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# Recent advances in understanding tourette syndrome, tic disorders and functional tics

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# Recent advances in understanding tourette syndrome, tic disorders and functional tics

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# Editorial: Recent advances in understanding Tourette syndrome, tic disorders and functional tics

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KEYWORDS

**Tourette syndrome, tic disorders, functional tics, interventions, diagnosis**

Editorial on the Research Topic
Recent advances in understanding Tourette syndrome, tic disorders and functional tics

The goal of this Research Topic was to present recent advances in our knowledge surrounding tic disorders. Tic disorders (TDs) are complex neurological conditions characterized by involuntary, persistent vocalizations and motor movements called tics. While tics are commonly associated with a diagnosis of Tourette syndrome, tics can appear as symptoms of other diagnoses, including an Unspecified Tic Disorder amongst others (1). Tics and functional tic-like behaviors (FTLBS) both appear repetitive and without appropriate context, and they can co-exist. However, compared to Tourette-related tics, FTLBS are often associated with a sudden onset and more complex movements. FTLBS are also associated with higher rates of anxiety and self-harm along with higher female predominance and a later age of onset (2).

Since the beginning of the COVID-19 pandemic, clinicians have noted a marked increase in presentations of these sudden and new onset of FTLBS (3). However, many misconceptions exist surrounding their source. Martindale and Mink provided an overview of how a series of pre-disposing factors, the psychological burden of the COVID-19 pandemic, as well as the rise in the use of social media and digital technology, may be implicated in the rise and spread of FTLBs. The wide-ranging impact of these FLTBS on daily life is also noted, with increases in school absenteeism along with disengagement with education. Using ten case studies, Owen et al. have highlighted that even in the absence of formal therapy, if young people with FTLBs are well-supported with the use of certain techniques, they can manage well at school.

There is strong evidence demonstrating that individuals with tic disorders experience a lower quality of life, with tics shown to have a pervasive impact on all aspects of daily living (4). For example, in Bamigbade et al. mothers revealed tics to be a barrier to positive mealtime experiences, affecting the child's ability to sit, drink and eat. Tics were also found to affect the geniality of mealtimes, with families often avoiding eating out of the

home environment due to the challenging and stressful experience of navigating the tics in public. Importantly, Taylor et al. noted the nature of the tics themselves to also have an impact on individuals with TS quality of life, with tics reported to be both physically and psychologically painful. The authors stress the need to understand tic-related pain in the long-term management of tic disorders.

Those with a tic disorder may have heightened awareness of their pain thresholds due to the interoceptive sensibility. For example, Naraparedy et al. reported on altered Interoceptive Sensibility in Adults with Chronic Tic Disorder (CTD), with increased anxiety-associated somatization and increased general body awareness shown. Importantly, in adults with CTD, anxiety-associated somatization was found to be more closely associated with females and obsessive-compulsive symptoms.

Obsessive-compulsive disorder and tic disorders can often co-occur, with individuals frequently presenting with distinct symptoms of CTD and/or OCD (5). However, there are also a subset of individuals with a condition which has been referred to as Tourettic OCD (TOCD), where patients show a specific overlap in tics, compulsions, and their preceding premonitory urges. Katz et al. reviewed the mounting evidence and suggested TOCD has its own distinct phenomenology including an earlier age of onset, male predominance, and specific symptom clusters.

Regarding treatment and management of tics, the European Society for the study of Tourette Syndrome (ESSTS) and the American Academy of Neurology have written guidelines for the management of TS recommending behavior therapy (BT) as a first-line intervention when psychoeducation alone is insufficient (6). Two approaches, habit reversal training (HRT; and its expanded version, Comprehensive Behavioral Intervention for Tics; CBIT) and exposure with response prevention (ERP), have gathered the strongest empirical support. However, a lack of trained therapists, pressures on already overstretched healthcare systems, treatment cost, and travel distance can impact on the availability of face-to-face treatment, with a lack of accessibility being more marked in non-English-speaking countries (7). Reflecting on barriers to treatment, Inoue et al. addressed the preliminary efficacy, feasibility, and acceptability of remotely administered group CBIT (RG-CBIT) in Japan. Positive findings were reported from all three children diagnosed with TS, with all showing a reduction in the severity of tics. Prato et al., also found online remote therapy to be as effective as face-to-face delivery in treatment of the severity of tics, levels of anxiety and obsessive-compulsive symptoms.

Khan et al. provided a synthesis of the research outlining the use of digitally delivered, remote therapy for tics, with promising evidence shown for reduction in the severity of tics in children, young people and adults. With the collective research on digital interventions so far demonstrating good adherence and engagement, although further research is required to understand its cost-effectiveness. However, it is also important to note that less than 40% of adults with TS respond well to CBIT. Ramsey et al. suggest urge intolerance to be one factor that might interact with treatment success. Given the predictive relationship premonitory urges has between tic severity and tic impairment, the authors argue that targeting urge intolerance to improve treatment response is an avenue for future research.

The role of gut bacteria in the symptomology of TS, as well as the possible use of prebiotics in the management of symptoms has recently been discussed. Wang et al. found the abnormal composition of gut microbiota to differentiate children with tic disorders from those without. High levels of Prevotella and Odoribacteis were identified in the tic disorder group, both of which have been associated with symptoms of irritable bowel syndrome (IBS-D), and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) respectively. Importantly healthy gut bacteria are essential to allow the body to absorb nutrients as well as influencing food cravings (8). Given Smith and Ludlow findings of high levels of food responsiveness and emotional overeating reported in the TS group, the role of gut bacteria in diet may warrant further exploration.

The work presented in this Research Topic emphasizes the complexity of tic disorders and their impact on everyday life. The future of digital interventions may offer an exciting new avenue to increase accessibility to treatment for those with a tic disorder.

## Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
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# Gut Microbiome Composition Abnormalities Determined Using High-Throughput Sequencing in Children With Tic Disorder

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**Object:** To investigate the distribution characteristics of gut microbiota in children with tic disorder (TD) and the possible role of these characteristics in the pathogenesis of TD.

**Methods:** The medical records of 28 children with TD treated at Wuxi Children's Hospital from January 1 to October 31, 2020, and 21 age-matched healthy children (controls) were included. The relative quantification of bacterial taxa was performed using 16S ribosomal RNA gene amplicon sequencing.

**Results:** There was no significant difference in the alpha diversity of gut microbiota between the TD and control groups. Analyses of beta diversity were able to differentiate the TD patients from the healthy controls based on their gut microbiota. At the phylum level, the two groups were mainly composed of four phyla, Firmicutes, Actinobacteria, Bacteroidetes, and Proteobacteria. There were significant differences in Firmicutes and Actinobacteria between the two groups ($P<0.05$). At the level of genera, the abundance of *Bifidobacterium* and *Collinsella* reduced while that of Ruminococcaceae unclassified, *Prevotella*, *Faecalibacterium*, *Coprobacillus*, and *Odoribacter* increased in the TD group compared to that in the control group. The intergroup differences were significant ($P < 0.05$).

**Conclusion:** The abnormal composition of gut microbiota in children with TD suggests that the change in gut microbiota may play an important role in TD development.

**Keywords: tic disorder, gut microbiota, high-throughput sequencing, 16S rRNA, abnormalities**

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## INTRODUCTION

Tic disorder (TD) is a childhood-onset neuropsychiatric and neurodevelopmental disorder (1, 2). Its main manifestations are involuntary, repetitive, rapid, purposeless, motor tics and/or vocal tics of one or more muscles. The age of onset of TD is 2–21 years, with TD most commonly developing between the ages of 5 and 10 years (3). TDs are more common among male patients than among female patients, with the male to female ration being 3–5:1. In recent years, the incidence of TD has increased (4). Currently, the incidence of TD in Chinese children is ∼6.1% (5). However, the etiology and pathogenesis of TD have not yet been fully explored. Most scholars believe that this disease may be the result of interactions among genetic factors, environmental factors, and neurotransmitters during the growth and development of children (6, 7).

Studies have shown that the gut microbiota is closely related to central nervous system diseases, such as epilepsy, autism spectrum disorder (ASD), and autism, attention deficit hyperactivity disorder (ADHD) (8–11). ADHD is the most common comorbidity of TD, and the two conditions share similar etiological characteristics and pathogenesis (12). Several previous studies have shown that the composition of the gut microbiota in children with ADHD was significantly different from that in healthy children (9, 10, 13). The gut is called the "second brain" or "gut-brain" in humans (14). The gut and brain interact through the bidirectional pathway of the brain-gut axis, which affects the central nervous system. The gut microbiota is the core of the microbiota-gut-brain axis, as an important mediator for the mutual adjustment of the brain and the gastrointestinal tract. It not only regulates the body's physiological functions but also changes the brain development trajectory of humans and animals, thereby regulating the behavior and cognitive functions of the host (15). Microbiota-generated metabolites, especially the neurotransmitters such as γ-aminobutyric acid (GABA), glutamate and histamine, could affect brain activity in the microbiota–gut–brain bidirectional communication (16). Therefore, an abnormal composition of the gut microbiota may lead to abnormal neurotransmitter secretion, which could promote the development of neuropsychiatric diseases. Zhao et al. reported that severe TD in a child was markedly ameliorated after fecal microbiota transplantation, promoting the consideration of the possible association between gut microbiota and TD development (17). We analyze the microecological distribution of the gut microbiota in children with TD and healthy controls by high-throughput sequencing methods.

# MATERIALS AND METHODS

## Subjects

Twenty-eight children with TD who visited the pediatric clinic of Wuxi Children's Hospital from January 2020 to October 2020 were selected as the research objects. The patients were aged 6–14 years, with the average age being 8.2 ± 1.2 years. Seventeen of the children were male and the rest were female; the disease duration in these children ranged from 6 months to 5 years. The criteria for TD patients consisted of the following: (1) diagnosed as TD through a comprehensive assessment according to the Expert Consensus on the Diagnosis and Treatment of Tic Disorders in Children (2017 Practical Edition) (18) and the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (19); (2) have never taken any medications to treat their TD before enrollment. The exclusion criteria were as follows: (1) a history of intellectual disability, autism, mood disorders, or other neuropsychiatric disorders; (2) presence of chorea, epilepsy, and other extravertebral diseases such as hepatolenticular degeneration, Parkinson's disease and athetosis; (3) a history of conditions such as obesity, precocious puberty, asthma, heart disease, gastrointestinal disease, and reproductive system defects; (4) use of systemic or local glucocorticoids, immunosuppressants, and antihistamines within 15 days before study enrollment; (5) presence of other co-morbidities related to Tourette syndromes such as ADHD or obsessive-compulsive disorder (OCD) and anxiety disorders; and (6) presence of other serious illnesses. Two senior neurological clinicians jointly assessed and completed the inclusion and exclusion of samples. Twenty-one children, 13 males and eight females, without TD who underwent health checkups in our hospital during the same period were included as the control group. They had no known physical illnesses or any of the aforementioned major neuropsychiatric diseases. The healthy children were aged 5–14 years, with an average age of 7.9 ± 2.0 years. The characteristics of the subjects are shown in **Table 1**. Both the control and TD groups did not receive antibiotics and probiotics within 2 months before enrollment. This study was approved by the ethics committee of Wuxi Children's Hospital (approval number: WXCH2019-08-006). All the enrolled participants and their family members signed an informed consent form.

**TABLE 1 |** Characteristics of patients with TD and healthy control children.

| | TD ($n = 28$) | Controls ($n = 21$) | *P*-values |
|---|---|---|---|
| Sex (*n*, %) | | | 0.585 |
| Boy | 17 (60.7) | 13 (61.9) | |
| Girl | 11 (39.3) | 8 (38.1) | |
| Age (mean ± SD) | 8.2 ± 1.9 | 7.9 ± 2.1 | 0.569 |
| Age, range | 6–14 | 5–14 | |
| BMI | 19.3 ± 1.9 | 18.8 ± 1.7 | 0.248 |

## Methods

### Sampling

Design of the *Record Form for Children with Tic Disorder* for collection of clinical data.

The form was designed to gather data on the child's general condition and date of TD onset, date of the first hospital visit for TD, first symptoms, current symptoms (specific symptoms of motor and vocal tics in children with TD), symptom frequency, daily activities, and learning and social situations. For each child enrolled in the TD group, 100 mg of fecal sample was collected in three sets of 2-mL sterile centrifuge tubes. The tubes were numbered according to the order of entry. Samples in two of the tubes were used for DNA extraction, and the remaining tube was reserved. All fecal samples were processed within 30 min after collection and then stored in a refrigerator maintained at −80°C.

### DNA Extraction, Library Construction, and Sequencing

The E.Z.N.A.® Soil DNA Kit (Omega Biotek) was used to extract DNA from samples in accordance with the operating instructions. After DNA extraction, the V3-V4 region of 16s rDNA was amplified by PCR. The PCR product was purified by 2% agarose gel electrophoresis, and the target fragment was cut and recovered. Qubit fluorometer was used to determine the DNA mass concentration of the library, and the KAPA Library Quantification Kit was used to quantitatively determine the molar concentration of the library DNA. After the library was mixed and denatured, the amplified products were

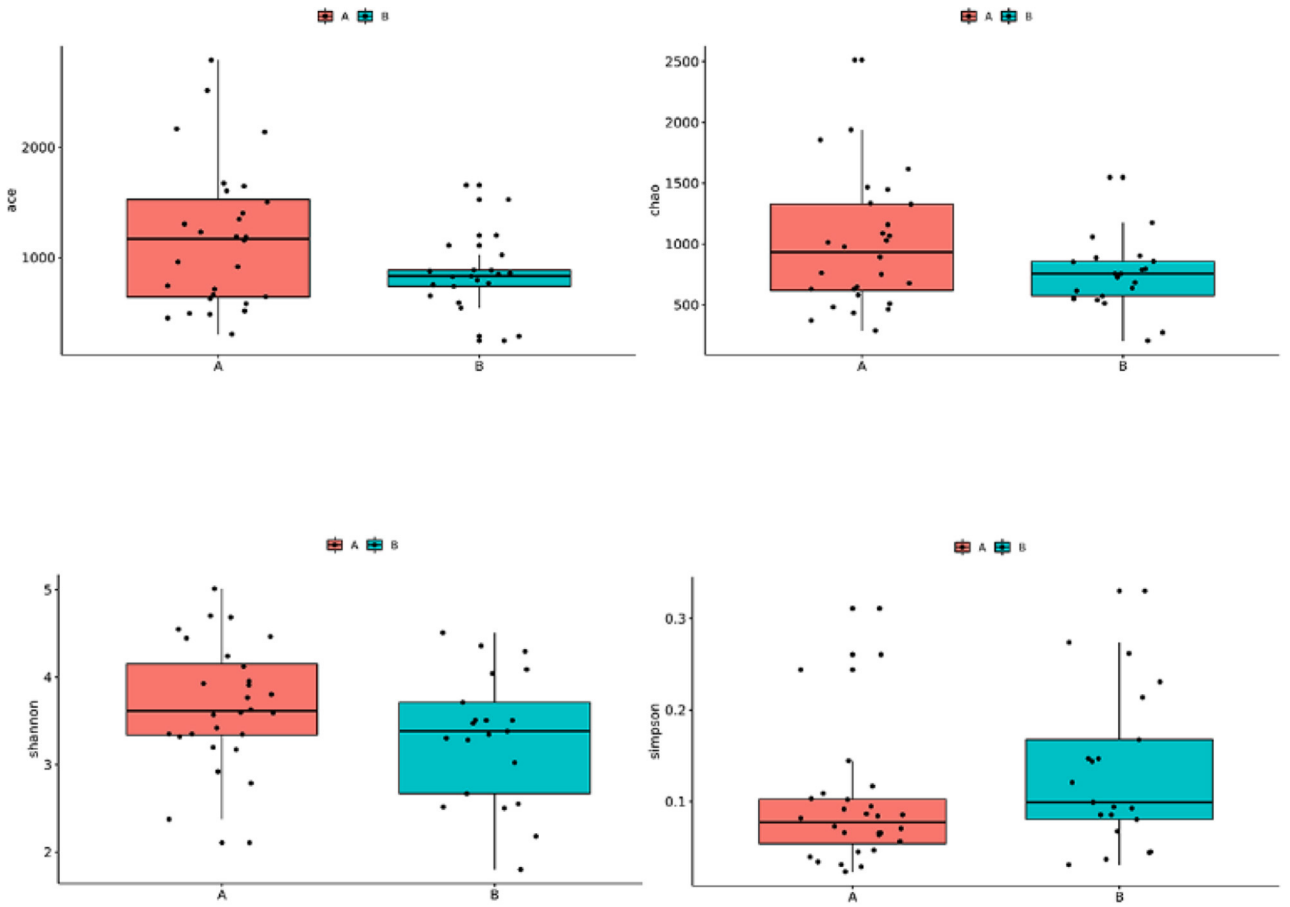


**FIGURE 1 |** Comparison of the alpha diversity of gut microbiota in children with TD and control children. Group A: TD group; Group B: control group.

subjected to paired-end sequencing on the Illumina Novaseq sequencing platform.

### Bioinformatics Analysis

Thecutadapt software was used to filter sequencing data to obtain high-quality clean data. The search software was used for sequence analysis and to classify sequences with a similarity of ≥97% as the same operational taxonomic units (OTUs). To obtain the species classification information corresponding to each OTU, sequences were compared with those in the Silva (SSU128) 16S rRNA database (http://www.arb-silva.de) to obtain the phylum to genus information for each OTU. The relevant analyses of the gut microbiota, including species annotation and evaluation, alpha diversity, beta diversity, and species difference analyses, were conducted using the I-Sanger cloud analysis platform (http://www.i-sanger.com/) of Meiji Biotechnology. Alpha diversity analysis is the analysis of species diversity in a single sample, which can reflect the richness and diversity of the microbial community. The commonly used metrics are the Shannon, Simpson, ACE, and Chao indexes, among which the ACE and Chao1 indexes reflect community richness and the Shannon and Simpson indexes reflect community diversity. Beta diversity analysis is a comparative analysis of the microbial community composition of different samples; it is used to evaluate differences between microbial communities. The commonly used analysis methods include principal component analysis, principal coordinate analysis (PCoA), unweighted pair group method with arithmetic mean analysis (UPGMA), and analysis of similarities (ANOSIM) (20).The Wilcoxon rank-sum test was used to analyze differences in the flora between children with TD and healthy children. $P < 0.05$ was considered statistically significant.

## RESULTS

### Characteristics of the Patients

In all, 28 children with TD were enrolled, including 17 males and 11 females. The patients were aged 6–14 years, with an average age of 8.2 ± 1.9 years. The disease duration range was 6 months to 5 years. The control group comprised 21 children, including 13 males and eight females. The controls were aged 5–14 years, with the average age being 7.9 ± 2.1 years. There were no statistically significant differences in sex and age between the two groups ($P > 0.05$).

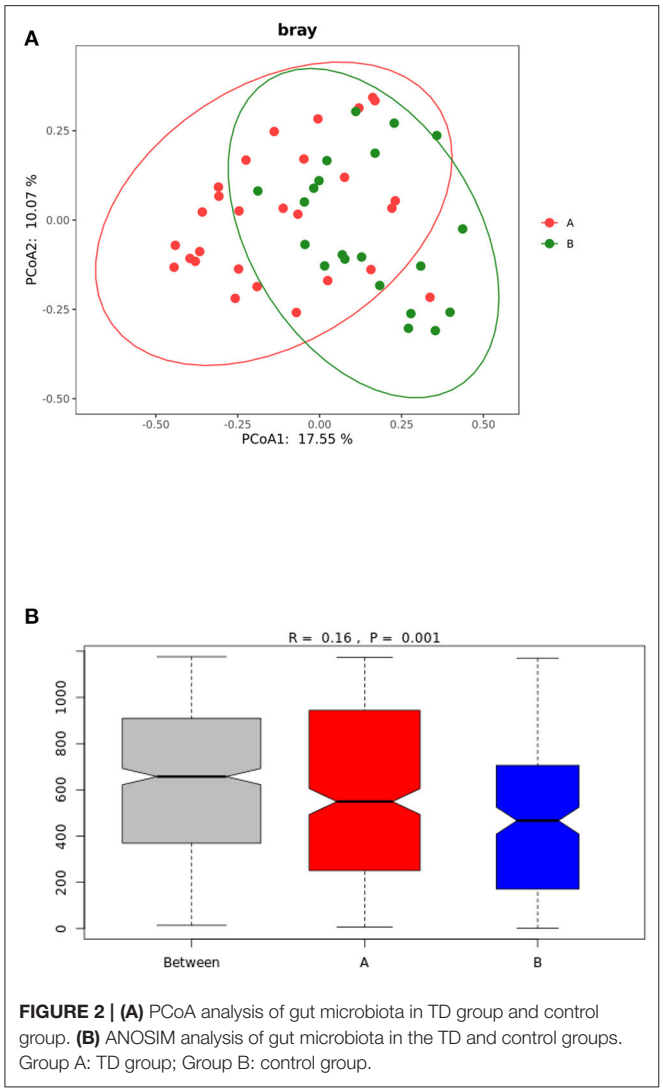


**FIGURE 2 | (A)** PCoA analysis of gut microbiota in TD group and control group. **(B)** ANOSIM analysis of gut microbiota in the TD and control groups. Group A: TD group; Group B: control group.

## Alpha Diversity Analysis

The Wilcoxon rank-sum test used to compare the TD and control groups showed no significant difference in the alpha diversity index (Shannon index, Simpson index, ACE index, Chao index) between the two groups ($P > 0.05$) (**Figure 1**).

## Beta Diversity Analysis

The beta diversity analysis (PCoA and ANOSIM) (**Figure 2**) showed significant differences between the gut microbiota of the TD and control groups ($P < 0.05$).

## Comparison of the Bacterial Composition and Structure

### Differences at the Phylum Level

Sequence analysis of the TD and the control groups showed that at the phylum level, the gut microbiota of the two groups belonged to 36 phyla, of which 35 phyla were in group A and 31 were in group B. Both groups were mainly composed of four phyla: Firmicutes, Actinobacteria, Bacteroides, and Proteobacteria (**Figure 3A**). The order of abundance in the TD group was as follows: Firmicutes, 68.64%; Bacteroidetes, 16.74%; Actinobacteria, 11.68%; Proteobacteria, 2.26%; and others, 0.68%. In contrast, the order of abundance in the control group was as follows: Firmicutes, 47.37%; Actinobacteria, 35.7%; Bacteroidetes 10.58%; Proteobacteria, 4.25%; and others, 2.11% (**Figure 3B**). The Wilcoxon rank-sum test was used to analyze the differences in species abundance between the two groups, and the results showed statistically significant differences in the abundances of Firmicutes ($P = 0.004$) and Actinobacteria ($P = 0.003$) between the TD and control groups.

