

Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders

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Abstract

Objective

To systematically evaluate the efficacy of treatments for tics and the risks associated with their use.

Methods

This project followed the methodologies outlined in the 2011 edition of the American Academy of Neurology's guideline development process manual. We included systematic reviews and randomized controlled trials on the treatment of tics that included at least 20 participants (10 participants if a crossover trial), except for neurostimulation trials, for which no minimum sample size was required. To obtain additional information on drug safety, we included cohort studies or case series that specifically evaluated adverse drug effects in individuals with tics.

Results

There was high confidence that the Comprehensive Behavioral Intervention for Tics was more likely than psychoeducation and supportive therapy to reduce tics. There was moderate confidence that haloperidol, risperidone, aripiprazole, tiapride, clonidine, onabotulinumtoxinA injections, 5-ling granule, Ningdong granule, and deep brain stimulation of the globus pallidus were probably more likely than placebo to reduce tics. There was low confidence that pimozide, ziprasidone, metoclopramide, guanfacine, topiramate, and tetrahydrocannabinol were possibly more likely than placebo to reduce tics. Evidence of harm associated with various treatments was also demonstrated, including weight gain, drug-induced movement disorders, elevated prolactin levels, sedation, and effects on heart rate, blood pressure, and ECGs.

Conclusions

There is evidence to support the efficacy of various medical, behavioral, and neurostimulation interventions for the treatment of tics. Both the efficacy and harms associated with interventions must be considered in making treatment recommendations.

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Glossary

AAN = American Academy of Neurology; ADHD = attention-deficit/hyperactivity disorder; CI = confidence interval; COI = conflict of interest; DBS = deep brain stimulation; GDDI = Guideline Development, Dissemination, and Implementation; rTMS = repetitive transcranial magnetic stimulation; SMD = standardized mean difference; TS = Tourette syndrome; YGTSS = Yale Global Tic Severity Scale.

This article summarizes the findings of a systematic review, conducted as the foundation of an American Academy of Neurology (AAN) practice guideline on the treatment of tics in people with Tourette syndrome (TS) and chronic tic disorders. A companion article summarizes the assessment and treatment recommendations and suggestions for future research. The complete and unabridged practice guideline (systematic review, recommendations, and suggestions for future research) is available at links.lww.com/WNL/A883 and includes full details of the methodology used, including the risk of bias assessment for each study, meta-analysis, and confidence in evidence determinations; space restrictions precluded more detailed description in this article.

TS is a neurodevelopmental condition that is characterized by the presence of multiple motor tics and at least 1 vocal tic that persists for at least 1 year.¹ Motor tics are defined as sudden, rapid, recurrent, and nonrhythmic movements. Vocal tics are essentially motor tics that involve the nasal or respiratory muscles, resulting in simple sounds such as sniffing, throat clearing or coughing, or complex vocalizations, including coprolalia, but they also may manifest with speech blocking or stuttering-like symptoms. Tics are often accompanied by specific behavioral symptoms.^{2,3} Persistent (chronic) motor tic disorder is characterized by the presence of motor tics only, which persist for more than 1 year. Persistent (chronic) vocal tic disorder is characterized by the presence of vocal tics only, which persist for more than 1 year. Epidemiologic studies that used current diagnostic criteria have consistently shown that the prevalence figures for TS in school children range from 0.4% to 1.5% across all cultures, while the prevalence of chronic tic disorders ranges from 0.9% to 2.8%.⁴ There are few population-based estimates of the prevalence of TS in adults; one recent population-based study found a prevalence of diagnosed TS of approximately 1 per 1,000.⁵ TS and chronic tic disorders are believed to share a common neurobiological origin, and we use the abbreviation TS throughout the article to refer to all individuals with primary chronic tic disorders.

