2024.01.24.24301734>

Isaacs DA, Bonnet K, Eckland MR, Markowitz K, Pena M, Schlundt DG. Perspectives from Adults with Tourette Syndrome | NDT [Internet]. Vol. 20, Neuropsychiatric Disease and Treatment. [https://www.dovepress.com/perspectives-from-adults-with-tourette-syndrome-on-research-priorities-peer-reviewed-fulltext-article-NDT;](https://www.dovepress.com/perspectives-from-adults-with-tourette-syndrome-on-research-priorities-peer-reviewed-fulltext-article-NDT) 2024. p. 257–69. Available at: <https://www.dovepress.com/perspectives-from-adults-with-tourette-syndrome-on-research-priorities-peer-reviewed-fulltext-article-NDT>

Keenan L, Bramham J, Dinca M, Coogan AN, Downes M. Sleep and daytime functioning in children with Tourette syndrome: A two-week case-control study with actigraphy and cognitive assessments. Sleep Med. 2024;113:313–27.

Li HH, Wang XF, Wang B, Jia FY. Vitamin D3 improves iminodipropionitrile-induced tic-like behavior in rats through regulation of GDNF/c-Ret signaling activity. Eur Child Adolesc Psychiatry. 2024;

Li L, Zhu N, Zhang L, Kuja-Halkola R, D’Onofrio BM, Brikell I, et al. ADHD Pharmacotherapy and Mortality in Individuals With ADHD. JAMA. 2024;331:850–60.

Loewenstern Y, Benaroya-Milshtein N, Belelovsky K, Bar-Gad I. Automatic identification of facial tics using selfie-video. January 10, 2024; Available at: <http://dx.doi.org/10.36227/techrxiv.170491562.24205217/v1>

Mahajan A, K. V, Dikshit N, Sandhu JK, Pallempati LL, Olivieri L. Gender Representation in Academic Publications of Tourette Syndrome Research: An Analysis of Authorship Trends. Cureus [Internet]. January 2024;16(1):e51520. Available at: <http://dx.doi.org/10.7759/cureus.51520>

Mohamed ZA, Xue Y, Bai M, Dong H, Jia F. Efficacy of differential reinforcement of other behaviors therapy for tic disorder: a meta-analysis. BMC Neurology [Internet]. January 2024;24(1). Available at: <http://dx.doi.org/10.1186/s12883-023-03501-2>

Nilles C, Martino D, Berg L, Fletcher J, Pringsheim T. What are the Key phenomenological Clues to Diagnose Functional Tic-Like Behaviors in the pandemic era?. Mov Disord Clin Pract. 2024;

Nilles C, Martino D, Pringsheim T. Testing the specificity of phenomenological criteria for functional tic-like behaviours in youth with Tourette syndrome. Eur J Neurol. 2024;:e16262.

Okun MS, Cagle J, Gomez J, Bowers D, Wong J, Foote KD, et al. Responsive deep brain stimulation for the treatment of Tourette syndrome. Sci Rep. 2024;14:6467.

Rotstein MS, Zimmerman-Brenner S, Davidovitch S, Ben-Haim Y, Koryto Y, Sion R, et al. Gamified closed-loop non-pharmacological intervention enhances tic suppression in children. medRxiv [Internet]. April 19, 2024; Available at: <http://dx.doi.org/10.1101/2024.04.17.24303913>

Sagalajev B, Lennartz L, Mokhtari N, Szpak M, Schüller T, Baldermann JC, et al. Phonic Tics in a Rat Model of Tourette Syndrome Enable Research on Symptom-Based DBS. bioRxiv [Internet]. 6AD; Available at: <http://dx.doi.org/10.1101/2023.08.06.551271>

Wang S, Xiong Z, Cui Y, Fan F, Zhang S, Jia R, et al. Placebo and Nocebo Responses in Pharmacological Trials of Tic Disorders: A Meta-Analysis. Mov Disord. 2024;

Wang Y, Fasching L, Wu F, Huttner A, Berretta S, Roberts R, et al. Interneuron loss and microglia activation by transcriptome analyses in the basal ganglia of Tourette syndrome (preprint). BioRxiv [Internet]. February 2024; Available at: <http://dx.doi.org/10.1101/2024.02.28.582504>

Zaher A, Leonards J, Reif A, Grimm O. Functional connectivity of the nucleus accumbens predicts clinical course in treated and non-responder adult ADHD (preprint). medRxiv [Internet]. 4AD; Available at: <http://dx.doi.org/10.1101/2024.01.04.24300820>

Zapparoli L, Devoto F, Mariano M, Seghezzi S, Servello D, Porta M, et al. Mapping Gilles de la Tourette syndrome through the distress and relief associated with tic-related behaviors: an fMRI study. Transl Psychiatry. 2024;14:7.

BNN Correspondents. Neurocrine Biosciences Faces Setback in Tourette Syndrome Study, Shares Tumble [Internet]. [https://web.archive.org/web/20240229062116/https://bnnbreaking.com/world/us/neurocrine-biosciences-faces-setback-in-tourette-syndrome-study-shares-tumble;](https://web.archive.org/web/20240229062116/https%3A//bnnbreaking.com/world/us/neurocrine-biosciences-faces-setback-in-tourette-syndrome-study-shares-tumble) 2024. Available at: [https://web.archive.org/web/20240229062116/https://bnnbreaking.com/world/us/neurocrine-biosciences-faces-setback-in-tourette-syndrome-study-shares-tumble](https://web.archive.org/web/20240229062116/https%3A//bnnbreaking.com/world/us/neurocrine-biosciences-faces-setback-in-tourette-syndrome-study-shares-tumble)