### Differences at the Genus Level

Sequence analysis was performed on children in the TD and control groups. At the genus level, the gut microbiota of the two groups belonged to a total of 167 genera, of which 159 genera were in group A and 140 were in group B. The differences between the samples were large, and the dominant bacteria were different between the two groups (**Figure 4A**). **Figure 4B** shows that the 10 most abundant genera in the gut microbiota of the TD group were *Faecalibacterium* (18%), *Bacteroides* (10.21%), *Bifidobacterium* (9.59%), Ruminococcaceae_unclassified (7.8%), *Streptococcus* (7.16%), Lachnospiraceae_unclassified (6.45%), Clostridiales_unclassified (4.07%), *Prevotella* (3.99%), *Romboutsia* (3.88%), and *Blautia* (3.87%). In contrast, the 10 most abundant genera in the gut microbiota of the control group were *Bifidobacterium* (31.69%), *Streptococcus* (7.87%), *Bacteroides* (6.84%), *Faecalibacterium* (6.69%), Lachnospiraceae_unclassified (5.78%), *Blautia* (3.33%), *Escherichia/Shigella* (3.23%), *Collinsella* (3.19%), Ruminococcaceae_unclassified (3.02%), and *Anaerostipes* (2.45%). In comparison with the control group, the TD group showed a significantly reduced abundance of *Bifidobacterium* ($P = 0.001$) and *Collinsella* ($P = 0.03$) and significantly increased abundance of Ruminococcaceae_unclassified ($P = 0.002$), *Faecalibacterium* ($P = 0.006$), *Prevotella* ($P = 0.002$), *Gemmiger* ($P = 0.022$), and *Odoribacter* ($P = 0.014$).

# DISCUSSION

TD is a neuropsychiatric disease, and its pathogenesis has not yet been fully explored. Evidence shows that gut microbiota can affect the development of the nervous system and may even cause or aggravate neurological diseases (21). In this study, the results of the α-diversity analysis of the gut microbiota in the TD group and the control group showed that the ace index, Shannon index, Simpson index, and Chaol index were not significantly different between the groups ($P > 0.05$). However, the beta diversity analysis showed that the gut microbial community of children with TD was significantly different from that of healthy children. In the analysis of flora species composition, the two groups showed differences in flora composition and abundance at the phylum and genus levels. In comparison with the control children, the TD group showed a significantly reduced abundance of *Bifidobacterium* and *Collinsella* and significantly increased abundance of*Ruminococcaceae*_unclassified, *Faecalibacterium*,

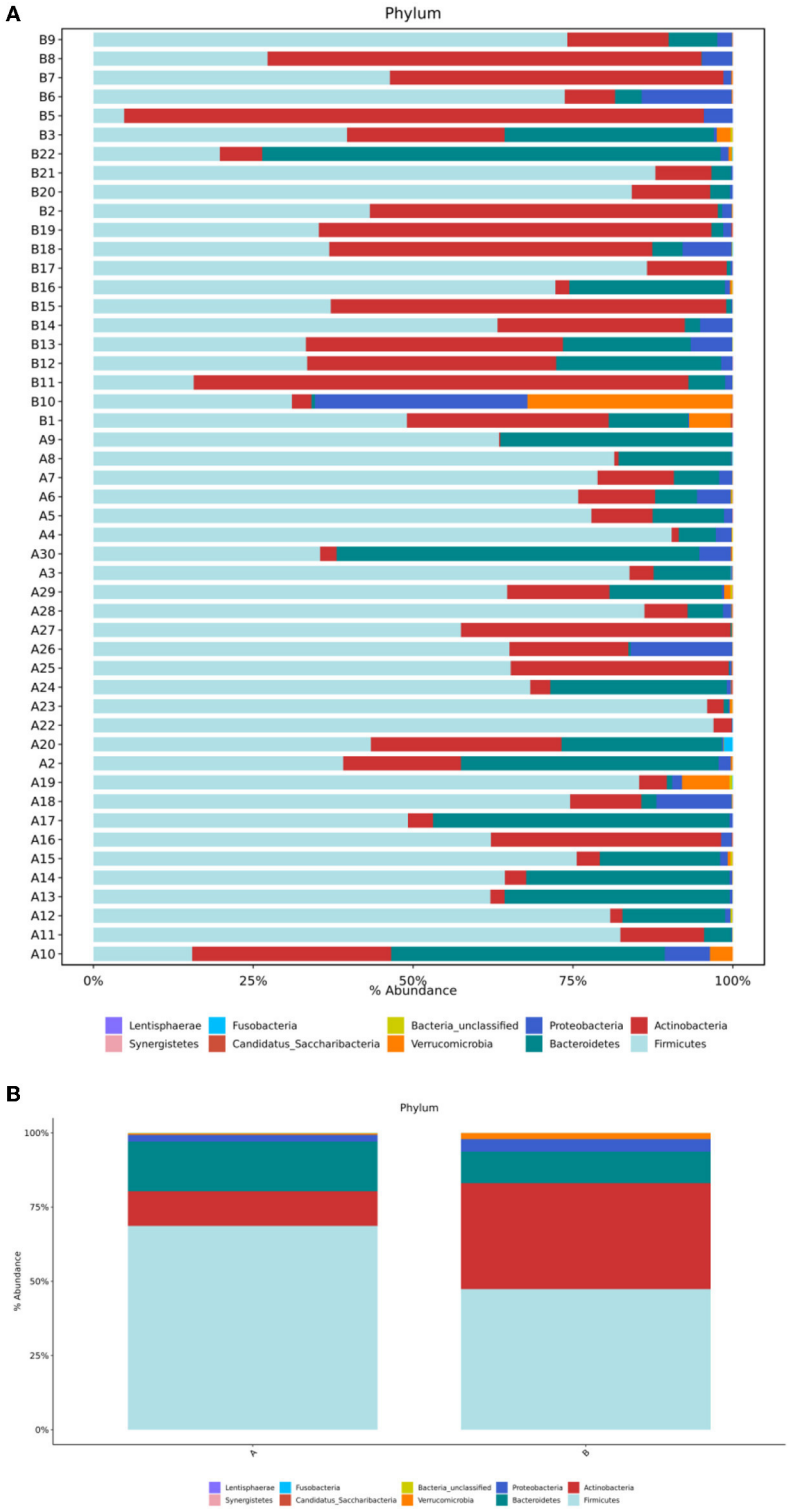


**FIGURE 3 | (A)** Structural composition analysis of the gut microbiota in each sample at the phylum level. **(B)** Comparison of relative abundance and composition of bacteria in the two groups at the phylum level. Group A, TD group; Group B, control group.

*Prevotella*, *Gemmiger*, and *Odoribacter*. As an important probiotic in the intestine, *Bifidobacterium* performs the functions of resisting harmful bacteria and regulating nutrition and the immune response and plays an important role in maintaining

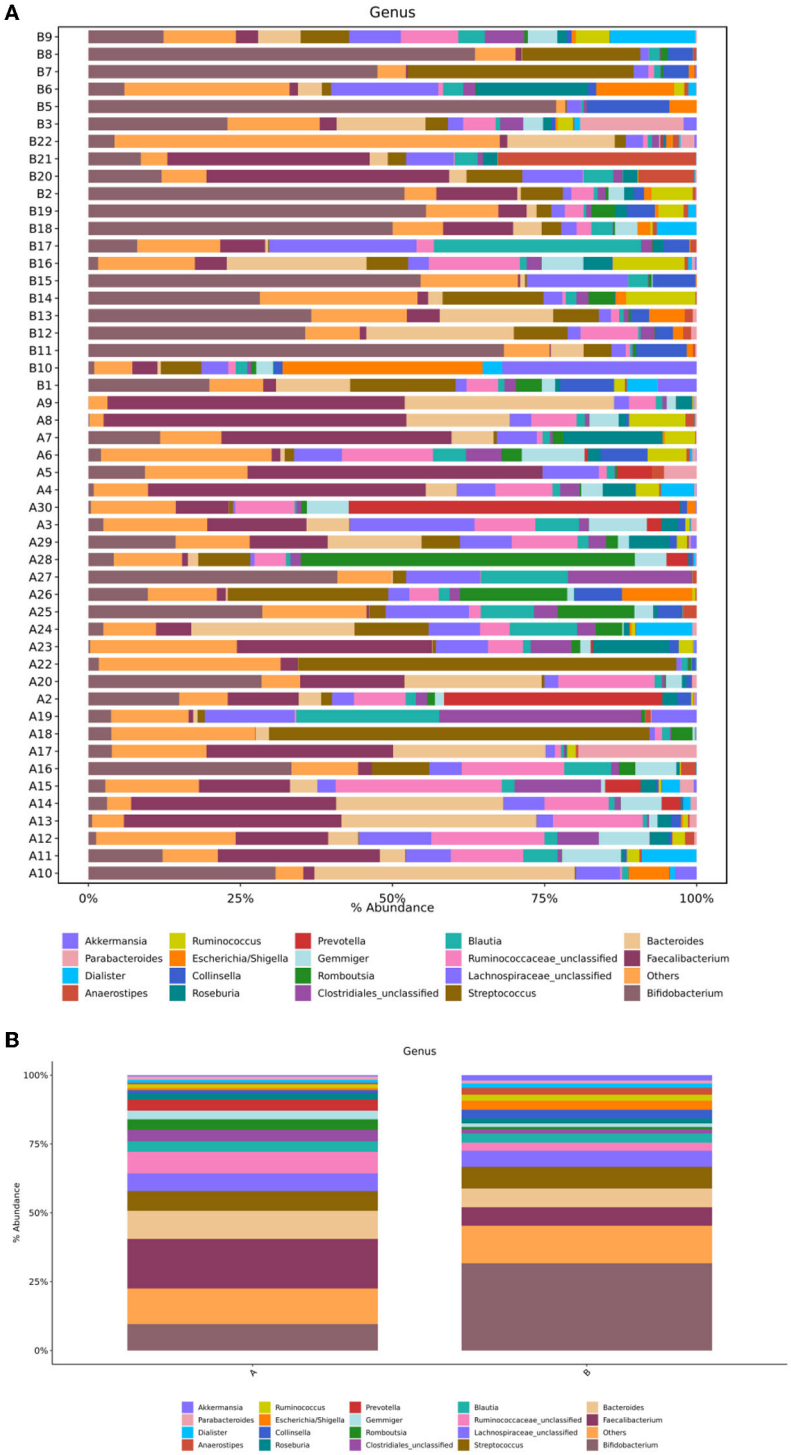


**FIGURE 4 | (A)** Structural composition analysis of the gut microbiota in each sample at the genus level. **(B)** Comparison of relative abundance and composition of bacteria in the two groups at the genus level. Group A, TD group; Group B, control group.

the intestinal microecological balance. A reduction in its content can activate the immune system in the intestine, leading to the occurrence of various diseases such as allergic diseases. Some studies in children suggest possible relationships between TS and allergic diseases, such that more research is warranted to clarify the specific nature of these relationships (e.g., longitudinal relationship between variables, whether it is correlational, causal). Given that the neural basis of TDs

are relatively understood, it will be important to understand whether and precisely how gut microbiota might impact relevant circuitry, as well as whether altered microbiota precede or are followed by the emergence of TD symptoms (22–24). The gut microbiota of allergic and non-allergic infants shows significant differences during the first year of life (25, 26). In comparison with normal infants and young children, the intestinal tract of allergic infants shows a reduced abundance of the beneficial bacteria *Bifidobacterium* and *Lactobacillus* and increased colonization of *Enterobacter* and *Staphylococcus*. *Lactobacillus* and *Bifidobacterium* have been shown to produce γ-aminobutyric acid (GABA), the primary inhibitory neurotransmitter (27). Reduced GABA concentration in the primary sensorimotor cortex has been suggested to contribute to both motor tics and sensory impairments in TD (28).The low abundance of *Bifidobacterium* can be speculated to cause allergies and affect the release of neurotransmitters in the gut-brain axis, impacting risk for developing TD. It is also possible that the presence of TD is a risk factor for altered gut microbiota through mechanisms not yet understood (e.g., children with TD often have early sensory intolerances which may limit diet, or children with TD may have been more frequently exposed to medications or other illnesses that alter gut microbiota). In recent years, the study of gut microbiota provides a new theoretical basis for probiotics in the treatment of nervous system diseases (29, 30). An increasing number of studies have shown that supplementation of probiotics can improve gut microbiota dysbiosis and play an important role in the treatment of allergic diseases and nervous system diseases (29–32). Limited studies suggest that probiotics may be associated with changes in cognitive function, which can reduce the risk of developing ADHD or ASD (30).This study provides a theoretical basis for the future use of *Bifidobacterium* to treat mild to moderate TD. Moreover, the abundance of *Collinsella* was shown to be reduced in children with TD, and *Collinsella* mainly produces some gas in the intestine, which is believed to be related to abnormal lipid metabolism. However, the relationship between TD and lipid metabolism has not been reported to date, and it needs to be further studied.

This study found an increased abundance of *Prevotella* in children with TD. *Prevotella* is closely related to irritable bowel syndrome (IBS-D), inflammatory bowel disease and other intestinal diseases (33). It contains enzymes that play an important role in the degradation of mucin, which may lead to an increase in intestinal permeability. *Prevotella* has also been confirmed to show a pro-inflammatory effect (34), and its increased expression level may lead to increased expression of inflammatory factors; the levels of inflammatory factors were also shown to be increased in children with TD (35). These inflammatory factors can pass through the blood–brain barrier to affect the development of the nervous system (36). Thus, an increased abundance of *Prevotella* may cause changes in the levels of inflammatory factors, which may also be involved in the pathogenesis of TD. This study also found an increased abundance of *Odoribacter* in children with TD. *Odoribacter* has been also shown to be closely related to neuropsychiatric diseases. In comparison with healthy children, children with pediatric acute onset neuropsychiatric syndrome (PANS) and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) show a significantly higher abundance of Odoribacter. The concept of PANS is relatively recent and is derived from research on PANDAS; PANDAS is now considered as a specific subset within the broader clinical spectrum of PANS (37, 38). Streptococcal infections have also been suggested to relate to Tourette's Syndrome (TS), a multifactorial and complex disorder that may, in some cases, match the criteria for PANDAS (39). While PANDAS has been proposed as an aetiological subtype of TS (40), the dopamine metabolism pathway is significantly attenuated in this condition, and the relative abundance of *Odoribacter* shows a significant positive correlation with the titer of anti-streptolysin O (37), suggesting that *Odoribacter* may affect the dopamine metabolism pathway and lead to the onset of TD. *Faecalibacterium* can exert anti-inflammatory effects by producing short-chain fatty acids, salicylic acid, and other metabolites. In children showing TD with comorbid ADHD, the abundance of *Faecalibacterium* is low. Studies have shown that changes in dietary structure affect the abundance of *Faecalibacterium*. Excessive intake of food with high monosodium glutamate, caffeine, artificial food dyes, flavorings, fat, sugar, and salt may have a connection with TD (41). In this study, the abundance of *Faecalibacterium*in the TD group increased, which may be related to the differences in the dietary structure of different children.

This study set strict inclusion and exclusion criteria for children with TD, included healthy children as controls, and strictly screened the included healthy children to exclude potential children with TD. The results indicated a decreased abundance of *Bifidobacterium* in the TD group, and the effectiveness of probiotics (Bifidobacterium) in improving TD in patients needs to be further studied. However, this study did not consider issues such as dietary differences, disease duration and a standardized measure of tic symptoms. Moreover, the large-sample studies are still lacking. In further studies, we plan to expand the sample size and stratify tic disorder cases, a questionnaire (including diet structure, lifestyle, health status, medical history, and heredity) will be designed to determine the correlation of TD with intestinal biomarkers and explore the correlation between the pathogenesis of TD and the gut microbiota.

In summary, children with TD showed an abnormal composition of the gut microbiota, suggesting that the microecology of the gut microbiota may have played an important role. In addition, exploration of the changes in the structure and diversity of the gut microbiota can provide clinical evidence for the diagnosis and treatment of children with TD.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are publicly available. This data can be found here: https://www-ncbi-nlm-

nih-gov.ezproxy.u-pec.fr/Traces/study/?acc=SRP346317&o=acc_s%3Aa.

## ETHICS STATEMENT

This study was approved by the Ethics Committee of Wuxi Children's Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

YW, HX, MJ, XH, JW, and YH participated in the design of the study, collected and analyzed the data, and drafted the manuscript. YW, MJ, and XH collected the data. YW, HX, and YH were responsible for analysis, analyzed the data, and contributed to drafting the manuscript. All authors read and approved the final manuscript.

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# A Randomized Controlled Trial Comparing Videoconference vs. Face-to-Face Delivery of Behavior Therapy for Youths With Tourette Syndrome in the Time of COVID-19

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**Objective:** To evaluate the clinical effectiveness of online remote behavior therapy, compared with face-to-face therapy in reducing tics and co-occurring disorders associated with the tics in a sample of youths with Tourette Syndrome.

**Design:** A randomized controlled trial. TS patients were randomized to receive face-to-face or online remote behavior therapy.

**Participants:** 40 children aged between 9 and 16 years affected by Tourette Syndrome.

**Results:** Online remote and face-to-face behavior therapy are equally effective in the treatment of tics and co-occurring disorders in children and adolescents affected by Tourette Syndrome. Both groups showed an improvement in the severity of tics, obsessive-compulsive symptoms, and anxiety symptoms, as assessed by neuropsychological findings. Online remote behavior therapy was more effective for reducing depressive symptoms than face-to-face behavior therapy.

**Conclusions:** Online remote behavior therapy is a promising tool for behavioral therapies for patients with Tourette Syndrome and may represents an alternative treatment option.

**Keywords: Tourette Syndrome, behavior therapy, COVID-19, telehealth, digital health interventions**

## INTRODUCTION

### Background

Tourette syndrome (TS) is a neurodevelopmental condition characterized by the presence of concomitant multiple motor tics and, at least one, vocal tic, that occurs for more than 1 year, in a patient <18 years old (1); DSM-V. The prevalence was even estimated to be 0.3–1% (2, 3), TS is more common in boys than in girls with a male-to-female ratio of 3–4/1 (4). Only 10–15% of individual patients with TS have tics only (pure TS) while the remaining patient population manifests comorbid attention deficit/hyperactivity disorder (ADHD), obsessive-compulsive behaviors/obsessive-compulsive disorder (OCB/OCD), autism spectrum disorders

(ASD), learning disabilities (LD), or other psychopathologies such as conduct disorder (CD), oppositional defiant disorder (ODD), anxiety disorders (AD) and depression (5, 6). Tics and co-occurring conditions are associated with functional impairment and contribute to decreases quality of life (7, 8). The etiology is complex and multifactorial. TS is polygenic, involving multiple common risk variants combined with rare, inherited or *de novo* mutations. These as well as non-genetic factors (such as perinatal events and immunological factors) are likely to contribute to the heterogeneity of the clinical phenotype, the structural and functional brain anomalies, and the neural circuitry involvement (4). Recently, the European Society for the study of Tourette Syndrome (ESSTS) wrote guidelines for the management of TS recommending psychoeducation as the initial intervention, and behavior therapy (BT) as a first-line intervention when psychoeducation alone is insufficient (9). Two approaches, habit reversal training (HRT; and its expanded version, Comprehensive Behavioral Intervention for Tics; CBIT) and exposure with response prevention (ERP), have gatered the strongest empirical support. (10–13). In situations where BT are ineffective, not available, not age-appropriate, or not the patient's or the family's preference, then pharmacological treatments should be considered.

## The Impact of the COVID-19 Epidemic on Children With Tic Disorders

The global pandemic caused by COVID-19 has created rapid changes to how people are able to carry out their normal lives, with impacts ranging from health and mortality through to those impacts brought about by social isolation rules and localized lockdowns. The social contexts for children and young people during this last year have been markedly different to what they had experienced before. Indeed, they have been subject to disrupted education at school and university, as well as hampered transition into training or the workforce for the first time (14, 15). Early results have indicated that adolescents may show an increase in symptoms of depression and anxiety, and that these are more concerned about the government restrictions designed to contain the spread of the virus, than the virus itself (16). Thus, they need our reassurance and help in these difficult times, supported by a network of informed health-care professionals. Perceived changes in tic severity during the lockdown were also recently described in school-age patients with tic disorders (17). In addition, during the global pandemic caused by COVID-19, it was reported a dramatic increase in functional tic-like behaviors in vulnerable children and adolescents after social media exposure (18, 19).

A promising development in increasing accessibility to behavioral treatments is the use of digital health interventions (DHIs) (20). Preliminary results suggest the effectiveness of DHIs for children and adolescents affected by tic disorders (21–23). In fact, telehealth will play an increasing role in the medical follow-up of patients with TS, likely beyond the end of the pandemic. However, it will be important to establish whether this type of care will be well accepted by patients and families alike (24).

# AIM OF THE STUDY

The present study aimed to evaluate the clinical effectiveness of online remote BT (or-BT), compared with face-to-face BT (ftf-BT) in reducing tics and co-occurring disorders associated with the tics in a sample of youths with TS. The study also aimed to compare the efficacy of the two treatments in improving severity of tics and other symptoms associated.

# MATERIALS AND METHODS

## Study Design

This pilot study was conducted at the Child and Adolescent Neurology and Psychiatry of the Medical and Experimental Department of Catania University. A total of 40 patients with a diagnosis TS, according to the Diagnostic and Statistical Manual for Mental Disorders (DSM-V), have been enrolled. Participants were randomly assigned to the face-to-face (ftf, $n = 20$) or online remote (or, $n = 20$) BT, using a simple randomization plan based on a random number list. Prior to enrolment, all participants provided written informed consent after receiving a complete explanation of the study and the assurance that the decision to participate in the study would not interfere with their treatment in any way. All parents gave written informed consent, and the subjects assented when possible. The study was conducted in accordance with the Declaration of Helsinki and approved by the local Ethics Committee (Catania 1) of Catania University Hospital.

## Participants

Eligible participants were patients aged 9–16 years of age with a primary diagnosis of TS according to DSM-V criteria (1), recruited from September 2020 to May 2021 at the outpatient clinic of the Child and Adolescent Neuropsychiatry Unit at Catania University Hospital. The inclusion criteria were tics of moderate severity as measured by the Yale Global Tic Severity Scale (YGTSS; >13 for subjects affected by TS and >9 for those affected by CTD) (25), and an intelligence quotient (IQ) >80. Exclusion criteria were primary psychiatric disorders different from TS, intellectual disability, previous BT for tics or initiation or adjustment of any psychotropic medication for tic within the previous 2 months. Comorbid ADHD, OCD, or AD was not considered exclusion criteria unless the disorder required immediate treatment or a change in the current treatment regimen.

## Clinical Assessment

The clinical assessment of the patients was performed at two time points during the study by a pediatric neuropsychiatrist (R.R.) with solid experience in tic disorders and possible comorbidities. Participants underwent the first assessment at baseline (T0), the second after 2 months (T1). At T0, the Wechsler Intelligence Scale for Children (WISC-IV) was administered to evaluate the IQ of patients (26). At baseline point (T0), patients were also assessed according to Yale Global Tic Severity Rating Scale (YGTSS), Children's Yale-Brown Obsessive-Compulsive Scale for Children (CY-BOCS), Premonitory Urge for Tic Scale (PUTS),

Multidimensional Anxiety Scale for Children (MASC), Child Depression Inventory (CDI) and the Conners' Parent Rating Scale (CPRS). Furthermore, after 2 months (T1), changes in symptoms severity were evaluated by the difference in the YGTSS, CY-BOCS, CPRS, CDI and MASC scales.