The majority of patients with TS, both in specialist clinics and in the community, report the presence of behavioral symptoms associated with their tics: most commonly obsessive-compulsive disorder (or obsessive-compulsive behavior) and

attention-deficit/hyperactivity disorder (ADHD).⁶ Lifetime prevalence of comorbid behavioral disorders is estimated to approach 90%.⁷ Patients with TS also report higher rates of impulse control, anxiety, and affective disorders compared with people in the general population.^{7,8} It is worth noting that the associated behavioral comorbidities often compromise the overall well-being of patients with TS to a much greater extent than tic severity.^{9,10}

The purpose of this systematic review is to assess all randomized controlled trials that evaluate the efficacy of medical and behavioral treatments for tics, including neurostimulation, and the risks associated with their use. The systematic review was performed to develop recommendations pertaining to the treatments of tics in children and adults with TS or chronic tic disorders. Antipsychotic medications have been commonly prescribed for this purpose since the 1960s. The adverse effects associated with antipsychotic medications, including movement disorders such as acute and tardive dystonia, tardive dyskinesia, akathisia, and drug-induced parkinsonism, and metabolic adverse effects, such as weight gain, hyperlipidemia, and hyperglycemia, have led clinicians to search for other effective treatments. In recent years, there has been a resurgence in the interest in behavioral treatments and neuromodulation for tics, yielding expanding evidence in this area.

Clinical questions

The systematic review for this practice guideline addressed the following questions:

1. In children and adults with TS or a chronic tic disorder, which medical, behavioral, and neurostimulation interventions, compared with placebo or other active interventions, improve tic severity?
2. In children and adults with TS or a chronic tic disorder, what are the risks of harm, including weight gain, elevated prolactin levels, sedation, drug-induced movement disorders, hypotension, bradycardia, and ECG changes with medical treatments, compared with placebo or other active interventions?

Description of the analytic process

In May 2016, the Guideline Development, Dissemination, and Implementation (GDDI) Subcommittee of the AAN recruited a multidisciplinary panel to develop the guideline, including 9 physicians, 2 psychologists, and 2 patient representatives. The patient representatives are both associated with the Tourette Association of America. All panel members

+ Supplemental Data

Full measurement set

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were required to submit online conflict of interest (COI) forms and copies of their curriculum vitae. All authors determined to have COI were not permitted to review or rate the evidence.

This evidence-based practice guideline follows the methodologies described in the 2011 edition of the AAN's guideline development process manual,¹¹ as amended to include use of the revised scheme for classifying therapeutic articles, the GDDI Guideline Topic Nomination Process scoring tool, and the change in order of steps for external review.

Study screening and selection criteria: Inclusion criteria for article selection

We included systematic reviews and randomized controlled trials on the treatment of tics in individuals with TS or chronic tic disorders that included at least 20 participants (10 participants if a crossover trial), except for neurostimulation trials, for which no minimum sample size was required. To obtain additional information on drug safety, we included cohort studies or case series that specifically evaluated adverse drug effects in individuals with TS.

Types of participants

We included individuals with TS or chronic tic disorders of any age or sex.

Types of intervention

We included any medical, behavioral, or neurostimulation (e.g., transcranial magnetic stimulation, deep brain stimulation [DBS]) intervention for tics.

Comparison group

We included studies that compared medical, behavioral, or neurostimulation treatments with placebo or other active treatments.

Types of outcome measures

We assessed the effect of all treatments on measures of tic severity and tic-related impairment. The preferred instrument for evaluation of tic severity and tic-related impairment was the Yale Global Tic Severity Scale (YGTSS), and when outcome results with this instrument were reported, they were used to calculate effect size. The YGTSS, the most extensively deployed rating scale for tics internationally, has displayed very good internal consistency, interrater reliability, and convergent and divergent validity.¹² Weight gain was assessed through reported measurements in kilograms. Elevated prolactin levels were evaluated by assessing mean changes in prolactin levels between groups, or mean prolactin levels at endpoint between groups. Drug-induced movement disorders were based on assessments that used validated scales, including the Extrapyrimal Symptoms Rating Scale, Barnes Akathisia Scale, Simpson Angus Scale, or the Abnormal Involuntary Movement Scale, or by clinician report. Sedation was evaluated by patient/parent/clinician report and

assessment. Hypotension and bradycardia were evaluated by assessing reported changes in systolic and diastolic blood pressure and heart rate with treatment and reported rates of presyncope and syncope. Reported ECG changes were also included.