## Measures

The YGTSS is a clinician-rated scale used to assess the motor and phonic tic severity considering the number, frequency, duration, intensity, and complexity of tics. It consists of separate motor and vocal tic checklists scored from 0 to 5 on two subscales for motor and vocal tics. The subscales were combined to produce a total tic severity score (ranging from 0 to 50). Another score ranging from 0 to 50 was assigned for global impairment due to tics (25).

The PUTS measures sensory and mental phenomena associated with premonitory urges in 10 items on a four-point scale (range 10–40). The first 6 items include itchiness, energy, pressure, tense feeling, incomplete, or a not "just right" feeling before performing a tic. The additional 4 items assess whether these feelings are experienced almost all the time before a tic, if they happen with every tic, if they go away after the tic is performed, and if subjects can stop the tics for a short period of time (27). To evaluate OCD, commonly associated with TS or CTD, the CY-BOCS, a semi-structured clinician-administered interview assessing the severity of obsessions and compulsions occurring over the past week across five areas (time, interference, distressing nature, effort to resist, control over obsessions and compulsions) was also administered (28). The CPRS is a useful tool for obtaining parental reports of childhood behavior problems that contains summary scales supporting ADHD diagnosis and quantifying ADHD severity (29). Finally, all participants completed the MASC, a self-report scale that robustly represents the factor structure of anxiety in children aged 8–18 years (30) and the Child Depression Inventory: a 27-item self-report instrument that assesses depressive symptoms in 7- to 17-year-olds (31).

## Behavior Therapy

BT was conducted according to the therapist manual developed by Verdellen et al. (32). Either HRT or ERP were conducted over eight weekly sessions. Sessions were 60 min in length. In awareness training, the therapist helps the patient to recognize the premonitory urge and to generate voluntary competing responses that are incompatible with the tic (habit reversal training) and/or increase their tolerance to the premonitory urge (exposure with response prevention). A ranking of the patient's tics is constructed according to tic severity and level of impairment, and then the patient learns to perform a voluntary movement to physically prevent performance of the tic during the competing response training. Patients were required to practice at home and parents were required to monitor tics for 15 min every day.

## Materials

To perform or-BT was used Skype©, a peer-to-peer VoIP software application providing free web-based videoconferencing and utilizing security features (including standard encryption algorithms and digital user authentication certificates). Treatment was delivered from a private clinic room, using a desktop computer and a high-speed university-based internet connection. All participants used their own home computer, high speed internet connection, and a web camera to connect with the therapist.

## Statistical Analysis

Categorical variables are summarized by absolute and percent frequencies, and differences between the two treatment groups were analyzed by the Fisher's exact probability test. Quantitative variables are summarized by means, standard deviations (SD), medians and range (minimum; maximum). We assessed the distribution of quantitative variables to determine their deviation from the normal distribution within each treatment group (Shapiro–Wilk test) and the homogeneity of variance among the two treatment groups (Levene test). Since the distribution of the test scores (YGTSS, YBOCS, MASC, CDI, CONNERS) was not normal in some treatment groups at some time points, we assessed the differences between groups and time-points by non-parametric methods. Specifically, for any subject and any variable we computed the mean (T1+T2)/2 (YGTSS_m, YBOCS_m, MASC_m, CDI_m, CONNERS_m) and the variation (T1-T2) (YGTSS_d, YBOCS_d, MASC_d, CDI_d, CONNERS_d) between the values at the two time-points. We then performed the Mann-Whitney U test to assess the difference between the two treatment groups in the mean values (main effect of treatment) and in the variations (interaction treatment-by-time), and the Wilcoxon matched paired test to assess the main effect of time. In the presence of a significant interaction treatment-by-time, we repeated the Wilcoxon test separately in the two treatment groups, applying the Bonferroni's correction to account for the two comparisons. Statistical analyses were performed using STATA release 16.0 software.

# RESULTS

## Sample Description

In this study, we enrolled a total of 40 subjects aged 9–16 years (Mean age = 13,5 ± 2,0; male (M)/female (F) = 36:4; male = 90,0%). All patients were affected by TS. The mean age of tic onset was 5,8 ± 1,2. Among the individuals diagnosed with TS, the most common comorbid psychiatric disorders were OCD (60%, $n = 24$), LD (42,5%, $n = 17$) and anxiety disorder (42,5%, $n = 17$). None of the patients had a concomitant depression, and only one patient was also affected by epilepsy. Only seven patients (17,5%) presented "pure-TS" phenotype. Seventeen (42,5%) received a pharmacological treatment (1 drug in 9, 2 drugs in 4, 3 drugs in 4) with no good response or a partial symptoms control. Participants presented a mean IQ of 103,8 (±10,6) and a mean PUTS score of 13,3 (±2,6). Demographic data and clinical features of all participants are displayed in **Table 1**.

## Baseline Characteristics

At baseline, no statistically significant differences were observed based on neuropsychological findings in the ftf- BT group vs. the or-BT group. The mean scores for YGTSS, CY-BOCS, and

**TABLE 1 |** Participant features.

| Variable | Total Sample ($n = 40$) | Online remote-BT ($n = 20$) | Face-to-face-BT ($n = 20$) | *p*-value |
|---|---|---|---|---|
| Male (%) | 36 (90.0%) | 18 (90.0%) | 18 (90.0%) | 1.000 |
| Age (mean, SD) | 13.5 (SD 2.0) | 13.3 (SD 2.0) | 13.8 (SD 2.0) | |
| Age of onset | 5.8 (SD 1.2) | 5.8 (SD 1.0) | 5.9 (SD 1.4) | 0.599 |
| Pharmacological Treatment (yes, %) | 17 (42.5%) | 9 (45.0%) | 8 (40.0%) | 1.000 |
| **Pharmacological Treatment (*n*, %)** | | | | 0.227 |
| 0 drug | 23 (57.5%) | 11 (55.0%) | 12 (60.0%) | |
| 1 drug | 9 (22.5%) | 4 (20.0%) | 5 (25.0%) | |
| 2 drugs | 4 (10.0%) | 4 (20.0%) | 0 (0.0%) | |
| 3 drugs | 4 (10.0%) | 1 (5.0%) | 3 (15.0%) | |
| **Pharmacological Treatment (yes, %)** | | | | |
| • Atypical antipsychotics | 14 (35.0%) | 9 (45.0%) | 5 (25.0%) | 0.320 |
| • Neuroleptic drugs | 3 (7.5%) | 0 (0.0%) | 3 (15.0%) | 0.231 |
| • SSRI | 5 (12.5%) | 2 (10.0%) | 3 (15.0%) | 1.000 |
| • Others | 7 (17.5%) | 4 (20.0%) | 3 (15.0%) | 1.000 |
| **Comorbid diagnosis (yes, %)** | | | | |
| • TS-only | 7 (17.5%) | 3 (15.0%) | 4 (20.0%) | 1.000 |
| • +OCD | 24 (60.0%) | 12 (60.0%) | 12 (60.0%) | 1.000 |
| • +LD | 17 (42.5%) | 8 (40.0%) | 9 (45.0%) | 1.000 |
| • +Anxiety | 17 (42.5%) | 9 (45.0%) | 8 (40.0%) | 1.000 |
| Total IQ | 103.8 (SD 10.6) | 104.0 (SD 9.3) | 103.6 (SD 12.0) | 0.653 |
| PUTS score | 13.3 (SD 2.6) | 13.6 (SD 2.9) | 13.1 (SD 2.3) | 0.622 |

*SD, standard deviation. p-values refer to Fisher's exact probability test in case of categorical variables (summarized by absolute and percent frequencies), and to Mann-Whitney U test in case of quantitative variables (summarized by means and SD). All tests are two-tail.*

MASC were slightly lower in the or-BT group vs. the ftf-BT group (YGTSS: mean 25.5, SD 10.5 vs. mean 25.8, SD 7.3, $p = 0.773$; CY-BOCS: mean 22.3, SD 12.0 vs. mean 22.7, SD 12.7, $p = 0.644$; MASC: mean 35.05, SD 16.8 vs. mean 36.15, SD 15.3, $p = 0.663$). Conversely, the mean scores for CPRS and CDI were slightly higher in the or-BT group vs. the ftf-BT group (CPRS: mean 21.15, SD 22.4 vs. mean 20.15, SD 17.2, $p = 0.363$; CDI: mean 4.45, SD 1.9 vs. mean 4.3, SD 2.6, $p = 0.574$).

## YGTSS Outcome

In general, patients in both groups showed a reduction in the severity of tic symptoms, as assessed by YGTSS scores, at T1. Mean YGTSS score at 2 months after randomization was 14,1 (SD 6,3) in the or-BT -group compared with 13,7 (SD 5,35) in the ftf-BT -group. The mean total decrease in YGTSS at 2 months was 12,05 (46,8%) in the ftf-BT -group vs. 11,4 (44,7%) in the or-BT -group. No statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the variation of the severity of tics as assessed by YGTSS between T0 and T1 ($p = 0.702$) (**Table 2**, **Figure 1**).

## CY-BOCS Outcome

Patients in both groups showed a reduction in the severity of obsessive-compulsive symptoms, as assessed by CYBOCS scores, at T1. Mean CYBOCS score at 2 months after randomization was 22,3 (SD 12,0) in the or-BT -group compared with 22,7 (SD 12,7) in the ftf-BT -group. The mean total decrease in CYBOCS at 2 months was 7,65 (33,7%) in the ftf-BT -group vs. 8,05 (36,1%) in the or-BT -group. No statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the severity of obsessive-compulsive symptoms as assessed by CYBOCS between T0 and T1 ($p = 0.680$) (**Table 2**, **Figure 1**).

## CPRS Outcome

Patients in both groups showed a reduction in the severity of core-ADHD symptoms, as assessed by CPRS scores, at T1. Mean CPRS score at 2 months after randomization was 21,15 (SD 22,4) in the or-BT -group compared with 20,15 (SD 17,2) in the ftf-BT -group. The mean total decrease in CPRS scores at 2 months was 5,45 (27,05%) in the ftf-BT -group vs. 6,85 (32,4%) in the or-BT -group. No statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the variation of the severity of these symptoms as assessed by CPRS between T0 and T1 ($p = 0.928$) (**Table 2**, **Figure 1**).

## MASC Outcome

Patients in both groups showed an improvement in MASC scores at T1. Mean MASC score at 2 months after randomization was 35,05 (SD 16,8) in the or-BT -group compared with 36,15 (SD 15,3) in the ftf-BT -group. The mean total decrease in MASC at 2 months was 13,6 (37,6%) in the ftf-BT group vs. 13,5 (38,5%) in the or-BT -group. No statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the

**TABLE 2 |** Outcome of neuropsychological findings.

| Variable | Time | Online remote-BT ($n = 20$) | Face-to-face-BT ($n = 20$) | *p*-values | Cohen's d |
|---|---|---|---|---|---|
| YGTSS | T0 | 25.5 (SD 10.5) | 25.8 (SD 7.3) | Group: 0.723 | 0.01 |
| | T1 | 14.1 (SD 6.3) | 13.7 (SD 5.4) | Time: <0.001** | 0.10 |
| | T1-T0 | −11.4 (SD 6.6) | −12.1 (SD 6.0) | Group*Time: 0.702 | |
| CYBOCS | T0T1 | 22.3 (SD 12.0) | 22.7 (SD 12.7) | Group: 0.723 | 0.06 |
| | | 14.3 (SD 6.6) | 15.1 (SD 7.2) | Time: <0.001** | 0.05 |
| | T1-T0 | −8.0 (SD 7.1) | −7.6 (SD 7.8) | Group*Time: 0.680 | |
| CPRS | T0 | 21.2 (SD 22.4) | 20.2 (SD 17.2) | Group: 0.260 | 0.02 |
| | T1 | 14.3 (SD 11.7) | 14.7 (SD 9.5) | Time: <0.001** | 0.14 |
| | T1-T0 | −6.9 (SD 11.8) | −5.5 (SD 8.1) | Group*Time: 0.928 | |
| CDI | T0 | 4.5 (SD 1.9) | 4.3 (SD 2.6) | Group: 0.973 | 0.16 |
| | T1 | 3.4 (SD 1.6) | 4.3 (SD 2.5) | Time: <0.001 | 0.95 |
| | T1-T0 | −1.1 (SD 1.5) | −0.0 (SD 0.2) | Group*Time: 0.002** *OnlineTime: 0.002** FtoF Time: 1.000* | |
| MASC | T0 | 35.1 (SD 16.8) | 36.2 (SD 15.3) | Group: 0.533 | 0.09 |
| | T1 | 21.6 (SD 10.1) | 22.6 (SD 5.4) | Time: <0.001** | 0.01 |
| | T1-T0 | −13.5 (SD 9.1) | −13.6 (SD 12.7) | Group*Time: 0.804 | |

*p-values refer to the non-parametric Mann-Whitney U test performed on the mean value of T0 and T1 (main effect of Group) and on the difference T1-T0 (interaction Group*Time), and Wilcoxon test performed in the overall group of patients (main effect of Time) or within each group (effect of Time separately assessed in the Online and in the Face-to-face groups). All tests are two-tail.*

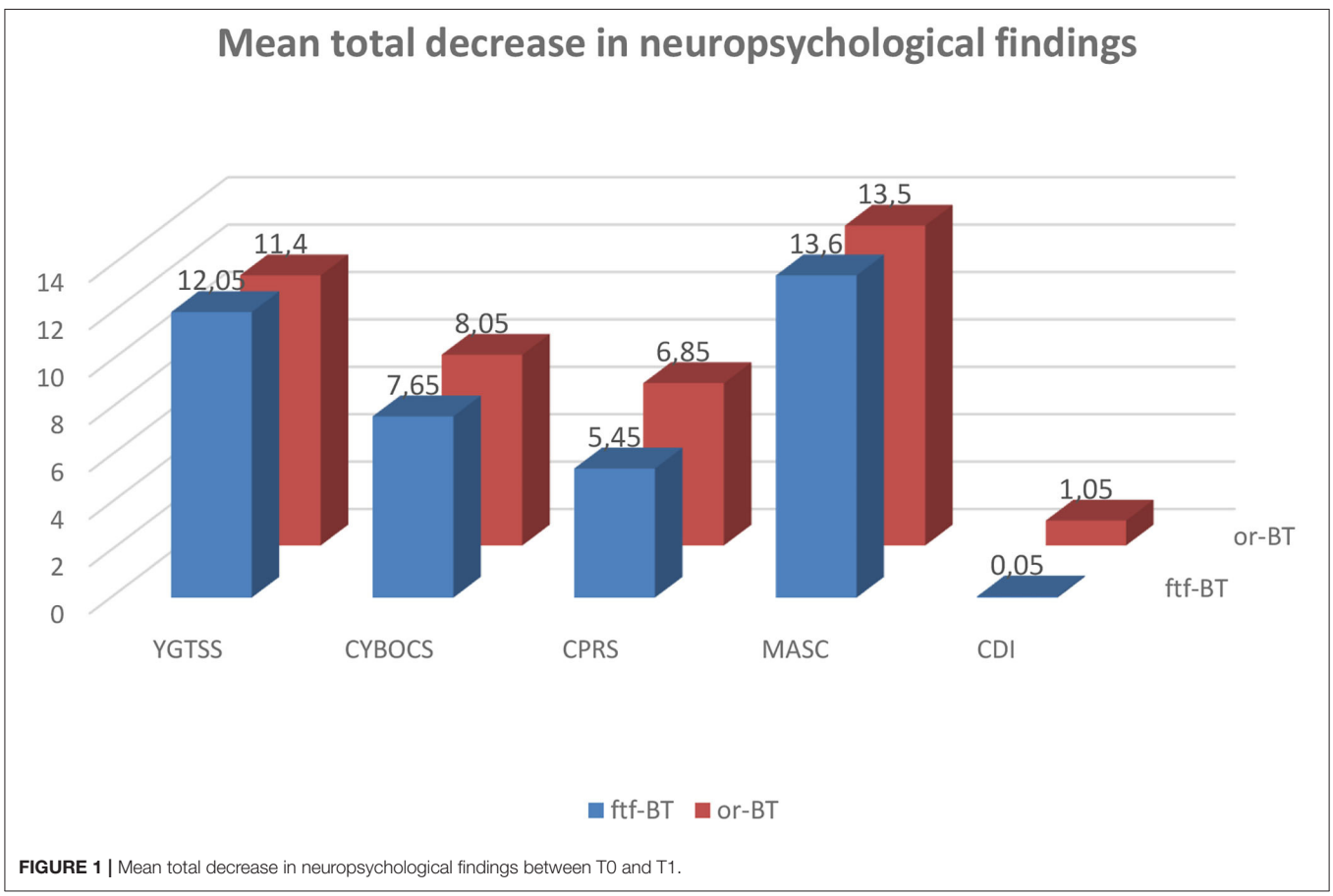


**FIGURE 1 |** Mean total decrease in neuropsychological findings between T0 and T1.

**TABLE 3 |** Summary of studies on online-remote BT in pediatric TS patients.

| Reference | Design | Interventions | Patients (*n*°) | Mean age | Outcome measures | Results |
|---|---|---|---|---|---|---|
| Himle et al. (33) | RCT | ICBT, F2F CBT | 18 | 11.6 | YGTSS | ICBT: 7.8 points reduction<br>FCBT: 6.5 points reduction |
| Ricketts et al. (21) | RCT | ICBT, WL | 20 | 12.7 | YGTSS | ICBIT > WL<br>ICBIT: 25.75 to 18.50<br>WL: 22.0 to 20.25 |
| Andrén et al. (22) | RCT | BIP TIC HRT, BIP ERP | 23 | 12.27 | YGTSS | BIP TIC HRT: 23.75 to 19.00<br>BIP TIC ERP: 23.45 to 21.18 |
| Hollis et al. (ORBIT) (20) | RCT | BIP TIC ERP, PE | 224 | 12.3 | YGTSS | BIP TIC ERP: 28.4 to 21.5<br>PE. 28.4 to 25.0 |

*WL, waitlist; ICBT, internet-delivered comprehensive behavioral therapy; F2F CBT, face-to face comprehensive behavioral therapy; BIP TIC HRT, internet-delivered habit reversal traning; BIP TIC ERP internet-delivered exposure and response prevention; PE, Psychoeducation; YGTSS, Yale Global Severity Scale.*

variation of the severity of anxiety symptoms as assessed by MASC between T0 and T1 ($p = 0{,}804$) (**Table 2**, **Figure 1**).

## CDI Outcome

Patients in both groups showed an improvement in CDI scores at T1. Mean CDI score at 2 months after randomization was 4,45 (SD 1,9) in the or-BT -group compared with 4,3 (SD 2,6) in the ftf-BT -group. The mean total decrease in CDI at 2 months was 0,05 (1,16%) in the ftf-BT group vs. 1,05 (23,6%) in the or-BT -group. Statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the severity of depressive symptoms as assessed by CDI between T0 and T1 ($p = 0.002$) (**Table 2**, **Figure 1**).

# DISCUSSION

This study investigates the efficacy of or-BT compared with ftf-BT in reducing tics and associated comorbid symptoms in youths with TS. So far, a few studies have evaluated the efficacy of BT remotely (20–22, 33). The first report about the efficacy of BT delivered via telehealth dates to a work by Himle et al. (33). These authors investigated the effectiveness of BT via videoconference in 10 TS patients compared with a face-to-face BT in 9 TS patients and demonstrated mean YGTSS reductions of 7.8 points for telehealth and 6.5 points for face-to-face (33% and 27% reductions from baseline, respectively) (33). Another 2016 RCT examined the delivery of BT via the Voice over Internet Protocol (VoIP) approach in 12 TS patient's vs. the waitlist control in 8 TS patients and found significantly greater reductions in clinician-rated and parent-reported tic severity in the VoIP-delivered BT group (21). Andrén et al. (22) also evaluated the feasibility of two existing BT protocols (HRT, ERP) into a therapist-guided and parent-guided online self-help format in a small pilot study. Both interventions resulted in reduced tic-related impairment, parent-rated tic severity and improved quality of life, and were again rated as highly acceptable, credible, and satisfactory (22). In addition, a multicentre, parallel group, single-blind RCT investigated the effectiveness of internet-delivered, therapist supported, ERP or psychoeducation and demonstrated a significant effect in treatment of tics in favor of therapist-supported ERP compared with supported psychoeducation (20). Previous studies regarding remote-BT conducted in pediatric TS patients are summarized in **Table 3**. Other studies have also reported the efficacy and safety of internet-delivered BT in the treatment of tics compared to ftf-BT for adults with chronic tic disorders (34, 35).

The results of this trial show that or-BT and ftf- BT are equally effective in reducing tic severity as measured by YGTSS scores. Furthermore, the mean total decrease in YGTSS at follow-up in both groups was higher (14,1 in the or-BT -group, 13,7 in the ftf-BT -group) respect to other recently reported samples (20–22, 33) (**Table 3**). Indeed, our results from the short follow-up assessment are more encouraging compared to the results reported in previous studies. Not only tics, but also co-occurring conditions were assessed and targeted for intervention in our study. No statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the severity of obsessive-compulsive symptoms and anxiety symptoms, as assessed by neuropsychological findings. Conversely, significantly greater reductions in depressive symptoms as assessed by CDI at T1 were found in the or-BT -group relative to ftf-BT group. Participants receiving or-BT demonstrated a mean reduction in CDI score of 1,05 (23,6%), higher to that observed in the ftf-BT group (mean total decrease = - 0,05; 1,16%). Between-group differences in clinician-rated severity of depressive symptoms did reach also statistical significance ($p = 0.010$). This may be probably attributable to the major impact of lockdown on their clinical course, and to the presence of other symptoms such as sleep disturbances or somatic complaints that amplified the vulnerability due to the restrictive social isolation. It is possible to hypothesize that fear of contracting virus has amplified the vulnerability to depressed moods in these children and adolescents. Future research should examine with more details the evolution and characteristics of possible secondary symptoms during lockdown.

The current study has several limitations. First, the sample size was small, limiting statistical power and detection of within-group effect sizes. Second, our study had a short follow-up period, and so a longer interventional period than 2 months may have been required to highlight the potential benefits of or-BT compared on ftf-BT. Third, our study did not include a non-BT

control group. Considering the lack of additional age-matched control-group and the relatively small sample size, the results should be considered as preliminary rather than conclusive. In addition, it would also be helpful to evaluate the effects of exposure to COVID-19-related stress on youth symptomatology. On the other hand, this study had also several strengths, including its randomized and controlled design, thoroughly considered inclusion and exclusion criteria, and the assessment of not only tics but also co-occurring conditions. In conclusion, our findings suggest that or-BT is a promising tool for behavioral therapies for patients with TS and may represents an alternative treatment option.

## CONCLUSIONS

This study suggest that or-BT is as effective as ftf-BT in the treatment of tics and co-occurring disorders in children and adolescents affected by TS or CTD. Despite this finding, further trials with larger samples are needed to confirm the beneficial effects of or-BT in treating patients with TS or CTD also affected by other comorbidities.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Local Ethics Committee (Catania 1) of Catania University Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

The trial was designed by RR. Treatment was provided by NM. Statistical analyses were performed by FC, in collaboration with AP. AP and LM drafted the original manuscript. RR, RB, and CV participated in constructive outline, discussions, and editing. All authors read and approved the final version of the manuscript.

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Altered Interoceptive Sensibility in Adults With Chronic Tic Disorder

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**Background:** Interoception refers to the sensing, interpretation, integration, and regulation of signals about the body's internal physiological state. Interoceptive sensibility is the subjective evaluation of interoceptive experience, as assessed by self-report measures, and is abnormal in numerous neuropsychiatric disorders. Research examining interoceptive sensibility in individuals with chronic tic disorders (CTDs), however, has yielded conflicting results, likely due to methodologic differences between studies and small sample sizes.

**Objective:** We sought to compare interoceptive sensibility between adults with CTD and healthy controls, adjusting for co-occurring psychiatric symptoms, and to examine the relationship of interoceptive sensibility with other CTD clinical features, in particular, premonitory urge.

**Methods:** We recruited adults with CTDs and sex- and age-matched healthy controls to complete the Multidimensional Assessment of Interoceptive Awareness, Version 2 (MAIA-2), as well as a battery of measures assessing psychiatric symptoms prevalent in CTD populations. CTD participants additionally completed scales quantifying tic severity, premonitory urge severity, and health-related quality of life. We conducted between-group contrasts (Wilcoxon rank-sum test) for each MAIA-2 subscale, analyzed the effect of psychiatric symptoms on identified between-group differences (multivariable linear regression), and examined within-group relationships between MAIA-2 subscales and other clinical measures (Spearman rank correlations, multivariable linear regression).

**Results:** Between adults with CTD ($n$ = 48) and healthy controls ($n$ = 48), MAIA-2 Noticing and Not-Worrying subscale scores significantly differed. After adjusting for covariates, lower MAIA-2 Not-Worrying subscale scores were significantly associated with female sex ($\beta$ = 0.42, $p < 0.05$) and greater severity of obsessive-compulsive symptoms ($\beta$ = –0.028, $p < 0.01$), but not with CTD diagnosis. After adjusting for severity of tics and obsessive-compulsive symptoms, a composite of MAIA-2 Noticing, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting subscales ($\beta$ = 2.52, $p < 0.01$) was significantly associated with premonitory urge.

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**Conclusion:** Study results revealed three novel findings: adults with CTD experience increased anxiety-associated somatization and increased general body awareness relative to healthy controls; anxiety-associated somatization is more closely associated with sex and obsessive-compulsive symptoms than with CTD diagnosis; and increased general body awareness is associated with greater severity of premonitory urges.

**Keywords: chronic tic disorder, Tourette syndrome, interoception, interoceptive sensibility, sensory impairment, tics**

## INTRODUCTION

Tics are sudden, recurrent, stereotyped, non-rhythmic movements (motor tics) or vocalizations (vocal tics), often preceded by an unpleasant sensation called a premonitory urge (1). Tourette syndrome (TS) is a neurodevelopmental disorder clinically defined by the presence of multiple motor tics and at least one vocal tic, with emergence of tics before 18 years of age and persistence of tics for at least one year (1). Individuals who experience only motor tics or only vocal tics but fulfill the remainder of the above TS diagnostic criteria are diagnosed with chronic (persistent) motor tic disorder or chronic (persistent) vocal tic disorder, respectively (1). TS, chronic motor tic disorder, and chronic vocal tic disorder exist along a single clinical spectrum (2), with shared underlying genetic architecture (3), and as such, these three disorders are often studied collectively under the label "chronic tic disorders" (CTDs).

While tics, a *discrete* motor phenomenon, and premonitory urges, a *discrete* sensory phenomenon, are the hallmark symptoms of CTDs, individuals with these disorders also manifest *pervasive* motor and sensory abnormalities. Relative to healthy controls, individuals with CTD exhibit altered movement timing (4, 5) and force (6), enhanced reinforcement learning of motor sequences (7), and diminished ability to lateralize fine motor movements (8, 9). Fine motor impairment in children with CTD predicts tic severity in adulthood (10). Sensorimotor integration is aberrant in those with CTD (11–13). The majority of adults and children with CTD endorse heightened sensitivity to commonplace environmental stimuli, a phenomenon termed sensory over-responsivity (14, 15). These clinical and behavioral findings of motor and sensory dysfunction align with neurophysiological (16–18), functional imaging (19–21), and structural imaging (22–25) investigations demonstrating abnormalities at multiple nodes and links of a distributed sensorimotor network in CTDs. Such abnormalities have been identified in primary motor cortex (22, 25, 26), supplementary motor area (19, 25, 26), primary sensory cortex (20, 22), superior parietal cortex (20, 22), insula (21, 27), several basal ganglia structures (20, 27, 28), and white matter tracts within the sensorimotor subcortical region (23, 29). Thus, motor and sensory dysfunction in CTDs is diffuse.

Both motor and sensory function are dynamically intertwined with interoception (30, 31). Interoception refers to the sensing, interpretation, integration, and regulation of signals about the body's internal physiological state (32–34). Interoception is a continuous, iterative process in which bottom-up afferent signals from the body are integrated in the insula with top-down signals from sensorimotor and frontal cortical regions (33–35). The primary function of interoception is to inform homeostatic drives (33). Numerous higher-order cognitive processes, including memory formation (31), emotion processing (31, 36), and self-representation (30, 31) rely on interoceptive input. Under the widely adopted conceptual framework posited by Garfinkel and Critchley (37), interoception is parsed into three sub-constructs: interoceptive accuracy (objective ability to detect bodily sensations, as assessed by physiological tasks, e.g., heartbeat detection tasks), interoceptive sensibility (subjective evaluation of interoceptive experience, as assessed by self-report measures), and interoceptive awareness (insight into one's interoceptive accuracy) (32). These inter-related constructs are dissociable (38–40) but appear to share a common neural substrate, the insula (34, 41–43). Individual differences in interoceptive accuracy (34, 41, 42) and interoceptive sensibility (41) have been linked to differences in insular function and structure. Interest in the three interoception sub-constructs and their neural bases has grown with mounting evidence of compromised interoception in numerous mental health and neurodevelopmental disorders (32, 34), including anxiety (44), depression (44), anorexia nervosa (45, 46), and autism spectrum disorder (47–49), to name a select few.

Two lines of evidence motivate research into interoception among CTD populations specifically. First, interoception plays a key role in motor, sensory, and emotional function (30, 31), domains frequently affected in CTDs (50). Second, as noted above, interoception is subserved by the insula, a structure strongly implicated in CTD pathophysiology (51). Enhanced understanding of interoception in CTDs may deepen insight into the phenotypes and neural mechanisms of these disorders.

To date, studies of interoception in CTD have yielded mixed results. Regarding interoceptive accuracy, adults with TS performed less accurately on a heartbeat counting task compared to healthy controls in one study (52) but not another (53). Given concerns that the heartbeat counting method inadequately indexes interoceptive accuracy (54), the latter study also employed a heartbeat discrimination task, finding no group difference between TS and healthy control samples on that task either (53). A pediatric study, also using the heartbeat counting task, identified reduced interoceptive accuracy in children with CTD compared to controls (55). Conflicting findings have similarly emerged from studies of interoceptive sensibility in CTD. Eddy et al. observed heightened interoceptive sensibility, as measured

by the Private Body Consciousness Scale (PBCS), in adults with TS relative to controls. Notably, in the TS group neither tic severity nor premonitory urge severity correlated with PBCS score (56). Conversely, Rae et al. found no significant difference between adults with TS and controls in interoceptive sensibility, as measured by the body awareness section of the Body Perception Questionnaire (BPQ) (53), but among TS participants BPQ score did correlate with both tic severity and premonitory urge severity (53). The relationship between interoception and premonitory urge is of particular interest given the insula plays a critical role in emergence of both phenomena (34, 41, 51). Divergent results between studies of interoception in CTD may have arisen from several possible factors, including methodologic differences in assessing interoceptive accuracy or sensibility, disparate eligibility criteria [e.g., Eddy et al. excluded individuals with TS who had psychiatric comorbidities (56) while Rae et al. did not (53)], and relatively small sample sizes [each adult study enrolled between 18 and 21 CTD participants (52, 53, 56); the sole pediatric study enrolled 29 CTD participants (55)]. Furthermore, none of the aforementioned studies adjusted their analyses for the presence or severity of mental health diagnoses that are known to be widespread in CTD populations. The most common comorbid mental health diagnoses among individuals with CTD include attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), anxiety, and depression, with respective lifetime prevalence rates of 54, 66, 36, and 30%. (57). Many with CTD who do not fulfill formal diagnostic criteria for ADHD, OCD, anxiety, and/or depression still exhibit symptoms of these disorders (58, 59). Each of these comorbid disorders has been associated with abnormal interoceptive accuracy (60–63) and/or sensibility (61, 63–65), and thus, each represents an important potential confound when investigating interoception in CTD. In sum, considerable ambiguity surrounds our understanding of interoception in CTDs.

In the current study, we sought to compare interoceptive sensibility between adults with CTD and healthy controls, adjusting for co-occurring mental health symptoms, and to examine the relationship of interoceptive sensibility with other CTD clinical features, in particular, premonitory urge. To do so, we recruited adults with CTD and sex- and age-matched healthy controls to complete the Multidimensional Assessment of Interoceptive Awareness, Version 2 (MAIA-2), as well as a battery of measures assessing psychiatric symptoms common in CTD populations. CTD participants additionally completed scales quantifying tic severity, premonitory urge severity, and health-related quality of life. We hypothesized the following: first, CTD and control participants would differ in interoceptive sensibility, with CTD participants exhibiting maladaptive interoceptive sensibility, given such a finding in one prior study of adults with TS (56); second, between-group differences in interoceptive sensibility would be partially attributable to between-group differences in co-occurring psychiatric symptom severity, given the known relationship between abnormal interoceptive sensibility and mental health disorders (61, 63–65); and third, after adjusting for other CTD clinical features, premonitory urge severity would positively correlate with interoceptive sensibility, given evidence of a strong correlation between these phenomena in one previous study (53).

# MATERIALS AND METHODS

## Participants

From February 2021 through February 2022, we recruited adults (≥18 years of age) with CTD and sex- and age-matched adults with no known neurologic or psychiatric diagnoses. English fluency was required for study enrollment. Adults with CTD were recruited from Vanderbilt University Medical Center (VUMC) Tourette Syndrome Clinic and institutional research registries. All CTD participants were interviewed, examined, and diagnosed with a CTD by an experienced movement disorders neurologist (D.I.) using Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria. Control participants were recruited via ResearchMatch, a web-based recruitment tool for clinical research (66). Controls completed all study activities online and were not interviewed or examined.

Control participants were one-to-one-matched on sex and age (±5 years) to CTD participants. TS and control participants who completed less than 50% of study measures were excluded from the matching process. All participants were asked to self-report history of any and all of the following conditions: tic disorder, OCD, ADHD, autism spectrum disorder, anxiety, and depression. Controls with a self-reported diagnosis of tic disorder, OCD, ADHD, or autism spectrum disorder were excluded from the matching process, but controls with a history of anxiety and/or depression were included. Data analysis was restricted to matched participants.

Participants provided electronic informed consent and received monetary reimbursement after completing all study activities. This study was approved by the VUMC Institutional Review Board and was conducted in accordance with the Declaration of Helsinki.

## Measures

**Table 1** lists the validated measures used in the study. More detailed information on each measure (e.g., number of items, score range, established cut-offs) is available in the **Supplementary Material**. A movement disorders neurologist (D.I.) administered the Yale Global Tic Severity Scale (YGTSS) (67) to all CTD participants, after which they were emailed unique hyperlinks to the study self-report measures in Research Electronic Data Capture (REDCap). REDCap is a HIPAA-compliant, web-based platform for data collection and storage (68, 69). CTD participants were requested to finish all study measures at their earliest convenience following the YGTSS to minimize time between the clinician-administered and self-report measures. Control participants were emailed unique hyperlinks to the same battery of self-report measures, with the exception that controls did not complete the Premonitory Urge to Tic Scale (PUTS) (70) or the Gilles de la Tourette-Quality

**TABLE 1 |** Participant demographic and clinical characteristics.

| Variable | Control ($n$ = 48) | CTD ($n$ = 48) | Wilcoxon rank-sum test for continuous variables |
|---|---|---|---|
| Sex (M: F) | 28: 20 | 28: 20 | |
| Age (years) | 31.5 (23.5–49.5)† | 31 (22–48.5) | $z$ = 0.23 |
| **Ethnicity** | | | |
| Hispanic or Latino | 4 | 1 | |
| Not Hispanic or Latino | 43 | 46 | |
| Unknown/Not reported | 1 | 1 | |
| **Race** | | | |
| American Indian or Alaska Native | 0 | 1 | |
| Asian | 2 | 1 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 6 | 1 | |
| White | 36 | 43 | |
| More than one race | 1 | 1 | |
| Unknown/Not reported | 3 | 1 | |
| **Co-occurring conditions, self-reported** | | | |
| ADHD | 0 | 16 | |
| OCD | 0 | 25 | |
| Anxiety | 4 | 27 | |
| Depression | 3 | 26 | |
| Autism spectrum disorder | 0 | 1 | |
| Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-5) | 7.5 (5–9.5) | 13 (9.5–16) | $z$ = –5.7*** |
| Dimensional Obsessive-Compulsive Scale (DOCS) | 9.5 (5–15.5) | 15.5 (7.5–28) | $z$ = –2.8** |
| Generalized Anxiety Disorder-7 (GAD-7) | 2.5 (0.8–4.5) | 9 (2.5–13) | $z$ = –4.6*** |
| Patient Health Questionnaire-9 (PHQ-9) | 2.5 (1–5) | 8 (4.5–15) | $z$ = –5.2*** |
| YGTSS Total Tic Score | – | 22.5 (15–30) | – |
| Premonitory Urge to Tic Scale (PUTS) | – | 25 (21.5–29) | – |
| Gilles de la Tourette-Quality of Life Scale (GTS-QOL) | – | 31.5 (19.4–51.4) | – |

†*Median (interquartile range).*
***$p < 0.01$; ***$p < 0.001$.*

of Life Scale (GTS-QOL) (71), both of which are tic disorder-specific. Estimated time to finish the online battery of self-report measures was 30–40 min.

To quantify interoceptive sensibility, we used the Multidimensional Assessment of Interoceptive Awareness, Version 2 (MAIA-2) (72). The MAIA-2 is a 37-item, self-report measure that assesses multiple facets of interoceptive sensibility. Each scale item is a statement to which respondents must select "never" (0) to "always" (5) on a six-point Likert scale. No total MAIA-2 score exists. Rather, individual scale items belong to one of eight MAIA-2 subscales: Noticing ("awareness of uncomfortable, comfortable, and neutral body sensations," per MAIA-2 developers' definition), Not-Distracting ("tendency not to ignore or distract oneself from sensations of pain or discomfort"), Not-Worrying ("tendency not to worry or experience emotional distress with sensations of pain or discomfort"), Attention Regulation ("ability to sustain and control attention to body sensations"), Emotional Awareness ("awareness of the connection between body sensations and emotional states"), Self-Regulation ("ability to regulate distress by attention to body sensations"), Body Listening ("active listening to the body for insight"), and Trusting ("experience of one's body as safe and trustworthy"). For each subscale, higher score signifies more of that construct. The original MAIA was developed via a mixed-methods process, involving concept and item development with an expert panel; focus group testing in instructors of body awareness therapies; cognitive interviewing; and assessment of internal consistency reliability, convergent validity, and incremental validity (73). Due to sub-optimal internal consistency reliability of two subscales of the original MAIA (Not-Worrying and Not-Distracting), the instrument underwent modifications, leading to creation of the MAIA-2 (72). The psychometric properties of the MAIA-2 were evaluated in a large community sample of 1,090 individuals (72). Notably, the MAIA-2 Not-Worrying and Not-Distracting subscales exhibited improved internal consistency reliability relative to the original MAIA versions of these subscales, but their Cronbach's $\alpha$ values remained slightly below the acceptable cutoff of 0.70 (Noticing 0.64; Not-Worrying 0.67) (72). Despite this limitation, we selected the MAIA-2 for use in the current study because the scale accounts for and differentiates between adaptive and maladaptive dimensions of interoceptive sensibility (74), whereas other scales primarily conceptualize interoceptive sensibility unidimensionally, as anxiety-related somatization (75).

To quantify symptom severity of psychiatric disorders commonly co-occurring with CTDs, all participants completed the following validated self-report measures: Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-5) (76), Dimensional Obsessive-Compulsive Scale (DOCS) (77), Generalized Anxiety Disorder-7 (GAD-7) (78), and Patient Health Questionnaire-9

(PHQ-9) (79). CTD participants were also administered the YGTSS, as noted above, as well as the PUTS and GTS-QOL.

## Statistical Approach

To provide non-parametric measures of central tendency and dispersion for continuous variables, we calculated medians and interquartile ranges. Missing item responses were imputed from mean, non-missing responses of all matched participants.

To examine internal consistency reliability of the MAIA-2 in the current sample, we computed McDonald's ω for each of the eight subscales across all participants. McDonald's ω is an estimate of internal consistency reliability that is robust when the assumption of τ-equivalence is violated and is thus more appropriate than Cronbach's α for most psychological self-report measures (80).

To examine between-group differences in interoceptive sensibility, we contrasted CTD and control group scores on each of the eight MAIA-2 subscales with the Wilcoxon-rank sum test. To account for multiple comparisons, we employed the false discovery rate-controlling procedure developed by Benjamini et al. (81). The magnitude of the Wilcoxon rank-sum test statistic functions as a non-parametric measure of effect size (82).

For MAIA-2 subscales with significantly different scores between the groups, we conducted secondary analyses to assess the effect of co-occurring psychiatric symptoms on the association between the MAIA-2 subscale and CTD diagnosis. To do so, we constructed multivariable linear regression models with the given MAIA-2 subscale as the dependent variable and the following as independent variables: sex, age, CTD diagnosis, ASRS-5 score, DOCS score, and GAD-7 score. PHQ-9 score was not included as an independent variable due to its strong correlation with GAD-7 score in both CTD ($r_s$ = 0.66) and control ($r_s$ = 0.73) groups. We next constructed a reduced model for the given MAIA-2 subscale, with the same set of independent variables except CTD diagnosis was removed. For each regression model, we plotted histograms of residuals to visually inspect for deviations from normality, plotted residuals against the independent variable to visually inspect for heteroskedasticity, calculated the Breusch–Pagan test statistic to quantify heteroskedasticity, calculated the variance inflation factor (VIF) for independent variables to identify significant multicollinearity (pre-specified as VIF > 5) (83), and performed a regression specification error test to assess for likelihood of omitted variables. Adjusted $R^2$ indexed model goodness-of-fit. Likelihood ratio tests and Akaike information criteria (AIC) were used to compare goodness-of-fit between full and reduced models. We conducted *post hoc t*-tests of the full models to examine the association between independent and dependent variables, with a pre-specified significance threshold of $p < 0.05$.

As an exploratory analysis, we contrasted MAIA-2 subscale scores between the subset of CTD participants with no reported ADHD or OCD and their sex- and age-matched controls. This analysis was performed to facilitate results comparison with other studies in which individuals with CTD were excluded for comorbid diagnoses of ADHD or OCD (56). We applied Benjamini et al's false discovery rate-controlling procedure to account for multiple comparisons (81). Of note, all other analyses discussed in the Methods section were conducted with data from the entire CTD cohort; only this exploratory analysis was conducted with data from a subset of the cohort.

To assess the interrelationship between measures within each participant group, we calculated Spearman's rank correlations ($r_s$) between scale scores, using the aforementioned false discovery rate-controlling procedure to account for multiple comparisons (81).

To further examine the association of interoceptive sensibility with premonitory urge in the CTD sample, we constructed a multivariable linear regression model with PUTS score as the dependent variable. Given our sample size, we were insufficiently powered to incorporate all eight MAIA-2 subscales into the model. We thus first sought to reduce the dimensionality of the MAIA-2 scale using hierarchical cluster analysis, with average linkage, on subscale scores from CTD participants. Prior to clustering, MAIA-2 subscale scores were standardized. A dissimilarity matrix, with the eight subscales as individual variables, was constructed using Euclidian distance as the metric. Based upon the dendrogram yielded by the cluster analysis of the MAIA-2 subscales, we identified a three-variable-cluster solution. For the premonitory urge regression model, the following served as independent variables: the three-variable solution to the MAIA-2 hierarchical cluster analysis, DOCS score, and YGTSS Total Tic Score. DOCS score and YGTSS Total Tic Score were selected as model covariates given the established association of premonitory urge severity with severity of obsessive-compulsive symptoms and tics (84–86). Study sample size precluded addition of other clinical variables and interaction terms into the premonitory urge regression model. We employed the same regression diagnostics outlined earlier in the Methods section.

Statistical analyses were conducted in STATA 15.0 and Excel 16.5.

# RESULTS

## Population

Forty-eight participants with CTD (46 with TS, 2 with chronic motor tic disorder) and 68 control participants completed more than 50% of study measures. From the pool of control participants, four were excluded due to self-reported history of ADHD ($n$ = 1), OCD ($n$ = 2), or both ($n$ = 1). From this remaining pool, 48 control participants were one-to-one sex- and age-matched to CTD participants. All subsequent analyses refer to matched participants. Data from the final cohort were > 99.9% complete, with missing responses only from single items of the PHQ-9 (for one participant) and GAD-7 (for two other participants). CTD participants completed self-report measures a median of 1 day (interquartile range 0 –9.5 days) following YGTSS administration.

**Table 1** contains demographic and clinical information for the matched sample. Age-matching was successful, with no significant difference in age between groups. The sample as a whole was predominantly non-Hispanic white, though the control population was slightly more diverse. Adults with CTD

endorsed significantly more severe symptoms of ADHD, OCD, anxiety, and depression relative to controls.

Internal reliability consistency for all eight MAIA-2 subscales, across the entire study population, was above the conventional threshold of 0.70, with McDonald's ω ranging from 0.74 –0.93. McDonald's ω for each MAIA-2 subscale is provided in the **Supplementary Material**.

## Between-Group Contrasts of MAIA-2 Subscale Scores

After controlling for the false discovery rate, CTD and control participant scores differed for two MAIA-2 subscales: Noticing and Not-Worrying (see **Table 2**). CTD participants were 65.8% (95% CI: 54.6–76.9%) more likely to have a higher MAIA-2 Noticing score than controls, while controls were 67.7% (95% CI: 56.8–78.5%) more likely to have a higher MAIA-2 Not-Worrying score than CTD participants. Respectively, findings suggest adults with CTD experience increased awareness of bodily sensations in general, as well as heightened worry in response to uncomfortable bodily sensations. Between-group difference for the MAIA-2 Trusting subscale approached significance ($p$ = 0.046), but significance did not survive correction for multiple comparisons.