The initial search was conducted in August 2016 and included MEDLINE, EMBASE, PsychINFO, CENTRAL, and ClinicalTrials.gov. The total number of references retrieved after duplicates were removed was 2,196. After 2 reviewers, working independently of each other, reviewed the abstracts and titles of these 2,196 references, the articles for 192 were selected and obtained for full-text review. This included 16 systematic reviews, for which the references of all included studies were examined for missing studies. Four additional studies were identified using this method. In total, 66 randomized controlled trials and 12 studies that evaluated drug safety were included in our analysis. Two nonconflicted panel members rated the class of evidence for each article according to the AAN scheme for classification of therapeutic articles (revised as denoted in a 2011 process manual amendment). Disagreements were resolved by a third panel member. Outcome data from included studies were extracted by the guideline methodologist and verified by a second panel member.

A repeat search was conducted in September 2017 to update our search results, with a total of 211 new abstracts retrieved after duplicate removal. Seven abstracts were selected for full-text review, and 3 articles met our inclusion criteria and were added to the analysis.

The effect size, or standardized mean difference (SMD), was calculated for each study intervention/outcome pair. The SMD expresses the size of the intervention effect relative to the variability observed in each study. For our analysis, an SMD of 0.20 was considered the minimal clinically meaningful difference for reduction in tic severity; effect sizes smaller than 0.10 were considered clinically unimportant. There were a number of studies that did not provide adequate data to reliably calculate effect sizes.^{13–20} If multiple studies were available that evaluated the same intervention/outcome pair, only those studies with the lowest risk of bias were used in formulating the confidence in evidence statements. A random effects meta-analysis was performed when appropriate to synthesize results of trials that studied the same intervention and outcome.

A modified form of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process was used to develop conclusions.²¹ The confidence in the evidence (high, moderate, low, or very low) is anchored to the error domain—class of evidence, indirectness of evidence, and precision of effect estimate—with the highest risk of error (see unabridged practice guideline for complete details on the evidence synthesis process).

Analysis of evidence

In children and adults with TS or a chronic tic disorder, which medical, behavioral, and neurostimulation interventions, compared with placebo or other active interventions, improve tic severity?

Unless otherwise specified, trial participants included both children (individuals aged 18 years and younger) and adults (individuals older than 18 years).

High confidence in the evidence

People with tics receiving the Comprehensive Behavioral Intervention for Tics are more likely than those receiving supportive psychotherapy to have reduced tic severity (SMD 0.56; 95% confidence interval [CI] 0.31–0.82, high confidence, 2 Class I studies^{22,23}).

Moderate confidence in the evidence

People with tics receiving the following interventions are probably more likely than those receiving placebo to have reduced tic severity:

- Haloperidol, SMD 0.59 (95% CI 0.11–1.06), 2 Class II studies^{24,25}
- Risperidone, SMD 0.79 (95% CI 0.31–1.27), 2 Class II studies^{26,27}
- Aripiprazole, SMD 0.64 (95% CI 0.31–0.97), 1 Class I study²⁸ and 1 Class II study²⁹ (children only)
- Tiapride, SMD 0.62 (95% CI 0.36–0.88), 1 Class I study³⁰ (children only)
- Clonidine, SMD 0.45 (95% CI 0.13–0.77), 1 Class I study³¹ and 2 Class II studies^{32,33}
- OnabotulinumtoxinA injections, SMD 1.27 (95% CI 0.51–2.03), 1 Class II study³⁴; confidence in evidence upgraded due to magnitude of effect
- Ningdong granule (as formulated by Zhao), SMD 0.97 (95% CI 0.45–1.49), 1 Class II study³⁵; confidence in evidence upgraded due to magnitude of effect (children only)
- 5-Ling granule, SMD 0.55 (95% CI 0.33–0.76), 1 Class I study³⁰ (children only)

People with tics and a comorbid diagnosis of ADHD receiving the following interventions are probably more likely than those receiving placebo to have reduced tic severity:

- Clonidine plus methylphenidate, SMD 0.72 (95% CI 0.22–1.22), 1 Class I study³¹ (children only)
- Methylphenidate, SMD 0.61 (95% CI 0.13–1.10), 1 Class I study³¹ (children only)
- Desipramine, SMD 1.13 (95% CI 0.47–1.79), 1 Class II study³⁶; confidence in evidence upgraded due to magnitude of effect (children only). Desipramine is now rarely used in children after several case reports of sudden death associated with the use of this medication.³⁷

People with tics receiving active DBS of the globus pallidus are probably more likely than those receiving sham DBS of the globus pallidus to have reduced tic severity (SMD 0.77 [95% CI 0.14–1.40], 2 Class II studies^{38,39} [adults only]).