Results of the multivariable linear regression analysis for the MAIA-2 Noticing and Not-Worrying subscales are shown in **Table 3**. Full and reduced models for these subscales satisfied the assumptions of multivariable linear regression, as assessed by the diagnostic procedures outlined in the Methods. The **Supplementary Material** contains histograms of the model residuals. For both the Noticing and the Not-Worrying subscales, the full models explained a statistically significant portion of the subscale score variance. However, the full model for the Noticing subscale explained a relatively low percentage of the score variance (adj $R^2$ = 0.09), and none of the selected independent variables were significantly associated with the subscale score. Adjusted $R^2$ and AIC values for the Noticing subscale full model were similar to those of the reduced model, and the goodness-of-fit did not significantly differ between these models, as determined by the likelihood ratio test, suggesting that CTD diagnosis did not significantly contribute to the Noticing subscale model goodness-of-fit. The full model for the Not-Worrying subscale explained a moderate percentage of the score variance (adj $R^2$ = 0.30), and sex and DOCS total score were significantly associated with the Not-Worrying subscale score, while CTD diagnosis was not. These findings indicate female sex and more severe obsessive-compulsive symptoms were associated with greater tendency to worry about uncomfortable bodily sensations. As with the Noticing subscale models, adjusted $R^2$ and AIC values for the full Not-Worrying models were similar to those of the reduced model, and the likelihood ratio test statistic from comparison of these models did not reach significance, suggesting that CTD diagnosis did not significantly contribute to the Not-Worrying subscale model goodness-of-fit.

Fifteen CTD participants reported no history of ADHD or OCD. The **Supplementary Material** contains full results from the comparison of MAIA-2 subscale scores and other scale scores between this CTD subset and their matched controls. Even within this subset, CTD participants exhibited more severe symptoms of ADHD, anxiety, and depression (see **Supplementary Material**). After correcting for multiple comparisons, group scores did not significantly differ for any of the scales. However, CTD participants without reported OCD or ADHD trended toward lower Self-Regulation subscale score ($z$ = 2.2, $p$ = 0.03) and higher Not-Worrying subscale score ($z$ = 1.7, $p$ = 0.09).

**TABLE 2 |** Between-group contrasts for MAIA-2 subscale scores.

| MAIA-2 subscale | Control ($n$ = 48) | CTD ($n$ = 48) | Wilcoxon rank-sum test |
|---|---|---|---|
| Noticing | 2.1 (1.0–3.0)† | 3.0 (2.1–3.5) | $z$ = –2.7* |
| Not-Distracting | 2.8 (2.0–3.8) | 2.7 (1.6–3.5) | $z$ = 1.3 |
| Not-Worrying | 3.1 (2.6–3.8) | 2.8 (1.8–3.2) | $z$ = 3.0* |
| Attention Regulation | 2.7 (1.8–3.1) | 1.9 (1.4–3.1) | $z$ = 1.2 |
| Emotional Awareness | 2.6 (1.7–3.2) | 2.8 (2.1–3.6) | $z$ = –1.0 |
| Self-Regulation | 2.8 (1.5–3.6) | 2.1 (1.3–3.0) | $z$ = 1.6 |
| Body Listening | 1.5 (0.7–3.0) | 1.3 (0.8–2.0) | $z$ = 0.6 |
| Trusting | 3.0 (2.7–4.0) | 2.7 (2.0–3.8) | $z$ = 2.0 |

†*Median (interquartile range).*
**Significant at p < 0.019 (threshold as determined by false discovery rate-controlling procedure).*

## Clinical Correlates of MAIA-2 Subscale Scores

Across the entire CTD participant group, select MAIA-2 subscale scores significantly correlated with scores from several other measures (see **Figure 1**). MAIA-2 Not-Worrying score negatively correlated with DOCS ($r_s$ = –0.53, $p < 0.001$), PUTS ($r_s$ = –0.44, $p < 0.01$), and GTS-QOL ($r_s$ = –0.45, $p < 0.01$) scores, indicating that higher Not-Worrying scores were associated with lower obsessive-compulsive symptom severity, lower premonitory urge severity, and higher health-related quality of life. MAIA-2 Trusting score negatively correlated with GAD-7 ($r_s$ = –0.42, $p < 0.01$), PHQ-9 ($r_s$ = –0.44, $p < 0.01$), and GTS-QOL ($r_s$ = –0.50, $p < 0.001$) scores, indicating that higher Trusting scores were associated with less anxiety, less depression, and higher health-related quality of life. In addition to MAIA-2 Not-Worrying score, PUTS score significantly correlated with MAIA-2 Emotional Awareness ($r_s$ = 0.35, $p < 0.05$) and Self-Regulation ($r_s$ = 0.34, $p < 0.05$) scores. GAD-7 and PHQ-9 were the measures most strongly correlated with GTS-QOL ($r_s$ = 0.75, $p < 0.0001$ and $r_s$ = 0.78, $p < 0.0001$, respectively). PUTS score did not significantly correlate with YGTSS Total Tic Score after correction for multiple comparisons ($r_s$ = 0.28, $p$ = 0.05). Notably, the degree of correlation between PUTS score and YGTSS Total Tic Score in our sample closely aligned with results from a recent meta-analysis examining the relationship between severity of premonitory urges and tics (84). The correlation matrix for control participants is available in the **Supplementary Material**.

In the hierarchical cluster analysis of MAIA-2 subscales within the CTD group, Not-Worrying and Not-Distracting were most dissimilar from the other six subscales (see dendrogram in **Supplementary Material**), in accord with several other

**TABLE 3 |** Regression model diagnostics and results for MAIA-2 Noticing and Not-Worrying Subscales.

| Dependent variable[§] | | Independent variables | VIF[†] | Breusch–Pagan test[‡] | Specification error test[^] | Independent variables significantly associated with dependent variable | Model goodness-of-fit indices | Likelihood ratio |
|---|---|---|---|---|---|---|---|---|
| MAIA-2 Noticing subscale score | Full | CTD diagnosis<br>Age<br>Sex<br>GAD-7 score<br>DOCS score<br>ASRS-5 score | 1.74<br>1.23<br>1.19<br>2.17<br>1.78<br>1.89 | $\chi^2(1) = 0.07$<br>$p = 0.80$ | $F(3,86) = 2.18$<br>$p = 0.10$ | – | $F(6,89) = 2.54$<br>$p < 0.05$<br>$R^2 = 0.15$<br>adj $R^2 = 0.09$<br>AIC[¶] = 322.6 | $\chi^2(1) = 0.77$<br>$p = 0.38$ |
| | Reduced | Age<br>Sex<br>GAD-7 score<br>DOCS score<br>ASRS-5 score | 1.19<br>1.18<br>1.97<br>1.78<br>1.51 | $\chi^2(1) = 0.01$<br>$p = 0.92$ | $F(3,87) = 2.16$<br>$p = 0.10$ | – | $F(5,90) = 2.92$<br>$p < 0.05$<br>$R^2 = 0.14$<br>adj $R^2 = 0.09$<br>AIC[¶] = 321.4 | |
| MAIA-2 Not-Worrying subscale score | Full | CTD diagnosis<br>Age<br>Sex<br>GAD-7 score<br>DOCS score<br>ASRS-5 score | 1.74<br>1.23<br>1.19<br>2.17<br>1.78<br>1.89 | $\chi^2(1) = 0.25$<br>$p = 0.62$ | $F(3,86) = 0.75$<br>$p = 0.52$ | Sex:<br>β = 0.42 (95% CI: 0.06–0.78)<br>$t = 2.3$, $p < 0.05$<br>DOCS score:<br>β = –0.028 (95% CI: –0.05 - –0.01)<br>$t = -3.1$, $p < 0.01$ | $F(6,89) = 7.77$<br>$p < 0.0001$<br>$R^2 = 0.34$<br>adj $R^2 = 0.30$<br>AIC = 238.1 | $\chi^2(1) = 2.99$<br>$p = 0.08$ |
| | Reduced | Age<br>Sex<br>GAD-7 score<br>DOCS score<br>ASRS-5 score | 1.19<br>1.18<br>1.97<br>1.78<br>1.51 | $\chi^2(1) = 0.29$<br>$p = 0.59$ | $F(3,87) = 0.57$<br>$p = 0.64$ | Sex:<br>β = 0.40 (95% CI: 0.03–0.76)<br>$t = 2.2$, $p < 0.05$<br>DOCS score:<br>β = –0.028 (95% CI: 0.05 - –0.01)<br>$t = -3.0$, $p < 0.01$ | $F(5,90) = 8.59$<br>$p < 0.0001$<br>$R^2 = 0.32$<br>adj $R^2 = 0.29$<br>AIC = 239.1 | |

[§]*Diagnostics and results are stratified into the full and reduced regression models, as noted by vertical text in the rightmost portion of this column.*
[†]*VIF, variance inflation factor.*
[‡]*$p < 0.05$ for Breusch–Pagan test indicates significant likelihood of heteroskedasticity.*
*∧$p < 0.05$ for regression specification error test indicates significant likelihood the model has omitted variables.*
[¶]*AIC, Akaike information criteria.*

studies (87–89). We thus generated a composite variable of the other six subscales (Noticing, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting) by averaging their scores. We then constructed a multivariable linear regression model with PUTS score as the dependent variable and the following as independent variables: MAIA-2 Not-Worrying score, MAIA-2 Not-Distracting score, MAIA-2 composite variable score (i.e., mean score from the six MAIA-2 subscales besides Not-Worrying and Not-Distracting), DOCS score, and YGTSS Total Tic Score (see **Table 4**). The model satisfied multivariable linear regression assumptions. The residuals histogram is provided in the **Supplementary Material**. Under this regression model, the MAIA-2 composite variable score, DOCS score, and YGTSS Total Tic Score were each independently associated with PUTS score. **Figure 2** plots PUTS score against the MAIA-2 composite variable score.

## DISCUSSION

In this study of interoceptive sensibility in adults with CTD, we identified three novel findings. First, only select dimensions of interoceptive sensibility (Noticing and Not-Worrying) differ between adults with CTD and healthy controls. Second, anxiety-associated aspects of interoceptive sensibility are more strongly associated with female sex and obsessive-compulsive symptom severity than with CTD diagnosis. Third, premonitory urge severity is significantly associated with interoceptive sensibility, even after controlling for severity of tics and obsessive-compulsive symptoms. We will discuss these findings sequentially.

In the current study, CTD participants endorsed a greater tendency to worry about sensations of bodily discomfort, as evidenced by their significantly lower MAIA-2 Not-Worrying subscale scores relative to controls. Two prior studies in adults with CTD used alternate self-report measures to quantify interoceptive sensibility: the Private Body Consciousness Scale (PBCS) (56) and the body awareness section of the Body Perception Questionnaire (BPQ) (53). The PBCS and the BPQ predominantly index a disposition to anxiety-associated somatization (48, 75, 90), similar to the MAIA-2 Not-Worrying subscale (41, 87, 88). Findings from these previous studies of interoceptive sensibility in CTD were discrepant: Eddy et al. identified increased interoceptive sensibility (as measured by the PBCS) in CTD participants relative to controls (56), whereas Rae et al. did not identify such a between-group

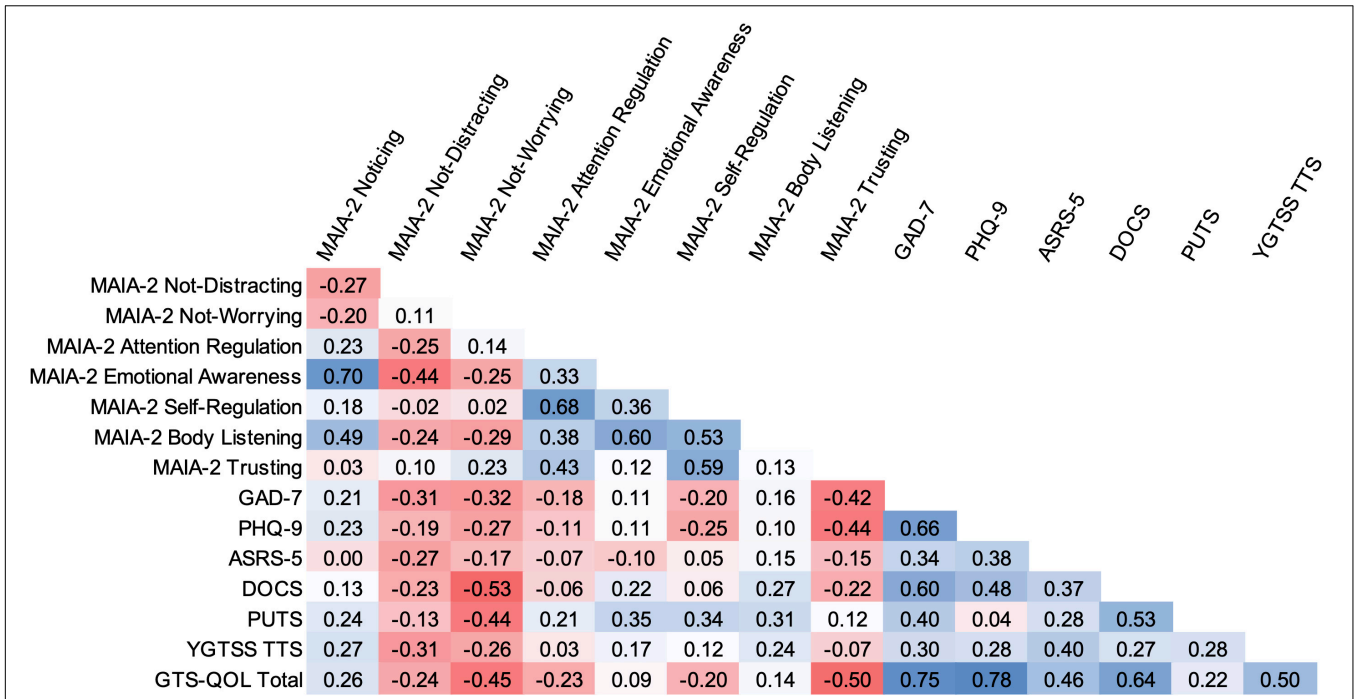


**FIGURE 1 |** Bivariate correlation matrix for CTD participants. Intensity of shading reflects magnitude of Spearman rank correlation, with blue indicating positive correlation and red indicating negative correlation. Correlations with absolute values ≥ 0.34 are significant, as per the false discovery rate-controlling procedure. TTS, Total Tic Score.

**TABLE 4 |** Regression model for PUTS.

| Dependent variable | Independent variables | VIF† | Breusch–Pagan Test | Specification error test | Model goodness-of-fit indices | Independent variables significantly associated with dependent variable |
|---|---|---|---|---|---|---|
| PUTS score | MAIA-2 Not-Worrying score<br>MAIA-2 Not-Distracting score<br>MAIA-2 composite variable score§<br>DOCS score<br>YGTSS Total Tic score | 1.55<br>1.43<br>1.14<br>1.53<br>1.34 | $\chi^2(1) = 0.19$<br>$p = 0.66$ | $F(3,39) = 2.79$<br>$p = 0.053$ | $F(5,42) = 7.03$<br>$p < 0.0001$<br>$R^2 = 0.46$<br>adj $R^2 = 0.39$<br>AIC¶ = 287.0 | MAIA-2 composite variable score:<br>β = 2.52 (95% CI: 0.79–4.24)<br>$t = 2.95$, $p < 0.01$<br>DOCS score:<br>β = 0.14 (95% CI: 0.02–0.25)<br>$t = 2.42$, $p < 0.05$<br>YGTSS TTS:<br>β = 0.08 (95% CI: 0.00–0.16)<br>$t = 2.02$, $p < 0.05$ |

§*MAIA-2 composite variable = mean of MAIA-2 Noticing, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting Subscale.*
†*VIF, variance inflation factor.*
¶*AIC, Akaike information criteria.*

difference (with the BPQ) (53). Importantly, neither of these studies incorporated sex or severity of co-occurring psychiatric symptoms into their analyses (53, 56). These clinical factors are critical considerations in studies of interoceptive sensibility given evidence of divergent interoceptive sensibility between the sexes (65, 91) and atypical interoceptive sensibility in depressive (92, 93), anxiety (94, 95), and obsessive-compulsive disorders (64). Among individuals with CTD, lifetime prevalence of depression, anxiety, and OCD is 30, 36, and 66%, respectively (57), highlighting the relevance of these conditions when researching interoception in CTD populations. In our sample, after adjusting for covariates, the MAIA-2 Not-Worrying subscale score was independently associated with sex and severity of obsessive-compulsive symptoms, but not with CTD diagnosis. Additionally, CTD diagnosis did not significantly contribute to model goodness-of-fit. Collectively, these findings suggest that observed between-group differences in anxiety-associated somatization were more attributable to obsessive-compulsive symptoms (since groups were sex-matched) than to CTD diagnosis. Female participants and participants with more severe obsessive-compulsive symptoms reported a greater tendency to worry about uncomfortable bodily sensations. These findings align with results from studies in non-tic disorder populations. In a large community sample ($n$ = 367), women and men

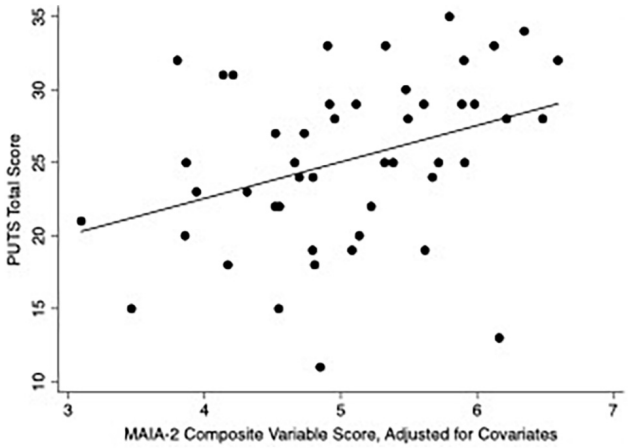


**FIGURE 2 |** Scatterplot of PUTS score versus MAIA-2 composite variable score. The MAIA-2 composite variable score is the mean of the scores from the following six MAIA-2 subscales: Noticing, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting. for the above plot, the composite score was adjusted for MAIA-2 Not-Worrying score, MAIA-2 Not-Distracting score, DOCS score, and YGTSS Total Tic Score, by inserting CTD-group median values for these variables into the regression model.

displayed distinct interoceptive sensibility profiles, with women tending to more frequently attend to bodily sensations, relate emotional state with bodily sensations, and experience distress with uncomfortable bodily sensations (96). Sex differences in interoceptive sensibility and accuracy are posited (91) to contribute to sex-specific vulnerabilities (91), symptom profiles (91, 97), and treatment responses (65) in anxiety and depression. Previous studies have revealed that individuals with OCD also exhibit heightened worry about uncomfortable bodily sensations, as well as greater tendency to distract themselves from bodily sensations and to experience the body as untrustworthy (64). In conjunction with this prior research, the current study findings suggest the relationships of sex and obsessive-compulsive symptoms with the anxiety-associated dimension of interoceptive sensibility are transdiagnostic. Results underscore the need to assess and adjust for sex and common co-occurring psychiatric symptoms when examining interoceptive sensibility in CTD.

Adults with CTD in the current study also reported an enhanced general awareness of bodily sensations, as reflected in their higher MAIA-2 Noticing subscale scores, compared to healthy controls. However, in the regression analysis, CTD diagnosis, severity of co-occurring psychiatric symptoms, and sex collectively explained a low percentage of the Noticing subscale score variance, and none of these variables were significantly associated with the subscale score. Furthermore, MAIA-2 Noticing subscale score did not significantly correlate with scores of any non-MAIA-2 measures in CTD or control participants. While all other MAIA-2 subscales assess an adaptive dimension of interoceptive sensibility, the Noticing subscale indexes a neutral dimension (74), with questions such as "I notice changes in my breathing, such as whether it slows down or speeds up." Notably, individuals with OCD also have elevated scores on this subscale (64). Further research with larger sample sizes may help to clarify the relationship of this Noticing dimension of interoceptive sensibility to other facets of the CTD phenotype.

CTD and control participants in our study did not significantly differ on any other MAIA-2 subscales. Between-group differences in the Trusting subscale scores approached significance ($p$ = 0.046), with the CTD group more likely to experience the body as untrustworthy. The increased tendency to distrust (lower Trusting subscale score) and to worry about bodily discomfort (lower Not-Worrying subscale score) are consistent with a maladaptive interoceptive sensibility profile. Dimensional profiles of interoceptive sensibility vary across mental health (64, 98–100) and pain (101, 102) disorders, and individual dimensions appear to have prognostic value in certain settings (65, 100, 103). Future studies of interoceptive sensibility in CTD should account for the multidimensionality of this construct.

The relationship between interoceptive sensibility and premonitory urge in CTD is of considerable interest given the phenomenological overlap and shared neural underpinnings (as will be discussed below) between these phenomena. In our sample, after controlling for severity of tics and obsessive-compulsive symptoms, premonitory urge was significantly associated with the composite of MAIA-2 Noticing, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting subscales. Higher score on this MAIA-2 composite variable was associated with more severe premonitory urge. The six subscales comprising this MAIA-2 composite variable have collectively been labeled a general measure of body awareness since, as a group, they reflect perception of bodily "changes and rhythms" rather than of bodily response to negative emotions (87). In contrast, the MAIA-2 Not-Worrying and Not-Distracting subscales focus on reactions to bodily pain and discomfort (87). The MAIA-2 Not-Worrying subscale, in particular, correlates closely with anxiety measures (41, 87, 88). Prior studies examining the association between premonitory urge and interoceptive sensibility in CTD have used measures of interoceptive sensibility that primarily assess anxiety-associated somatization: Rae et al. (using the BPQ) observed a significant correlation between urge and interoceptive sensibility (53), while Eddy et al. (using the PBCS) did not (56). Neither study accounted for co-occurring psychiatric diagnoses or symptoms in their analyses. It is notable that in the current study, premonitory urge severity correlated more strongly with the MAIA-2 Not-Worrying subscale ($r_s$ = –0.44) than with the other MAIA-2 subscales. However, after controlling for the multiple dimensions of interoceptive sensibility, as well as for severity of obsessive-compulsive symptoms and tics, the general measure of body awareness was significantly associated with premonitory urge severity, while the Not-Worrying subscale was not.