Low confidence in the evidence

People with tics receiving the following interventions are possibly more likely than those receiving placebo to have reduced tic severity:

- Pimozide, SMD 0.66 (95% CI 0.06–1.25), 3 Class II studies,^{24,40} confidence in evidence downgraded due to imprecision
- Ziprasidone, SMD 1.14 (95% CI 0.32–1.97), 1 Class II study⁴¹ (children only)
- Metoclopramide, SMD 1.14 (95% CI 0.33–1.95), 1 Class II study⁴² (children only)
- Guanfacine, SMD 0.45 (95% CI 0.03–0.87), 1 Class I study⁴³ and 2 Class II studies,^{44,45} confidence in evidence downgraded due to imprecision (children only)
- Topiramate, SMD 0.91 (95% CI 0.11–1.71), 1 Class II study⁴⁶
- Tetrahydrocannabinol, SMD 0.62 (95% CI 0.01–1.22), 1 Class II study⁴⁷ and 1 Class III study⁴⁸ (adults only)

For people with tics and a comorbid diagnosis of ADHD, atomoxetine does not worsen tics relative to placebo (1 Class II study⁴⁹) (children only).

Very low confidence in the evidence

There is insufficient evidence to determine whether people with tics receiving the following interventions are more or less likely than those receiving placebo to have reduced tic severity:

- Baclofen, SMD 0.55 (95% CI –0.39 to 1.49) 1 Class II study⁵⁰; confidence in evidence downgraded due to imprecision (children only)
- Levetiracetam, SMD 0.22 (95% CI –0.38 to 0.82), 1 Class II study⁵¹; confidence in evidence downgraded due to imprecision (children only)
- N-acetylcysteine, SMD 0.45 (95% CI –0.27 to 1.17), 1 Class II study⁵²; confidence in evidence downgraded due to imprecision (children only)
- Omega-3 fatty acids, SMD 0.69 (95% CI 0.00–1.39), 1 Class II study⁵³; confidence in evidence downgraded due to imprecision (children only)
- Ningdong granule (as formulated by Wang), 1 Class II study¹⁷ (children only)
- Nicotine, SMD 0.38 (95% CI –0.14 to 0.90), 1 Class III study⁵⁴ (children only)
- Nicotine patch added to haloperidol, SMD 0.71 (95% CI 0.17–1.25), 1 Class III study⁵⁵ (children only)
- Mecamylamine, 1 Class II study¹⁶ (children only)
- Flutamide, 1 Class I study¹⁴ (adults only)
- Riluzole, SMD 0.17 (95% CI –0.91 to 1.25), 1 Class I study⁵⁶; confidence in evidence downgraded due to imprecision (children only)

- D-serine, SMD -0.04 (95% CI -1.13 to 1.05), 1 Class I study⁵⁶; confidence in evidence downgraded due to imprecision (children only)
- Ondansetron, SMD 0.53 (95% CI -0.20 to 1.25), 1 Class III study⁵⁷
- Pramipexole, SMD 0.00 (95% CI -0.53 to 0.53), 1 Class II study⁵⁸; confidence in evidence downgraded due to imprecision (children only)
- IV immunoglobulin, SMD 0.50 (95% CI -0.24 to 1.24), 1 Class II study⁵⁹; confidence in evidence downgraded due to imprecision
- Deprenyl, SMD 0.47 (95% CI -0.05 to 0.99), 1 Class II study⁶⁰; confidence in evidence downgraded due to imprecision (children only)

There is insufficient evidence to determine whether people with tics receiving the following interventions are more or less likely than those receiving an alternate intervention to have reduced tic severity:

- Haloperidol vs pimozide, SMD 0.11 (95% CI -0.41 to 0.62), 2 Class II studies,^{24,25} confidence in evidence downgraded due to imprecision
- Risperidone vs pimozide, SMD 0.24 (95% CI -0.51 to 0.99), 2 Class II studies, confidence in evidence downgraded due to imprecision
- Risperidone vs clonidine, SMD -0.19 (95% CI -1.06 to 0.68), 1 Class II study,^{e1} confidence in evidence downgraded due to imprecision (children only)
- Aripiprazole vs risperidone, SMD 0.17 (95% CI -0.34 to 0.68), 1 Class II study,^{e2} confidence in evidence downgraded due to imprecision (children only)
- Clonidine vs levetiracetam, SMD 0.86 (95% CI -0.03 to 1.75), 1 Class II study^{e3} (children only)
- Habit reversal therapy vs exposure and response prevention, SMD 0.25 (95% CI -0.40 to 0.90), 1 Class II study,^{e4} confidence in evidence downgraded due to imprecision
- Habit reversal therapy vs educational group treatments, SMD 0.55 (95% CI -0.17 to 1.27), 1 Class II study,^{e5} confidence in evidence downgraded due to imprecision (children only)
- Face-to-face habit reversal therapy vs habit reversal therapy through video conferencing, SMD 0.24 (95% CI -0.70 to 1.18), 1 Class II study,^{e6} confidence in evidence downgraded due to imprecision (children only)
- Habit reversal therapy by video conferencing vs wait list control, SMD 0.24 (95% CI -0.65 to 1.14), 1 Class II study,^{e7} confidence in evidence downgraded due to imprecision (children only)
- Relaxation therapy vs minimal therapy, 1 Class III study²⁰ (children only)
- Biofeedback vs sham, 1 Class III study¹⁵ (adults only)
- Active DBS of the thalamus vs sham DBS of the thalamus, SMD 1.58 (95% CI -0.12 to 3.28), 1 Class III study^{e8} (adults only)
- Active DBS of the centromedian-parafascicular complex vs sham DBS of the centromedian-parafascicular complex,

SMD 0.99 (95% CI -0.28 to 2.26), 1 Class III study^{e9} (adults only)

- Continuous theta burst transcranial magnetic stimulation of the supplementary motor area vs sham transcranial magnetic stimulation, SMD -0.15 (95% CI -1.29 to 0.99), 1 Class II study^{e10}; confidence in evidence downgraded due to imprecision
- Repetitive transcranial magnetic stimulation (rTMS) of the supplementary motor area vs sham stimulation, SMD 0.19 (95% CI -0.69 to 1.07), 1 Class II study,^{e11} confidence in evidence downgraded due to imprecision (adults only)
- rTMS of the left motor or prefrontal cortex vs sham stimulation, 1 Class III study¹³

In children and adults with TS or a chronic tic disorder, what are the risks of harm, including weight gain, elevated prolactin levels, sedation, drug-induced movement disorders, hypotension, bradycardia, and ECG changes with medical treatments compared with placebo or other active interventions?

Data on harms related to the use of DBS can be found in the complete and unabridged practice guideline.

Weight gain

People with tics receiving risperidone are probably more likely to gain weight than people receiving placebo (moderate confidence, 2 Class II studies^{27,e1}).

People with tics receiving aripiprazole are probably more likely to gain weight than those receiving placebo (moderate confidence, 1 Class I study²⁸ and 1 Class II study²⁹) (children only).

People with tics receiving aripiprazole are possibly more likely to have an increase in body mass index and waist circumference than people receiving placebo (low confidence, 1 Class II study²⁹) (children only).

People with tics and a comorbid diagnosis of ADHD who are receiving atomoxetine are possibly more likely to have a decrease in body weight than people receiving placebo (low confidence, 1 Class II study⁴⁹) (children only).

Elevated prolactin levels

People with tics receiving pimozide are possibly more likely to have increased prolactin levels than people receiving placebo (low confidence, 1 Class II study²⁴).

People with tics receiving haloperidol are possibly more likely to have increased prolactin levels than people receiving placebo (low confidence, 1 Class II study²⁴).

People with tics receiving metoclopramide are possibly more likely to have greater increases in prolactin levels than people receiving placebo (low confidence, 1 Class II study⁴²) (children only).

Sedation

People with tics receiving risperidone are possibly more likely to experience fatigue and somnolence than people receiving placebo (low confidence, 1 Class II study²⁶).

People with tics receiving aripiprazole are possibly more likely to experience sedation and somnolence than people receiving placebo (low confidence, 1 Class II study²⁹) (children only).

People with tics receiving tiapride are probably more likely to experience higher rates of physical tiredness and sleep disturbances compared with people receiving placebo (moderate confidence, 1 Class I study³⁰) (children only).