The above finding has potential therapeutic implications. Premonitory urges are experienced by 80–90% of adolescents and adults with CTD and are more distressing than tics for many patients (51). Premonitory urges also serve as an integral component of comprehensive behavioral intervention for tics (CBIT), an evidenced-based therapy for tics with a

treatment effect size similar to approved medications (104) and sustained benefit for at least six months post-treatment (105). During CBIT, patients are first trained to self-monitor for a specific tic and its associated premonitory urge (104). Patients then learn to implement a volitional movement physically incompatible with the tic (a so-called competing response) when the premonitory urge is detected. Given CBIT's operational reliance on premonitory urge, one might speculate that severity of urges would portend better response to this intervention. However, in a pooled analysis of adults and children with CTD ($n$ = 248), baseline severity of premonitory urges predicted less improvement with CBIT (106). In that same analysis, severity of premonitory urges failed to improve at the end of the 10-week CBIT treatment period, even though tic severity significantly decreased (106). This and other evidence (107, 108) demonstrate that severity of tics and premonitory urges are dissociable, and in fact, decoupling of the premonitory-urge tic complex is one mechanism by which CBIT is postulated to exert its effect (105). Ultimately, the presence of the premonitory urge itself may be less clinically important than the valence attached to the urge. Under this theoretical framework, a key function of CBIT is to facilitate re-appraisal of premonitory urges as non-threatening phenomena that permit adaptive behaviors. More generally, re-tuning conscious and subconscious responses to somatic sensations is commonly employed in numerous behavioral interventions across various disorders. For example, addition of interoceptive training to standard therapies for anxiety disorders (109, 110), eating disorders (111), and select pain disorders (112, 113) yields incremental benefit in mitigating symptoms, demonstrating the transdiagnostic utility of such an approach. A more refined understanding of the relationship between interoceptive sensibility and premonitory urge may allow further optimization of behavioral therapies for CTD.

The current study assessed interoceptive sensibility, but interoceptive accuracy is also aberrant in CTDs. Both adults (52) and children (55) with CTD exhibit reduced interoceptive accuracy, as gauged by a heartbeat counting task. Notably, another study comparing adults with CTD and healthy controls did not identify between-group differences in a heartbeat counting task or a heartbeat discrimination task, but the investigators did observe that the discrepancy between interoceptive accuracy and interoceptive sensibility (so-called trait interoceptive predictive error) was significantly greater in CTD participants (53). This discordance between interoceptive accuracy and interoceptive sensibility suggests these individuals experience heightened subjective responses to bodily signals but exhibit a diminished ability to objectively detect those signals (53). High trait interoceptive predictive error is also evident in individuals with autism spectrum disorder (49, 114) and anxiety (49). Some investigators propose, under a Bayesian predictive coding framework, that the mismatch between interoceptive accuracy and interoceptive sensibility is more relevant than either phenomenon considered in isolation (49, 115, 116).

Both interoceptive accuracy (34, 41, 42) and interoceptive sensibility (41) are subserved by the insula, a structure strongly implicated in CTD pathophysiology as well (51). The insula is functionally segregated into posterior, ventral anterior, and dorsal anterior subdivisions (61). Bottom-up interoceptive signals from the body are received in the posterior insula and there integrated with exteroceptive and proprioceptive inputs (34). This information is then relayed to the ventral anterior and dorsal anterior insula where it is assimilated with top-down emotional and cognitive input from other cortical and sub-cortical structures, yielding a complex, topographically-organized representation of the bodily state contingent on physiology, affect, and prior beliefs (30, 34, 61). In accord with this empirically grounded model, individual differences in insular structure and function predict interoceptive accuracy and interoceptive sensibility. Enhanced hemodynamic activity in the right insula predicts healthy individuals' accuracy in a heartbeat detection task (42), and increased gray matter volume in the same region correlates with increased task accuracy and increased subjective awareness of bodily sensations (42). Maladaptive dimensions of interoceptive sensibility (specifically, decreased attentional control and increased distraction and worry) are associated with increased hemodynamic activity in a distributed network involving the insula, somatosensory cortex, motor cortex, and cingulate cortex (41). Given the critical role of the insula in subserving interoception and given the altered interoception in CTDs, it is unsurprising that abnormalities in insular structure and function have been observed in CTD populations. In TS, the insula exhibits reduced cortical thickness (117), reduced $GABA_A$ receptor binding (27), and enhanced functional connectivity with frontal and striatal regions (118). Of the clinical manifestations of CTD, the insula is most clearly linked with premonitory urge. Severity of premonitory urges correlates with left insula cortical thickness (117) and with extent of functional connectivity between the right insula and the bilateral supplementary motor areas (118). In the one to two seconds preceding a tic, when premonitory urges are subjectively experienced, a diffuse cortical network involving the insula activates (119, 120). These tic disorder-specific findings align with the wider literature demonstrating that the insula subserves urge-to-action (51) and provides essential input to inform movement (30). Future research is needed to explore the relationship of insular structure and function to interoception anomalies in CTDs.

Additionally, given evidence of interoception abnormalities in many neurodevelopmental and mental health disorders, cross-disorder comparisons of interoception are of prime interest. In particular, research directly comparing interoception between CTD and OCD populations would significantly advance insight into the transdiagnostic impact of altered interoception. As discussed previously, one dimension of interoceptive sensibility, anxiety-associated somatization, is prevalent in both CTD and OCD samples (56, 61, 64). Furthermore, among both CTD and OCD populations, many individuals experience "not just right" sensations (51, 64). In CTD, such sensations manifest as premonitory urges with this specific quality (51), while in OCD, the sensations occur in the context of repetitive behaviors (64). Severity of "not just right" sensations in OCD correlates

with overall tendency to notice bodily sensations (as indexed by the MAIA Noticing subscale) (64). Recent translational work showed that distinct facets of interoceptive sensibility in OCD are differentially associated with insula functional connectivity (121). Cross-disorder investigations promise to further elucidate the neural mechanisms underpinning the sensory dysfunction evident in CTD and OCD.

Our study has several notable limitations. First, while our sample size was larger than previous studies examining interoceptive sensibility in CTD, we may have been underpowered to detect possible between-group differences across all dimensions of interoceptive sensibility. Second, due to the study sample size and number of variables under consideration, our regression analyses did not incorporate interaction or medication terms. Third, co-occurring psychiatric symptoms were quantified with self-report scales rather than gold-standard clinician-administered measures, though the scales employed demonstrate good convergent validity with clinician-administered instruments (76–79). Last, the majority of CTD participants were recruited from a tertiary care clinic, and across both CTD and control groups, participants were predominantly white and non-Hispanic. Both of these issues undermine generalizability of the study findings to the broader, diverse CTD population. The relevance of study findings to the pediatric CTD population is also unclear. One study has examined interoceptive accuracy in children with CTD (55), but to our knowledge, no studies have assessed interoceptive sensibility in this population, precluding results comparison between pediatric and adult CTD samples.

Despite the above limitations, study results revealed three novel findings: adults with CTD experience increased anxiety-associated somatization and increased general body awareness relative to healthy controls; anxiety-associated somatization is more closely associated with sex and obsessive-compulsive symptoms than with CTD diagnosis; and increased general body awareness is associated with greater severity of premonitory urges. Future research is warranted to determine the therapeutic relevance of interoceptive sensibility for CTDs and to clarify the translational links between interoceptive sensibility, interoceptive accuracy, and CTD neurobiology.

## DATA AVAILABILITY STATEMENT

The raw, de-identified data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Vanderbilt Human Research Protections Program. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

AN and DI conceived and designed the study, with assistance from CC. ME and DI implemented the study protocol and collected the data. AN and DI performed the statistical analysis and drafted the initial manuscript. ME, HR, and CC critically reviewed and revised the manuscript. All authors approved the submitted version of the manuscript.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.914897/full#supplementary-material

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# The Rise of Functional Tic-Like Behaviors: What Do the COVID-19 Pandemic and Social Media Have to Do With It? A Narrative Review

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**Background:** There has been a rise in explosive onset of tic-like behaviors during the COVID-19 pandemic. Historically, this is an uncommon phenomenology of functional movement disorders across all ages. Both the psychological burden of the pandemic and social media usage have been implicated in the rise of these tic-like behaviors.

**Methods:** This paper provides a narrative review of the literature on chronic tic disorders, functional tics, and mass functional illness with particular focus on the key distinguishing features, role of social media, and the role of COVID-19.

**Results:** The COVID-19 pandemic has profoundly affected the mental health of many individuals, including children, adolescents, and their caregivers. Implementation of lockdowns, lifestyle disruptions, school closures, and social distancing have driven a surge in social media and digital technology use. The combination of predisposing factors, the psychological burden of the COVID-19 pandemic, and social media are implicated in the rise and spread of tic-like behaviors; which may represent a modern-day form of mass functional illness. While many of the features overlap with functional tics, there are emerging distinctive features that are important to recognize. A more encompassing term, *Functional Tic-Like Behaviors,* is used to better reflect multiple contributing factors.

**Conclusion:** Knowledge of these differences is essential to mitigate downstream health effects and poor outcomes.

**Keywords: tourette, tic, functional tic, functional movement disorders, mass psychogenic illness, TikTok, COVID-19, tic-like behavior**

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## INTRODUCTION

In December 2019, a novel coronavirus (COVID-19) was discovered in Wuhan, China. By March 11, 2020, the World Health Organization (WHO) declared a global pandemic of severe acute respiratory syndrome due to coronavirus-2 (SARS-CoV-2)[1]. This led to implementation of lockdowns, lifestyle disruptions, school closures, and social distancing. To date, there

[1]World Health Organization. (2020). Director-General media briefing on COVID-19. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-$-$11-march-2020 (Accessed 11/4/2021).

have been 246 million confirmed cases and 4.9 million deaths from COVID-19 worldwide[2].

There is mounting evidence of potential neurological and psychological sequela of COVID-19. Peripheral and central neurological complications of COVID-19 infections have reported (1–5) as have rising rates of stress, anxiety, depression, and behavioral problems (6).

During this time, there has been an increase in functional tics (FT) and functional tic-like behaviors (FTLB). Abrupt onset, atypical progression of symptoms, poorly localized premonitory sensation, high-degree of suggestibility, lack of suppressibility, and complete distractibility help distinguish FT from chronic tic disorders (CTD), including Tourette Syndrome (TS). Previously an uncommon phenomenology of functional movement disorders (FMD) (7–11), the rise in FTLB presents an opportunity to understand the overlapping and distinguishing features of this disorder from CTD and FT. Both social media and the psychological burden of the COVID-19 pandemic have been implicated in this increase.

As research in this area is rapidly evolving, the purpose of this article is to provide a narrative summary of our current understanding of FT, FTLB, and mass functional illness, with particular focus on the distinguishing features, social media, and the role of COVID-19. Early recognition of FT and FTLB is essential for improved outcomes (12, 13).

## METHODS

A narrative review was chosen as the synthesis method due to rapidly evolving research in this area. The literature search was conducted using PubMed, Embase, and Web of Science between 2006 through 2021. A modified Patient Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) figure is included (**Figure 1**). A combination of search terms produced 6,925 results. Initial search terms included "tic" or "tourette" and "COVID," "social media," "TikTok," "functional," "psychogenic," or "like-behavior." Both "functional" and "psychogenic movement disorders" in context of COVID and pediatrics were also searched. Additionally, the various names for mass functional illness were searched. Inclusion criteria included English literature with publication dates between 2006 and 2021. No specific type of study or age range were excluded from the search. Use of the term functional yielded many non-relevant results related to functional imaging, disability, and anatomy. After removal of duplicates, non-relevant, and non-English literature, as well as backwards snowballing, 118 articles were included for final review. Given the topic of social media, additional publicly available content was included in the review as noted in the footnotes.

## Chronic Tic Disorders

Tics are sudden, rapid, non-rhythmic movements or vocalizations, which occur in 1 in 5 school-aged children (14). Chronic Tic Disorders (CTD), including Tourette Syndrome (TS), are developmental neurobiological disorders characterized by multiple motor and/or vocal tics for at least 1 year. Co-occurring conditions such as attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and anxiety occur in 90% of individuals with CTD (15–19).

Tics begin gradually in early childhood, fluctuate, and change over time (16, 18, 20). There is a male predominance of tics, 4:1 male to female ratio, which diminishes in adulthood (18, 20, 21). For the vast majority of individuals with CTD, tics peak in the peri-pubertal period and improve through adolescence (20).

Tics often begin as simple motor tics and progress over time in a rostro-caudal distribution (22). Tics are preceded by a premonitory urge, often localized to the affected body region (23). Premonitory urges are an itch, tension, need or unpleasant sensation that builds with voluntary suppression and is relieved by completing the tic (24, 25). Recognition of premonitory urges tends to occur between 8 and 10 years old, although is reported by the majority of individuals with CTD (24, 26, 27).

Whether the phenotype of TS is different in affected females is poorly understood. There are conflicting reports on the sex-differences of comorbidity prevalence (16, 18, 21, 28–32). Some studies have reported TS-affected females have later onset of tics (16, 33, 34), later peak of tic severity (29, 34), motor tic severity (32, 33), and lower likelihood of tic remission; however, others have shown conflicting results or no significant sex-differences in these factors (18, 28, 32, 33, 35).

Complex tics, including coprophenomena, echophenomena and self-injurious behaviors (SIB) are often misunderstood by the public (36). Risk of coprophenomena such as obscene gestures (copropraxia) or words (coprolalia) increases with age and co-occurring conditions. Coprolalia is three times more common than copropraxia, with a lifetime prevalence of 8–18.5 and 5.7% respectively and often occurs within 5 years of tic onset (18, 37–39).

Echophenomena refers to the repetition of other's actions (echopraxia) or sounds/words (echolalia). In the original publications from Georges Gilles de la Tourette, the persistence of echophenomena beyond normal expected childhood development was essential for the diagnosis of TS (40). Given the heterogeneity of CTD, echophenomena are now considered a distinctive feature rather than a requirement for diagnosis (41), with an estimated lifetime prevalence 43–56% (42, 43).

SIB can occur in 4–53% of individuals with CTD (18, 44, 45). Estimates vary depending on the definition of SIB, which can range from skin picking or scratching, biting, head banging, or self-hitting, to more severe symptoms such as self-cutting, body deformation, or self-mutilation (46). Rarely, individuals affected with TS can have life-threating symptoms (44, 47).

**Abbreviations:** COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome due to coronavirus-2; FMD, functional movement disorder; FT, functional tics; FND, functional neurological disorder; CTD, chronic tic disorders; TS, Tourette Syndrome; ADHD, attention deficit-hyperactivity disorder; OCD, obsessive-compulsive disorder; MFI, mass functional illness; PNES, psychogenic non-epileptic spells; MSMI, mass social media-induced illness; UNESCO, United Nations Education, Scientific and Cultural Organization.

[2]World Health Organization. (2020). Coronavirus (COVID-19) Dashboard. https://covid19.who.int/ (Accessed 11/2/2021).

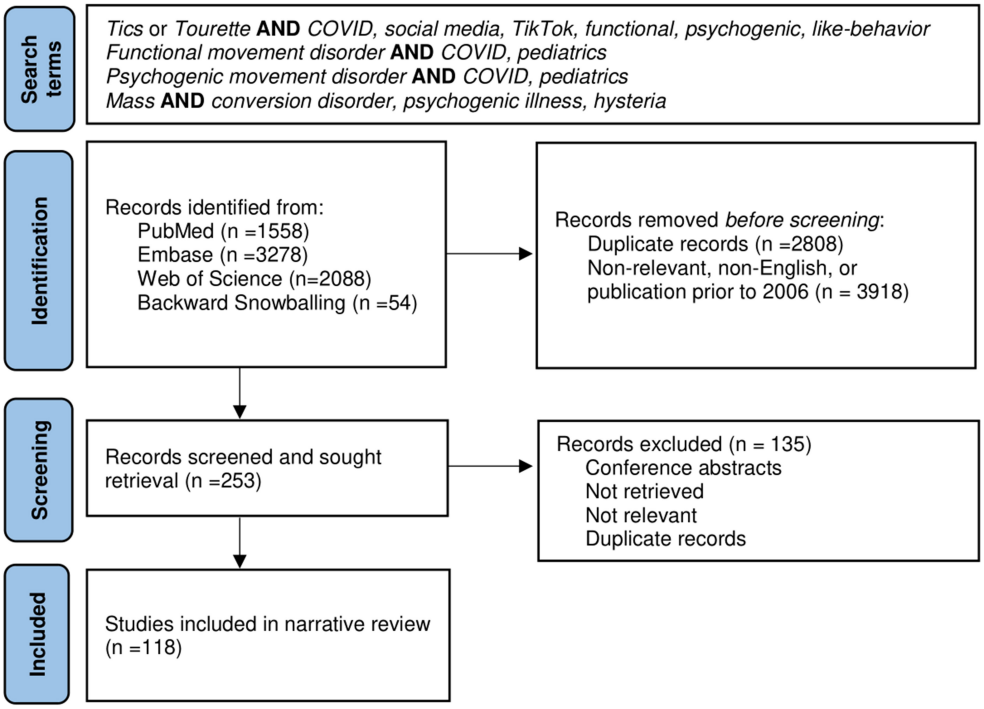


**FIGURE 1 |** Modified Patient Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Figure.

## Functional Movement Disorders

Functional movement disorders (FMD) are a common presentation in neurology clinics (48). Many different terms have described these disorders including conversion disorder, psychogenic, nonorganic, medically unexplained, and hysteria (49, 50). Although *psychogenic* and *functional* are often use interchangeably, *functional* is the preferred terminology. Functional is freer of stigma and more reflective of the current understanding of the pathophysiology on FMD, which suggest a neurobiological basis of these disorders (12, 49, 51, 52). A combination of predisposing, precipitating, and perpetuating factors play a role in development of FMD. Psychosocial stressors, low socioeconomic status, psychiatric comorbidities, female gender, and adverse experiences may increase risk of FMD. It is hypothesized that both epigenetic and genetic factors may contribute to FMD, but current evidence is limited (53). Additionally, brain maladaptation and plasticity may serve as perpetuating factors for FMD (12, 49, 54–56). The Diagnostic and Statistical Manual for Mental Disorders–Fifth Edition (DSM-5) adopted new emphasis on diagnosing based on positive features and removed the necessity of a precipitating stressor as with many patients none are found (57).

## Epidemiology of Functional Tics

The true prevalence of FMD is hard to discern given diagnostic uncertainty, inconsistent terminology, and variability of utilized billing codes (48, 58). Diagnosis relies on inconsistencies and incongruences with known movement disorders. Across all ages, tremor, dystonia and gait disorders are the most common phenomenology of FMD, and FT were rarely reported (13, 59–61).

Estimates of pediatric FT prevalence vary from 0 to 17% (61–64). The rarity of FT may be attributed to the challenge in distinguishing FT from CTD. Many of the positive features used to diagnose FMDs such as distractibility, suggestibility, and fluctuating course are common amongst CTD. Clinical expertise and prior case studies suggest there are some key distinguishing features (10, 12, 65–68). While most individuals with pre-existing FMD reported no change in symptoms with the COVID-19 pandemic, there has been a dramatic increase in new FT (7–11, 69, 70).

## Clinical Phenomenology of Functional Tics

FT have key clinical characteristics that distinguish them from CTD. FT present in adolescents often without a prior history of tics. There is a 3:1 to 9:1 female predominance in FTs. This is in contrast to CTD, which are heavily male dominant (13, 20, 59, 61, 71). Common features include abrupt onset followed by a static or progressive course, high-degree of suggestibility, and complete distractibility. FT lack suppressibility, build up with voluntary suppression, or relief upon completion of the tics (65, 66). Although the presence or absence of a premonitory urge is less definitive, when present in FT it is less often localized to the area of the tic-like behavior (11, 72, 73).

Unlike CTD, FT include complex and large amplitude movements at onset (11). Complex tics such as pali-, echo-, and copro-phenomena are less common in FT and are often more complex, variable, longer in duration, or context-dependent (72, 74, 75). The progression of FT tends to disregard the expected rostro-caudal distribution seen in CTD (66, 76). Frequently other functional neurological or somatic symptoms are present (65, 66).

Some studies note a lack of family history of tics in individuals with FT; however, an important caveat is that there may be a heredity component to FMD (51, 65, 77, 78). There is also potential for false-negative family history, as some may not recognize they had tics previously. Alternatively, a false-positive family history can occur given the prevalence of CTD. Additionally, while a precipitating event can occur, it is important to note stressors and adverse experiences are risk factors rather than requirements for diagnosis (13, 50, 64, 65). Treatment resistance to typical tic medications may also occur (65, 66).

## Mass Functional Illness

Mass Functional Illness (MFI), also known as mass psychogenic illness, mass hysteria, mass conversion disorder, or mass sociogenic illness, is "the rapid spread of illness signs and symptoms affecting members of a cohesive group" (79). MFI has been described for many centuries and occurs in varied cultures, ethnic groups, and religious settings (79, 80).

Historically, there are two categories of MFI: anxiety or motor phenomena. Anxiety MFI is characterized by transient, benign symptoms typically resolving within 24 h when there is a sudden, extreme stress or perceived threat in a cohesive group (81). Symptoms can include dizziness, headache, fatigue or hyperventilation. Motor MFI typically presents with gradual onset of motor symptoms including hyper- or hypo-kinetic movements, gait abnormalities and speech difficulties. Symptoms evolve over weeks to months and gradually remit.

Over the past two decades there has been increased motor presentations. There are many examples throughout recent history of MFI including outbreaks of non-epileptic spells, weakness, twitching, and gait abnormalities often in adolescent females (82–86)[3].

Perhaps one of the most notable relevant examples was the outbreak of sudden onset of tic-like behaviors in August 2011 through January 2012 at Le Roy High School in Western New York State (68). The 19 affected individuals (18 females, 1 male), who did not belong to the same social group initially, formed a new social group based on their common disorder. Similarly, there were two outbreaks of hiccups and vocal tic-like behaviors of over a dozen students in two nearby Massachusetts high schools in November 2012 and January 2013 (87).

Like FMD, females have been reported to have a higher propensity to MFI (88, 89). A recent meta-analysis of gender differences showed 2.4:1 female predominance of MFI in children and adolescent (90). These outbreaks become the target of substantial media attention as well as thorough investigations into exposures, recent vaccinations, or environmental triggers (90–93).

## Role of Social Media

Presence of movement disorders on social media is not novel. Review of videos on YouTube in 2011 by movement disorder specialists revealed 66% of movement-related videos were FMD (94). Interestingly enough, 18% (5,450/30,095) of movement-related videos reviewed were categorized as tic-related content.

Historically, MFI has been limited to a cohesive group; however, in the modern-day era, social media breaks the geographic barriers that typically confine such symptoms. Bartholomew was one of the first to propose the role of social media in MFI (81, 87). YouTube and Facebook were implicated in the spread of tic-like behaviors in Le Roy, as affected individuals were uploading videos of their symptoms onto these social media sites[4,5,6,7].

A similar phenomena occurred in Germany in June 2019 when German Neurologists saw a vast rise in FT strikingly similar to a popular YouTube Channel "Gewitter im Kopf [Thunderstorm in the Brain]", staring a young man Jan Zimmerman (95, 96). The channel gained rapid popularity and has more than 2.2 million subscribers and 312 million views[8]. Zimmerman has a similarly large presence across multiple platforms. Individuals presented with near identical complex movements, vocalizations, and unique words or phrases often seen in Zimmerman's videos. Given the specific role of social media, a more specific term was suggested - mass social media-induced illness (MSMI) (95).