People with tics receiving clonidine are probably more likely to experience sedation than people receiving placebo (moderate confidence, 1 Class I study³¹ and 1 Class II study³³).

People with tics receiving guanfacine are probably more likely than those receiving placebo to have drowsiness (moderate confidence, 1 Class I study⁴³) (children only).

Drug-induced movement disorders

People with tics receiving pimozide are probably more likely to have extrapyramidal symptoms than people receiving placebo (moderate confidence, 2 Class II studies⁴⁰).

People with tics receiving haloperidol are possibly more likely to have extrapyramidal symptoms than people receiving pimozide and placebo (low confidence, 1 Class II study^{24,25}).

People with tics receiving risperidone are possibly more likely to have higher parkinsonism scores on the Extrapyramidal Symptom Rating Scale than people receiving placebo (low confidence, 1 Class II study²⁶).

People with tics receiving risperidone are possibly more likely to require antiparkinsonian medication than people receiving placebo (low confidence, 1 Class II study²⁶).

Blood pressure

People with tics and a comorbid diagnosis of ADHD receiving desipramine are possibly more likely to have an increase in diastolic blood pressure than people receiving placebo (low confidence, 1 Class II study³⁶) (children only).

Heart rate

People with tics and a comorbid diagnosis of ADHD receiving atomoxetine are possibly more likely to have an increase in heart rate than people receiving placebo (low confidence, 1 Class II study⁴⁹) (children only).

People with tics and a comorbid diagnosis of ADHD receiving desipramine are possibly more likely to have an increased heart rate than people receiving placebo (low confidence, 1 Class II study³⁶) (children only).

ECG changes

People with tics receiving pimozide are possibly more likely to have a prolonged QT interval than people receiving placebo and haloperidol (low confidence, 1 Class II study²⁵).

Discussion

This systematic review summarizes the evidence for efficacy and harms of interventions for the treatment of tics in individuals with TS and chronic tic disorders. While there is evidence to support the efficacy of several treatments, knowledge gaps remain. Many of the interventions have only been studied in one randomized controlled trial of short duration, with modest sample sizes. The inherent features of tic disorders, with waxing and waning of symptoms over time, placebo effects, as well as suppression of tics during clinical encounters, may confound symptom assessment in clinical trials. There remains a great need for randomized controlled trials of interventions for tics to further evaluate both long-term efficacy and safety. The accompanying practice guideline makes recommendations based on the findings of this systematic review, acknowledging the limitations of the currently available evidence and strongly encouraging psychoeducation and shared decision-making regarding treatment needs and priorities.

Author contributions

Dr. Pringsheim: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Holler-Managan: study concept and design, acquisition of data, analysis or interpretation of data, critical revision of the manuscript for important intellectual content. Dr. Okun: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Jankovic: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Piacentini: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Cavanna: study concept and design, critical revision of the manuscript for important intellectual content. D. Martino: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Müller-Vahl: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Woods: study concept and design, critical revision of the manuscript for important intellectual content. M. Robinson: study concept and design, critical revision of the manuscript for important intellectual content. E. Jarvie: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Roessner: study concept and design, critical revision of the manuscript for important intellectual content. Dr. Oskoui: study concept and design, acquisition of data, analysis or interpretation of data, critical revision of the manuscript for important intellectual content. This guideline was endorsed