The benefits and risks of social media remain controversial. Some argue that social media and digital technology help maintain social connection despite social distancing and lockdowns (97). Social media can also serve as a platform for individuals to share their experiences, advocate, and educate about medical conditions including tics. However, drawing attention to tics and/or exposure to other's tic-like behaviors may serve as precipitating or perpetuating risk factors for both FT and CTD. While social media provides access to communities that may not be readily available locally, this may also serve as a medium for continued spread of FT. Additionally, overuse of social media is associated with anxiety, depression, and

[3]The New York Times. (2007). Mysterious illness strikes teenage girls in Mexico. https://www.nytimes.com/2007/04/16/world/americas/16iht-mexico.3.5306132.html (Accessed 10/26/2021).

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[6]TODAY. (2012). Facebook, YouTube could be spreading 'mystery illness,' doctor says. https://www.today.com/health/facebook-youtube-could-be-spreading-mystery-illness-doctor-says-1C9381793 (Accessed 10/26/2021).

[7]Huffpost. (2014). When Social Media Makes Something Go Viral In Real Life. https://www.huffpost.com/entry/dont-look-now-social-medi_b_5534200 (Accessed 10/26/2021).

[8]YouTube. (2005). Gewitterimkopf. https://www.youtube.com/c/gewitterimkopf/about (Accessed 10/28/2021).

psychological distress all of which may serve as risk factors for FT (98, 99).

## TikTok Tics

Tic-related videos are gaining popularity across social media and the rapid spread of tic-like behaviors is a global phenomenon. On TikTok alone, hashtags of #tourette (4.9 billion views) and #tic (3.1 billion) have grown substantially during the COVID-19 pandemic[9], hence what some are calling "TikTok Tics".

TikTok is a popular social media platform where users can create, watch and share short videos. TikTok has experienced a surge in monthly active users between January 2018 and August 2020. Globally TikTok's active monthly users has grown from 54 million users in January 2018 to over 1 billion users as of September 2021[10,11]. For comparison of active monthly users across other social media platforms Facebook has 2.9 billion, YouTube 2.3 billion, WhatsApp 2 billion, Instagram 1.4 billion, Snapchat 538 million, and Twitter 436 million[12].

It is important to note that tic-related videos have grown substantially across multiple social media platforms and are not exclusive to TikTok. For example, TikTok influencer Evie Meg, better known as @thistrippyhippie, has 14 million followers for her tic-like behavior but also 791k followers on Instagram and 25 million views on YouTube[13,14,15]. Her videos often feature complex movements, coprophenomena, unique triggers and context-dependent tics. This influencer discloses her diagnosis of FND and features other videos of functional dystonia and psychogenic non-epileptic spells (PNES).

Two studies assessed the phenomenology of tic-like behavior on TikTok based on expert review. Both studies found a high degree of coprophenomena, context-dependence, aggression toward others, and self-injurious behavior (7, 100). Tic-like behaviors were highly variable and nonstereotyped. While tic-like behavior often involved the face and neck, there was a higher percentage of movements involving arms or body. Tic severity was overall severe with a high degree of tic attacks reported. There was a female predominance with 64.3% female, 17.6% male, and 14.3% nonbinary based on self-report of gender identity in the user's profile (7). Mean age reported was 18.8 years old although limitations included lack of age disclosure as well as unclear timing of video to onset of symptoms (7).

While these descriptive analyses are important to exploring the relationship of social media and tic-like behaviors, these conclusions were based on observations of social media videos rather than in-depth in-person evaluations. Additionally, negative portrayals of CTD are more popular on social media (101) and may influence the phenomenology reviewed by these two studies.

There has been some question of secondary gain in use of social media. Many of these social media influencers have merchandise for purchase (7). Jan Zimmerman sells merchandise, a book and recently released a Google app with his most popular vocal tics including "tics of the month." Evie Meg released her new book "My Non-Identical Twin: What I'd like you to know about living with Tourette's" (7, 102, 103). It is important to note that factitious disorders and malingering are distinctly different from FMD and are beyond the scope of this article.

## Functional Tic-Like Behaviors

While many of the features overlap with FT, there are emerging distinctive features (**Figure 2**, **Supplementary Table 1**). A more encompassing term is used, *Functional Tic-Like Behaviors* (FTLB) to better reflect the combined role of social media and the pandemic.

FLTB have a female predominance (11) with the exception of one report from Germany (96), which had a male predominance. It is possible that this is related to the German social media influencer previously discussed. Median age of FTLB onset ranges from 14.2 to 15.3 years old with initial presentations being abrupt onset, non-fluctuating, and predominately complex tic-like behavior (11, 96, 104). Studies note a higher prevalence of tic-like behavior involving the trunk and extremities relative to the expected rostro-caudal progression seen in CTD (11, 96, 104). Pringsheim et al. reported a higher proportion of anxiety and depression diagnoses in FTLB compared to primary tic disorders (11), whereas others have found no significant difference (96).

FTLB are associated with high prevalence of coprophenomena, odd words or phrases, self-injurious (SIB) and non-obscene socially inappropriate behavior (NOSIB) (7, 71). Additionally, unique or contextual triggers such as particular words, flashing lights, or loud noises can trigger the tics or tic attacks (96, 104). Common SIB include hitting, punching or slapping one's self. Conversely, NOSIB can present as hitting others, throwing or hitting objects (11, 104). Tic attacks and presence of other functional or somatic symptoms were commonly reported (104). There are more limited data and variability in the degree of suppressibility, family history of tics, and presence of premonitory urge in patients with FTLB (11, 96). Careful questioning may endorse exposure to tic-related videos on social media; however, it should be considered one of many risk factors and is not always found (11, 96).

Although the predominance of adolescent females is reported, other sociodemographic features associated with FTLB remain unknown. Further exploration of risk factors and social determinants of health would be useful for prevention and intervention planning.

[9]TikTok. (2016). Tag: Tourette's. https://www.tiktok.com/tag/tourettes?lang=en (Accessed 10/28/2021).

[10]CNBC. (2021). TikTok says 1 billion people use the app each month. https://www.cnbc.com/2021/09/27/tiktok-reaches-1-billion-monthly-users.html (Accessed 10/27/2021).

[11]TikTok. (2021) TikTok Newsroom: Thanks a billion!. https://newsroom.tiktok.com/en-us/1-billion-people-on-tiktok (Accessed 10/27/2021).

[12]Datareportal. (2021) Global Social Media Stats. https://datareportal.com/social-media-users (Accessed 10/27/2021).

[13]Social Blade. (2018). User Summary: This Trippy Hippie - YouTube. https://socialblade.com/youtube/channel/UCJHvN0zYgO2ZLjePERRLjKQ (Accessed 10/28/2021).

[14]Social Blade. (2018). User Summary thistrippyhippie – TikTok. https://socialblade.com/tiktok/user/thistrippyhippie (Accessed 10/28/2021).

[15]Social Blade. (2018) User Summary eviemeg – Instagram. https://socialblade.com/instagram/user/eviemeg (Accessed 10/28/2021).

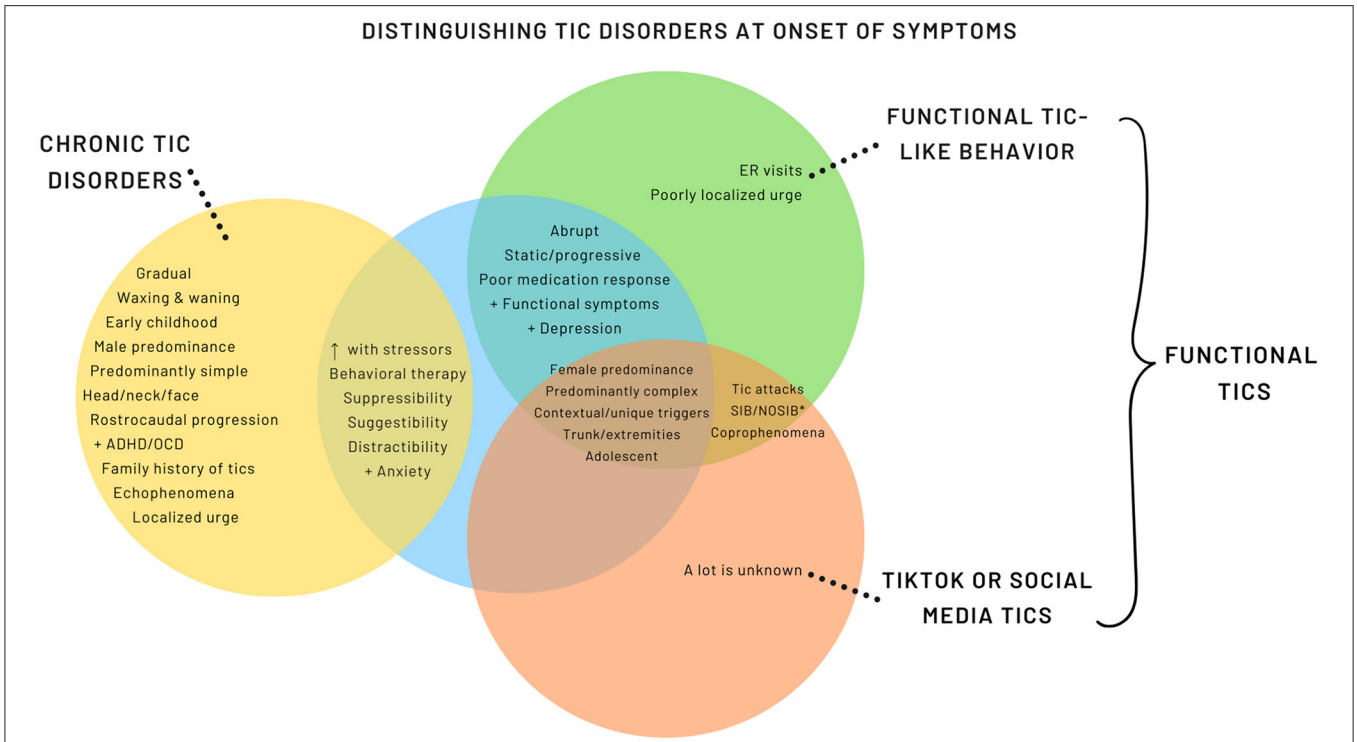


**FIGURE 2 |** Distinguishing Tic Disorders at Onset of Symptoms. *SIB, Self-injurious behavior; NOSIB, Non-obscene socially inappropriate behavior.

## Role of the COVID-19 Pandemic

There is mounting evidence on the neurological sequela of COVID-19 infections including new development of movement disorders. Although one may consider post-infectious or infectious phenomena of COVID-19, a recent review of de novo movement disorders related to COVID-19 infections did not report any cases of new tics or tic-like behavior (105).

However, the COVID-19 pandemic has profoundly affected the mental health of many individuals, including children and adolescents. Nearly 168 million children globally missed an entire year of school due to COVID-19 according to the United Nations Education, Scientific and Cultural Organization (UNESCO). In April 2020, 1.5 billion learners were affected by school closures in 195 countries and as of November 2021, 55 million learners were still impacted by school closures with lower socio-economic statuses disproportionally affected (106)[16,17].

Prior studies demonstrated both short- and long-term psychological effects of pandemics/epidemics including increased post-traumatic stress symptoms, anxiety, depression, helplessness, and risky behaviors (107–113). The overall rates of depression and anxiety are higher during COVID-19 than prior pandemics (114), with increased risk in females, adolescents, and remote learners (106, 107, 114–121). Periods of intense stress, such as the pandemic, can be associated with increased functional symptoms (122–124).

Parental stress, mental health, and wellbeing are also impacted during the pandemic, which is associated with poorer child wellbeing (125–128). Disruptions from the pandemic altered diets, sleep schedules, and social relationships. Additionally, parents reported interrupted access to medical care and to their support networks. Parents and/or caregivers suffered from isolation, employment changes, food insecurity, housing instability, and financial constraints all while balancing remote-learning and their child's wellbeing (125). Lower socioeconomic status, younger parents, and families of healthcare workers have been reported to be at increased risk of poorer wellbeing (129, 130). Additionally, there are increased reports of childhood adverse experiences during the pandemic, such as witnessed domestic violence, emotional abuse, and physical abuse (131, 132).

There has been an overall increase in new FMD presenting to neurology clinics during the COVID-19 pandemic (10). Despite this increase, individuals with preexisting FMD did not show significant variability or worsening of their symptoms during the pandemic (133). However, up to two-thirds of parents or individuals reported worsening of CTD symptoms (134, 135). Children with neurodevelopmental disorders, such as CTD, report higher behavioral and psychological impacts of the pandemic compared to peers (136). The same is true for

[16]UNESCO. (2021). Education: From disruption to recovery. https://en.unesco.org/covid19/educationresponse#schoolclosures (Accessed 11/01/2021).
[17]UNESCO. (2020). 1.3 billion learners are still affected by school or university closures, as educational institutions start reopening around the world, says UNESCO. https://en.unesco.org/news/13-billion-learners-are-still-affected-school-university-closures-educational-institutions (Accessed 11/1/2021).

children with preexisting mental health diagnoses (125). Acute psychosocial stressors, routine disruption, and increased mental health burden likely play a role in symptom exacerbation or development; however, these relationships need to be further explored (137).

## DISCUSSION

Knowledge of these disorders are vital in mitigating downstream health effects and poor outcomes. A common concern in FMD is fear of misdiagnosis; however, in the modern medical setting the frequency of misdiagnosis is consistently low (138, 139). Recognition of the positive features to support a diagnosis of FMD is essential. While behavioral therapy is the first line treatment for both FMD and CTD, it is critical to establish the diagnosis early and engage familial support (12, 140). Longer duration of symptoms before diagnosis and pre-existing personality disorders lead to poorer outcomes (141, 142). A multidisciplinary approach is essential in effective treatment and psychological support is crucial. The overall mental health burden of the pandemic poses challenges for accessibility to knowledgeable therapists and mental health resources.

Clinicians should also be mindful that FTLBs may co-occur in individuals with CTD or other neurological conditions (143). A sudden or explosive emergence of atypical tic-like behaviors should raise concern of functional overlay (144, 145). Failure to recognize this can lead to unnecessary medication trials, sense of pseudo-refractoriness, potential invasive surgical procedures or delay in diagnosis (61, 146, 147).

The role of social media in these tic-like behaviors has gained significant media attention, which likely contributes to parental fear and uncertainty. Explosive onset of FTLB can be both bothersome and intrusive to the daily function of the individual and their family. This may result in missed days at school, parental missed days of work, missed social events, and/or financial constraints that impacts parental stress and wellbeing. Many patients with explosive onset of FTLB are utilizing emergency room services (9). FMD admissions have higher work-up rates but shorter length of stays. In 2017, the estimated US economic impact of ER and inpatient care of FNDs was more than $1.2 billion annually, comparable to other high-utilization neurological conditions such as refractory epilepsy or demyelinating disorders (58). Recognition of FTLB may reduce unnecessary admissions, diagnostic testing, medication trials, time to treatment, and economic impacts.

The impact this global phenomena has had on the CTD community must also be considered. A look through the comments on these influencers' videos suggests a step backwards in awareness, attitudes, and stigmatization of not only CTD but also FMD community. In CTD, female gender, tic severity and complex tics increase stigmatization risk, which is associated with lower quality of life, depression, and lower self-esteem (36, 148–151). The commonality of these features with FT and FTLB may contribute to ongoing public misconception of individuals with CTD and FMD. Future research should aim to understand the intricacies of stigmatization in these disorders.

Lastly, the rarity of FT previously may have limited our understanding of this disorder. With the rise of FTLB, there is an opportunity to evaluate overlapping and distinguishing features of FT, FTLB, and CTD to establish evidence-based guidelines for evaluation and treatment. Previous studies have suggested some common predisposing factors between CTD and FT such as family history, adverse experiences, and psychosocial stressors (11, 72). Lastly, the etiology of FLTB is likely multifactorial. Future research is necessary to better define the relationship between social media, the pandemic, and these entities as well as further understand shared predisposing, precipitating, and perpetuating factors.

## AUTHOR CONTRIBUTIONS

JMM: conceptualized, drafted the initial manuscript, reviewed, and revised the manuscript. JWM: conceptualized, critically reviewed the manuscript for important intellectual content, and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fped.2022.863919/full#supplementary-material

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# Digital and remote behavioral therapies for treating tic disorders: Recent advances and next steps

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The rapid expansion of access to and engagement with digital technology over the past 15 years has transformed the potential for remote delivery of evidence-based digital health interventions (DHIs). Digital and remote behavioral interventions have the potential to address current gaps in the provision of evidence-based therapies in healthcare services. As the lack of access to behavioral treatments for people with tic disorders is a pressing issue across the world, there is great potential for DHIs to close this treatment gap. Here, we present a critical synthesis of the recent key advances in the field of digitally delivered, remote therapy for tics, outlining the research evidence for the clinical and cost-effectiveness and acceptability of digital or remotely delivered therapy. We found five trials aimed at reducing tic severity in children and young people and one trial for adults. The evidence supports the clinical utility of DHIs to deliver tic therapies, which shows promise in being clinically efficacious compared to an active control. Furthermore, DHIs in trials show good adherence and engagement and are acceptable to patients. The role of human support (including therapists and parents for young people) is likely to be important to encourage adherence. DHIs, where the main therapeutic content is delivered *via* web-based chapters, are likely to reduce clinical time, and maintain intervention fidelity, but further research is required to understand cost-effectiveness. Despite utilizing randomized controlled trials, only two trials were sufficiently powered to address efficacy and only one trial explored contextual factors that may influence engagement. Moreover, only one trial followed patients for >12 months, thus further long-term follow-ups are required. Specifically, we note that despite an emerging evidence base, DHIs for tics are yet to be routinely implemented in healthcare provision in any country. Drawing on the existing evidence, we conclude by

proposing a stepped care model, in which digital therapy is implemented as a widely accessible first-line treatment using a purely online or therapist-supported approach.

KEYWORDS

**tics, Tourette syndrome, review, digital interventions, behavioral therapy, treatment**

## Introduction

Tic disorders, such as Tourette syndrome (TS), affect around 1% of children (1) and around 0.05% of adults (2) and are associated with a range of co-occurring behavioral, motor, and emotional conditions which can have a profound impact on children's and adult's quality of life, school/work experience and peer relationships (3). Although pharmacological interventions can be useful for people with tic disorders, behavioral and educational approaches are generally recommended in guidelines as a first line intervention (4). However, access to evidence-based behavioral therapies is limited due to the small number of highly trained therapists based in a few specialist centers with an uneven geographical distribution of services relative to demand. Digital health interventions (DHIs) provide the opportunity to widen access to psychoeducation and evidence-based behavioral therapies and thus reduce the severity and impact of debilitating conditions such as tic disorders.

Although studies have shown that DHIs can be efficacious in reducing symptom severity in people with tic disorders (5), no DHIs for tic disorders have yet to be implemented into routine clinical care. Digital delivery encompasses different types of treatment with varying active ingredients. The treatments are based on established techniques including Habit Reversal Therapy (HRT), in which patients learn to detect tics and use a competing response (usually an incompatible action) to control them; Comprehensive Behavioral Intervention for Tics (CBIT), which combines HRT with relaxation, functional analysis, and social support; Exposure and Response Prevention (ERP), in which patients learn to suppress their tics (response prevention) while tolerating urges to tic (exposure); and psychoeducation, where the focus is on the history, prevalence, and risk typically associated with tic disorders, and advice on healthy habits but with no information on tic control. Here, we review the recent key advances in the field of digitally delivered and remote therapy for tic disorders, outlining the research evidence for the clinical efficacy and cost-effectiveness and acceptability of these therapies. Efficacy refers to evidence gathered within tightly controlled trials whereas effectiveness refers to trials conducted in real-world settings. We explore strengths and limitations in the research design as well as investigating differences in the therapeutic approaches (i.e., type of therapy, use of blended human support, mode of delivery) of research to date. In doing so, we outline gaps for future research; examine the importance of the human factor in digital modalities, and implications for future care pathways as well as recommendations for practice. This paper examines the evidence for the efficacy of DHIs for tic disorders, which can be used to inform future research looking into the effectiveness of these interventions in order to assess the potential for implementation.

## Overview of digital and remote therapies

Recent advances in the use of digital technology have coincided with increasing rates of mental health and behavioral problems in young people and a growing demand for mental health services that outstrips supply and the capacity of traditional therapeutic approaches to respond. Thus, health services are turning to digital modalities to reach a larger proportion of the population (e.g., people who may be under provided for by standard face-to-face care) in a more efficient and patient-centered manner. DHIs refer to interventions delivered *via* technologies using a range of digital modalities, such as smartphones, applications ("apps"), wearable devices, robotics, websites, social media, or text messaging. DHIs can be used as a platform to help treat a range of physical and psychiatric disorders (6) promote positive health behaviors (7) and even improve outcomes of people with long term conditions (8). There is considerable optimism within the medical community that digital technologies–especially apps used on smartphones, tablets, and watches–could open a new frontier for the implementation of interventions to aid in the recovery from a range of disorders (9). Despite there being an estimated 350,000 health apps available to download across the major app stores (10), the vast majority have little or no evidence base.

These digital interventions may be delivered with varying degrees of human support. On one end of the spectrum, the intervention is delivered in a purely self-directed manner, with no therapist or human support. On the other end of the spectrum, the technology may be simply used as a vehicle for a therapist to remotely deliver therapeutic content in real-time (such as cognitive behavioral therapy delivered *via* videoconferencing). In the middle, there is a more "blended"

approach whereby the technology platform is used to deliver the core therapeutic content with therapist support. This support may be provided synchronously or asynchronously (i.e., immediate or delayed responses) and be limited to only motivational or trouble-shooting advice or provide an adjunct to the therapeutic content (11).

For this review, we performed a non-systematic literature search using key terms such as digital interventions and tic disorders in databases including PsychINFO, PubMed, Embase, Central, Web of Science, and Medline. We also consulted with our clinical expert team to see if we omitted any studies of relevance. Studies were selected if the intervention aimed to improve the diagnostic symptomology of the tic disorder and was delivered *via* a website, mobile application ("app"), social media, email, or other form of digital technology. The intervention could include human support in its delivery and there was no restriction on targeted age. The search resulted in six trials for review.

## Videoconference delivered therapy for tic disorders

Initially, DHIs could only be delivered through desktop computers either locally or *via* modem connectivity meaning that users needed to be in a specific location to access the intervention. Indeed, the first two studies using digital modalities to deliver therapeutic content to people with tic disorders used videoconferencing software ("Skype"). Himle et al. (12) carried out the first pilot randomized controlled trial (RCT) within the realm of digital therapy for tic disorders (see Table 1 for summary of included studies). Extending on the findings of a previous pilot trial (13), they compared videoconferencing delivered CBIT to face-to-face CBIT for 8–17-year-olds with tics in USA. Participants ($N = 20$) attended 8 weekly sessions of CBIT at one of two university-based tic disorder specialty clinics over 10 weeks. Therapists were doctoral level psychologists with extensive CBIT training and experience, and study personnel were on hand to help participants connect to the remote therapist and to manage any technical difficulties. The primary outcome was tic severity as measured on the Yale Global Tic Severity Scale Total Tic Score (YGTSS-TTS) (14). The researchers found a statistically significant reduction in tic severity scores from baseline to 10-week follow-up (post-intervention) in both groups. Although the mean reduction in YGTSS-TSS in the videoconferencing group (7.8-point reduction) was greater than that of the face-to-face group (6.5-point reduction), this did not reach statistical significance between groups. Furthermore, positive treatment response as measured on the Clinical Global Impressions Improvement (CGI-I) (15) scale showed similar between group findings, with 80% being classified as treatment responders in the videoconferencing group compared to 75% in the face-to-face condition. This study indicated that videoconferencing was at least as efficacious as face-to-face therapy. Moreover, a measure of treatment credibility was similar between the two modes of delivery. Overall, this was the first RCT to show promising findings with regards to both positive outcomes and treatment acceptability in the domain of DHIs for tics.