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Disclosure

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clinical time; and has received financial or material support from Pfizer Pharmaceuticals, the National Institute of Mental Health of the NIH, and from the academic entity of 501C3s, the TAA, TLC Foundation for BFRBs, and the Pettit Family Foundation. A. Cavanna has had nonfinancial competing interests at the Royal College of Psychiatrists, Faculty of Neuropsychiatry, Movement Disorders; has received funding for travel from the TAA; has served as a journal editor, an associate editor, or an editorial advisory board member for *Behavioral Neurology* and *Epilepsy and Behavior*; has received royalties from Oxford University Press; and has received personal compensation from speakers' bureaus with UCB Pharma, Eisai, and Janssen-Cilag. D. Martino has no disclosures to report. K. Müller-Vahl has nonfinancial competing interests as a member of the TAA medical advisory board, the scientific advisory board of the German Tourette Association (TGD), the board of directors of the German (ACM) and the International (IACM) Association for Cannabinoid Medicines, and the committee of experts for narcotic drugs at the federal opium bureau of the Federal Institute for Drugs and Medical Devices (BfArM) in Germany; has received consultant's honoraria from Abide Therapeutics, Fundacion Canna, and Therapix Biosciences, and speaker's fees from Tilray, and is a consultant for Zynerva Pharmaceuticals; has 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" and is an associate editor for *Cannabis and Cannabinoid Research*; has performed several clinical studies related to Tourette syndrome, including randomized controlled trials using cannabinoids and behavioral therapy; has received financial or material research support from the German Ministry of Education and Research (BMBF), German Research Society (Deutsche Forschungsgemeinschaft [DFG]), European Union, Tourette Gesellschaft Deutschland e.V., Else-Kroner-Fresenius-Stiftung, and GW, Almirall, Abide Therapeutics, and Therapix Biosciences; and has received royalties from Medizinisch Wissenschaftliche Verlagsgesellschaft Berlin. D. Woods has a nonfinancial competing interest as a member of the TAA Medical Advisory Board; has received royalties from Guilford Press, Oxford University Press, and Springer Press; and has received honoraria from speaking from the TAA. M. Robinson has a nonfinancial competing interest in serving as co-Chair for the Massachusetts State Chapter of the Tourette Association of America Board of Directors. E. Jarvie has declared a nonfinancial competing interest in serving as member of the Wisconsin Tourette Syndrome Association Board of Directors. V. Roessner serves on an advisory board for the German Tourette Society and the German Society of Obsessive-Compulsive Disorder; has received funding for travel from Actelion, Lilly, MEDICE, Novartis, and Shire; serves as a journal editor, associate editor, or member of an advisory board for *European Child and Adolescent Psychiatry*, *Zeitschrift für Kinder- und Jugendpsychiatrie, Neuropsychiatrie, Behavioral Neurology*, and *Scientific Reports*; has received honoraria from Actelion, Lilly, MEDICE, Novartis, and Shire; has received

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in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com. For complete information on this process, access the 2011 AAN process manual, as amended.¹¹

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Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders

Tamara Pringsheim, Yolanda Holler-Managan, Michael S. Okun, et al.

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Teaching NeuroImages: The zigzag edging sign of adult-onset neuronal intranuclear inclusion disease

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In the article “Teaching NeuroImages: The zigzag edging sign of adult-onset neuronal intranuclear inclusion disease” by Chen et al.,¹ the second-to-last sentence in the first paragraph should read “FMR1 CGG permutation was not present.” The publisher regrets the error.

Reference

1. Chen L, Chen A, Lei S, et al. Teaching NeuroImages: The zigzag edging sign of adult-onset neuronal intranuclear inclusion disease. *Neurology* 2019;92:e2295–e2296.

Opinion and Special Articles: Self-management in epilepsy Web-based seizure tracking applications

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In the article “Opinion and Special Articles: Self-management in epilepsy: Web-based seizure tracking applications” by Casassa et al.,¹ first published online November 19, 2018, NIH Grant T32NS048005 should have been listed as a funding source. The authors regret the error.

Reference

1. Casassa C, Rathbun Levit E, Goldenholz DM. Opinion and Special Articles: Self-management in epilepsy: web-based seizure tracking applications. *Neurology* 2018;91:e2027–e2030.

Cost of illness in Charcot-Marie-Tooth neuropathy Results from Germany

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In the article “Cost of illness in Charcot-Marie-Tooth neuropathy: Results from Germany” by Schorling et al.,¹ first published online March 27, 2019, the published-online-ahead-of-print version should have presented figures in USD rather than euros. They are presented correctly in the April 23 issue. The editorial office regrets the error.

Reference

1. Schorling E, Thiele S, Gumbert L, et al. Cost of illness in Charcot-Marie-Tooth neuropathy: results from Germany. *Neurology* 2019;92:e2027–e2037.

Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders

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In the article “Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders” by Pringsheim et al.,¹ first published online May 6, 2019, the data supplement link in the first paragraph should have been: links.lww.com/WNL/A882. The authors regret the error.

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1. Pringsheim T, Holler-Managan Y, Okun MS, et al. Comprehensive systematic review summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology* 2019; 92:907–915.