Following on from this study, Ricketts et al. (16) conducted a similar RCT also in USA, however, they compared videoconferencing CBIT to a waitlist control. Participants ($N = 20$) were 8–16-year-olds and therapeutic content was delivered by a therapist located in a university-based tic disorders specialty clinic. However, in contrast to Himle et al. (12), participants accessed videoconferencing therapy from home. Both the child and their parent were required to be present for sessions, although for mature older adolescents (i.e., those who were 16 years) this was waived and they could attend alone. Treatment consisted of two 1.5-h sessions followed by six 1-h sessions occurring over a 10-week period. Parents were urged to reward children to help their engagement rates and participants were financially rewarded by the study team for completion of both the baseline assessment and the post-assessment. The study found no statistically significant difference in tic severity scores between the videoconferencing and waitlist group. However, in the videoconferencing group there was a significant within-group reduction in tic severity scores between baseline and follow-up (10-weeks post baseline) which was not observed in the control group. Furthermore, there were a significantly higher proportion of treatment responders in the videoconferencing CBIT group (33.3%) relative to waitlist control (0%) and parent acceptability ratings were high. Given the small sample sizes, it is unlikely that the samples of either Himle et al. (12) or Ricketts et al. (16) were powered to detect the effect of DHIs on clinical outcomes, however, the findings provide preliminary support and acceptability of DHIs for tics.

## Web-based internet therapy for tic disorders

Whilst the two studies described showed promising findings and potentially opened a new frontier for delivering evidence-based treatments *via* digital modalities, either the participants and/or the therapists had to be present at a clinic for the sessions and the technology was used as a vehicle to aid remote human therapist delivery of the intervention: it doesn't address a critical factor affecting access which is the lack of highly trained therapists. As digital technology progressed exponentially in the years since the Ricketts et al. (16) study in 2016, there was a move away from videoconferencing to mobile, remote technology, which allowed more flexibility for participants to complete sessions at their own pace at a setting of their choosing. Moreover, smartphones could now be integrated to send SMS

TABLE 1 Summary of included studies.

| Reference | Design, number of arms, comparator, sample size and study location, setting | Sample demographics and baseline tic severity | Intervention and modality | Length/ dosage, follow-ups | Comorbidities | Outcome measures | Human support with intervention | Adherence and engagement | Summary of main findings |
|---|---|---|---|---|---|---|---|---|---|
| Himle, et al. (12) | RCT 2 arms, F2F CBIT, *N* = 20, USA, clinic | Children (8-17 yrs old, M = 11.6), 94% male, 28% on tic medication, 67% TS only, baseline YGTSS-TTS = 23.7 | Internet-accessed Videoconference (Skype) CBIT | 8 weekly sessions of CBIT delivered over 10 weeks. FU = post-treatment (week 10), and at 4-months | 33% anxiety, 28% ADHD, 22% OCD | YGTSS*, CGI-S and CGI-I, PTQ, WAI, TAQ | Therapist supported | 2 dropped out before primary analysis; both in F2F group | The intervention group showed a mean YGTSS-TTS reduction of 7.8 points and the F2F group showed a mean reduction of 6.5 points. Within-group ES for the two treatment delivery modalities were ES = 0.54 and ES = 0.75, for intervention and F2F. The intervention group showed a mean YGTSS-TTS reduction of 6.4 points at follow-up and the F2F group showed a mean reduction of 4.2 points. Within-group effect sizes for the two delivery modalities were ES = 0.39 and ES = 0.41, for intervention and F2F. |
| Ricketts et al. (16) | RCT 2 arms, WLC, N=20, USA, clinic and home based | Children (8-16 yrs old, M=12.1), 64.9% male, 95.8% Caucasian, 35% on tic medication, 75% TS only, baseline YGTSS-TTS = 25.75 | Internet-accessed Videoconference (Skype) CBIT | Treatment consisted of two 1.5-h sessions followed by six 1-h sessions occurring over a 10-week period. FU = 10-week post treatment | 25.8% ADHD, 8.3% OCD | YGTSS*, CGI-I, PTQ, CPTR, CSQ, TAQ, VSQ | Therapist and parent supported | Only 1 patient discontinued treatment as they sought treatment for OCD instead | In the intervention group there was a statistically significant decrease of 7.25 points in YGTSS-TTS total scores from baseline to post-assessment. In the WLC group, the 1.75-point decrease on the YGTSS-TTS total scores from baseline to post-assessment was not significant. |

*(Continued)*





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TABLE 1 Continued

| Reference | Design, number of arms, comparator, sample size and study location, setting | Sample demographics and baseline tic severity | Intervention and modality | Length/ dosage, follow-ups | Comorbidities | Outcome measures | Human support with intervention | Adherence and engagement | Summary of main findings |
|---|---|---|---|---|---|---|---|---|---|
| Andrén et al. (17) | Pilot RCT 2 arms, No comparison between groups, $N = 23$, Sweden, home based | Children (8-16 yrs old, M = 12.3), 65% male, 17.5% on tic medication, baseline YGTSS-TTS = 23.6 | Internet delivered ERP and HRT | 10 chapters over 10 weeks. FU = post-treatment and 3 (primary endpoint), 6 and 12-month | 39% ADHD, 13% OCD | YGTSS*, CGAS, CGI-S and CGI-I, PUTS, GTS-QOL, adapted child version of the WSAS, OCI-Child version, CDI-S, PTQ, WSAS-Y (parent), SMFQ | Therapist and parent supported | Average number of completed chapters was 7.92 (for both children and parents) in the ERP group, and 7.36 (children) and 7.09 (parents) in the HRT group. 6 children (50%) and 5 parents (42%) in the ERP group, and 5 children and parents (45%) in the HRT group completed all 10 chapters. None lost to FU. | Significant reduction on the YGTSS-TTS for internet ERP, but not for internet HRT. Within-group Cohen's $d$ was 1.12 for internet ERP and 0.50 for internet HRT. |
| Rachamim et al. (19) | Feasibility and effectiveness study with crossover design, 2 arms, WLC, N=41, Israel, home based | Children (7-18 yrs old, M = 11.26), 70.7% male, 24.4% on tic medication, baseline YGTSS-TTS = 22.72 | Internet delivered CBIT | 9 modules over 9 weeks. FU = post-treatment, 3 and 6-months | 43.9% ADHD, 31.7% OCD | YGTSS*, CGI-I, CGAS, ADIS, PTQ, Revised CPRS, OCI, SCARED, LSAS, RSES, CDI | Therapist and parent supported | 23 completed 9 modules. Participants completed a mean of 8.8/9 modules. Reasons for stopping ($n = 2$) included a lack of motivation and self-discipline. | A significant interaction was found for the YGTSS-TTS between time-point and group [$F_{(1,39)} = 9.96$, $p = 0.003$, large effect]. At post-intervention (time 2), the YGTSS-TTS was significantly reduced in the internet CBIT arm only. Internet CBIT was associated with a mean YGTSS-TTS reduction of 6.60 points ($p < 0.001$) compared with a mean YGTSS-TTS reduction of 0.94 points ($p = 0.51$) in the WLC arm. This 6.60 points difference was clinically meaningful, with an ES of within-group Cohen's $d = 0.91$, large effect. |

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TABLE 1 Continued

| Reference | Design, number of arms, comparator, sample size and study location, setting | Sample demographics and baseline tic severity | Intervention and modality | Length/ dosage, follow-ups | Comorbidities | Outcome measures | Human support with intervention | Adherence and engagement | Summary of main findings |
|---|---|---|---|---|---|---|---|---|---|
| Hollis et al. (18) | RCT 2 arms, Internet Psychoeducation, $N = 224$, UK, home based | Children (9-17 yrs old, M = 12), 79% male, 87% White, 13% on medication for tics, baseline YGTSS-TTS = 28.4 | Internet delivered ERP | 10–12 weeks of 10 chapters for both child and parent. FU = 3-, 6-, 12- and 18-months post-randomization | 27% anxiety disorder, 25.5% ADHD, 22.5% ODD | YGTSS*, CGI-I, CGAS, CASUS, CHU9D, SDQ, PTQ, modified version of the Hill and Taylor side-effects scale, MFQ, SCAS, PUTS, C&A-GTS-QOL | Therapist and parent supported | 204 (91%) received the minimum intervention (at least first 4 chapters) and were treatment completers (99 in the ERP group and 105 in the psychoeducation group). 186 (83%) were followed up 6 months after randomization (93 in the ERP group and 93 in the psychoeducation group). | Mean total decrease in YGTSS-TTSS at 3 months was 4.5 (16%) in the ERP group vs. 1.6 (6%) in the psychoeducation group, and at 6 months was 6.9 (24%) in the ERP group vs. 3.4 (12%) in the psychoeducation group. The estimated mean difference in YGTSS-TTSS change between the groups at 3 months was −2.29 points (95% CI −3.86 to −0.71) in favor of ERP, with an ES of −0.31 (95% CI −0.52 to −0.10) |

*(Continued)*



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TABLE 1 Continued

| Reference | Design, number of arms, comparator, sample size and study location, setting | Sample demographics and baseline tic severity | Intervention and modality | Length/ dosage, follow-ups | Comorbidities | Outcome measures | Human support with intervention | Adherence and engagement | Summary of main findings |
|---|---|---|---|---|---|---|---|---|---|
| Haas et al. (20) | RCT 3 arms, Placebo and F2F CBIT, *N* = 161, Germany, home based | Adults (112 males, 49 females, mean age = 35.6 yrs old, range = 18–62 yrs), 40.4% on tic medication, baseline YGTSS-TTS = 24.37 | Internet delivered CBIT | 8 sessions over 10 weeks. FU = 5 weeks after start of treatment (V2), 1 week after end of treatment (V3; primary endpoint), and 2 follow-up visits at 3 (V4) and 6 months (V5) | Not reported | YGTSS*, Modified RVBTRS, Adult Tic Questionnaire, GTS-QoL, PUTS-9, CGI-S and CGI-I, Y-BOCS, Conners' Adult ADHD Rating Scales, BDI-II, BAI, WAI-SR | No human support | 108 (67.1%) were considered as compliant until V3. Rate of non-compliance was lowest in the placebo group (22.9%) and similarly high in both treatment groups | Internet CBIT group showed a larger tic reduction [2.54 (−3.53; −1.55)] in comparison to the placebo group [−1.26 (−2.16; −0.35)] at V3. Difference in YGTSS-TTS change to baseline between placebo and internet CBIT was −1.28 (−2.58; 0.01). Significance for superiority of internet CBIT was narrowly missed and the null hypothesis could not be rejected as the upper 95% CI limit was marginally above 0. Difference in YGTSS-TTS change to baseline between internet CBIT and F2F CBIT at V3 was 0.98 [−1.01; 2.96]. Since the upper bound of the 95% CI was below the non-inferiority margin of 3; non-inferiority of internet CBIT in comparison to F2F CBIT could be observed. |

*Primary outcome measure. ADHD, attention deficit hyperactivity disorder; ADIS, Anxiety Disorders Interview Schedule; CBIT, Comprehensive Behavioral Intervention for Tics; CDI, Children's Depression Inventory; CGAS, The Children's Global Assessment Scale; CGI-I, Clinical Global Impression-Improvement Scale; CGI-S, The Clinical Global Impression-Severity scale; CHU9D, Child Health Utility instrument; CPRS, Child-Parent Relationship Scale; CPTR, Children's Perception of Therapeutic Relationship; CSQ, Client Satisfaction Questionnaire; ERP, Exposure and Response Prevention; ES, effect size; F2F, Face-to-face; FU, Follow-up; GTS-QOL, Gilles de la Tourette Syndrome-Quality of Life Scale; HRT, Habit Reversal Therapy; LSAS, Liebowitz Social Anxiety Scale; MFQ, Mood and Feelings Questionnaire; OCD, obsessive compulsive disorder; OCI, Obsessive-Compulsive Inventory; ODD, Oppositional defiant disorder; PTQ, Parent Tic Questionnaire; PUTS, Premonitory Urges for Tic Disorders Scale; RCT, randomized controlled trial; RSES, Rosenberg's Self-Esteem Scale; RVBTRS, Rush Video-Based Tic Rating Scale; SCARED, Screen for Child Anxiety Related Disorders; SCAS, Spence Children's Anxiety Scale; TAQ, Treatment Acceptability Questionnaire; TAU, Treatment as usual; TS, Tic syndrome; TTS, Total Tic Score; VSQ, Videoconferencing Satisfaction Questionnaire; WAI, Working Alliance Inventory; WLC, wait-list control; WSAS, Work and Social Adjustment Scale; YGTSS, Yale Global Tic Severity Scale.



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or emails as an adjunct to regular face-to-face therapy with therapeutic content delivered by web-based chapters. Andrén et al. (17) were the first to take advantage of this new technology in the tic disorder domain. They conducted a pilot RCT in Sweden evaluating two types of internet-delivered behavioral therapies: ERP and HRT. Participants ($N = 23$) were 8–16-year-olds who completed 10 web-based chapters of remote therapeutic content, similar to a self-help book, over 10 weeks with parental support. Parents had separate logins to the online platform and were able to access extended versions of the treatment content. Specifically, parents learnt about parental coping strategies, social support, and functional analysis (i.e., examining the causes and consequences of behavior). They also had access to a therapist who did not deliver any therapeutic content. Therapists were supervised, graduate psychologists who were trained in the use of the platform and were mainly responsible for engaging participants and responding to any queries *via* the online platform or SMS. Therapists answered queries *via* the online platform, which related to understanding treatment content delivered in the web-based chapters and any technical difficulties, but they did not provide any new treatment content relating to ERP/HRT. The researchers found that there was a significant reduction on the YGTSS-TTS for the ERP group, but not for the HRT group 3-months post-intervention. Within-group Cohen's *d* was 1.12 for ERP and 0.50 for HRT. In addition, 9 participants (75%) in the ERP group and 6 participants (55%) in the HRT group were classified as treatment responders according to the CGI-I and children and parents rated both treatments as credible and satisfaction at post-treatment was high in both groups. Adherence and engagement were excellent in both groups.

The Andrén et al. (17) study showed promising findings that tic severity can be reduced with the use of remote therapist supported internet delivered behavioral therapy, but the study was not powered to explore clinical efficacy. Hollis et al. (18) expanded on this pilot by conducting a large RCT in England using the same online platform as Andrén et al. (17) with the content translated into English language. In total, 224 participants aged between 9 and 17 years were randomized to receive either internet ERP or online delivered psychoeducation as an active control. ERP was chosen as the active therapeutic intervention based on the findings from Andrén et al. (17) which suggested that ERP may be more acceptable and feasible to deliver in an online format. Aligned with the pilot Swedish study, participants were required to work through 10 chapters of content over 10 weeks with parental and therapist support. Parents had their own chapter content to work through which gave them tools to help support their child during treatment as well as more information on tic disorders and related conditions. The therapists' role was to answer any queries and engage participants but not deliver any therapeutic content. The findings showed that at 3 months post-baseline there was significant reduction in tics in the ERP group (4.5, 16% YGTSS-TTS reduction) compared to the psychoeducation group (1.6, 6% YGTSS-TSS reduction). The estimated mean difference in YGTSS-TTS change between the groups at 3 months was −2.29 points in favor of ERP, with an effect size of −0.31 (95% CI −0.52 to −0.10). There was also a significantly greater positive treatment response with ERP at 3 months (36%) than with psychoeducation (20%). Adherence and engagement in both groups was excellent and the perception of treatment suitability, credibility and satisfaction was high across both groups. Although a full economic analysis is to be reported in the long-term follow-up Online Remote Behavioral Intervention for Tics (ORBIT) paper, preliminary analysis showed that the fixed and variable costs including wider healthcare costs of delivering the behavioral therapy (ERP) were higher compared to psychoeducation [£159 (95% CI 53–370) more per participant]. As the study did not compare to standard face-to-face therapy it is not possible to understand cost-savings compared to standard tic services. However, the authors indicate that given the total therapist time in the trial was an average of 2.5 h delivered by a less-experienced therapist compared to typically 9–10 h of highly skilled therapist time required for face-to-face therapy, it is possible this would be cost-effective. In sum, this was the first adequately powered RCT that showed internet delivered behavioral therapy with low intensity human support could reduce tic severity offering a new approach to breaking down barriers in accessing evidence-based treatments.

Two further trials have been conducted that evaluated remote digital behavioral therapies using a web-based delivery approach. One used a crossover design and was carried out in Israel by Rachamim et al. (19). They compared caregiver-guided self-help internet delivered CBIT to a waitlist control group in a sample of 41 children and adolescents (7–18 years). The therapeutic content was delivered *via* nine web-based chapters over 9 weeks, and participants had parental support with access to a therapist, who provided support but did not deliver any therapy. At post-intervention, the YGTSS-TTS was significantly reduced in the internet CBIT arm only with a mean YGTSS-TTS reduction of 6.60 points compared with a mean YGTSS-TTS reduction of 0.94 points in the waitlist arm. The 6.60 points difference had an effect size of within-group Cohen's $d = 0.91$, indicating large effect. All but one of the participants in the internet CBIT group (95%) were rated as treatment responders.

The final study was carried out by Haas et al. (20) in Germany and the sample was 161 adults. This was the only study in the literature conducted in an adult population. They compared self-directed internet CBIT delivered *via* web-based chapters to placebo and face-to-face CBIT, with participants completing 8 sessions over 10 weeks. The study found no significant difference in efficacy between web-based and face-to-face delivered CBIT (non-inferiority) and although the web-based CBIT group showed a larger tic reduction compared to the placebo condition, this fell short of statistical significance. Overall, these two studies further add to the

promising findings that digital technology could be used to deliver evidence-based behavioral treatments to people with tic disorders.

## Strengths and limitations

In critically appraising the evidence of DHIs for people with tic disorders, one must consider the inherent strengths and limitations within the respective studies. All but one of the studies employed a randomized controlled design, which is considered the "gold standard" for efficacy studies. However, most were not sufficiently powered to address efficacy. All but two of the included trials had small sample sizes (i.e., <50), which means that studies were probably underpowered to reliably detect clinically meaningful effects. One intrinsic methodological limitation of many therapeutic intervention trials is the great difficulty in blinding participants and those delivering treatment (21), thus introducing a high risk of bias. This can be partially mitigated by having outcome assessors (such as YGTSS assessors) who are blind to arm allocation, which was done in all the presented trials.

Before any new technology can be implemented in routine practice, it is important to understand the costs of an intervention to the healthcare system. Economic evaluations can be used to inform decisions about the economic impact and relative value for money of DHIs. It can assess whether differences in costs between the intervention and competing alternatives can be justified in terms of health and non-health benefits. However, only one of the papers included a full health economic analysis (18). Moreover, only one of the included trials was conducted in an adult population and whilst the sex distribution in the included studies is typical for a tic disorder population, a large proportion of participants in the studies were white, which may limit the generalizability of the findings concerning ethnicity. Another criticism of the included studies is the lack of long-term follow up data. It is imperative to understand the sustainability of digital interventions, however most of the included trials were of limited follow up with only one of the trials measuring outcomes beyond 12-months (18, 22).

Furthermore, there is an issue with generalizing the findings to routine practice. As a small proportion of participants in the included trials had comorbidities, this may not reflect the reality of standard practice especially as research suggests that around 85–88% children with tic disorders have at least one psychiatric comorbidity (23). The reported studies incorporated a range of therapeutic content and approaches, differed in their level of human involvement, and had varied comparators and modalities of delivery, which could have affected participant interaction and consequently, efficacy (24). Further research is required to understand better as to what works best and for whom.

Despite these limitations, the included studies reported promising findings that give cause for optimism in utilizing digital technology for people with tic disorders. First, all participants who received the digital treatments in the respective studies showed some improvement in tic severity from baseline to primary endpoint as measured on the YGTSS-TTS, which ranged in a mean reduction of 4.5 points in Hollis et al. (18) to 7.8 points in Himle et al. (12). Although these reductions were over a similar timeframe, the Hollis et al. (16) study had a far larger sample size which may explain the discrepancy in tic reduction between the two studies. Furthermore, a larger proportion of those who received a digital intervention showed positive treatment response compared to controls. The effect sizes, tic reduction, and responder statuses of included studies are comparable to previous studies assessing face-to-face therapeutic interventions for tic disorders (25, 26). Another positive outcome, which was found in the ORBIT trial, is that digital ERP could be delivered with around one quarter of the therapist contact time (also at a lower level of training) compared to evidence-based face-to-face behavioral therapy. Therapists required limited training in how to use the ORBIT platform and support the intervention. These are positive findings as they show that digitally enabled behavioral therapy has similar efficacy but lower costs than regular face-to-face therapy, and, if delivered as a first-line behavioral intervention, could allow more people to access evidence-based non-pharmacological interventions. Another strength of the trials is that they all used a validated and reliable measure, namely the YGTSS. As the YGTSS is a subjective, clinician-rated measure, it is imperative that researchers are trained and supervised throughout the trial in how to conduct this measure. Indeed, four out of the six trials included in this review explicitly mentioned training their YGTSS assessors.

Aside from efficacy, before any new intervention can be adopted in routine healthcare, assessments must be made on how acceptable and/or credible participants found it. This is particularly important when evaluating modern advancements such as digital therapies. Indeed, all included studies showed that participants were highly satisfied with the treatments and found the mode of delivery acceptable/credible. Another consideration is the extent to which the intervention was safe to deliver and use, which is generally captured in the form of adverse event reporting. All but two studies explicitly recorded and reported on adverse events. Although a few serious adverse events in total were reported across the included studies, none were related to the treatment, suggesting that all interventions were safe to use. Finally, all trials had low attrition and high engagement rates with the intervention. As high attrition and low engagement rates are a common problem in digital health research (27, 28), this not only shows the need that this population have for an evidence based behavioral treatment

but that the included interventions appeared to be engaging to users. However, it is worth noting that all but one of the studies involved human support which may have positively impacted on engagement rates.

## Future research for tic-related digital interventions

Primarily, it would be important for any future work to supplement the limitations highlighted above. Only one of the included studies assessed the cost-effectiveness of the digital intervention, which is likely to be an important consideration for policymakers. A cost-effectiveness evaluation would be much needed in future research of digital interventions for tic disorders to help policymakers make decisions on adoption to routine healthcare. All but one of the interventions in this review contained an element of human interaction, either with synchronous contact by videoconferencing or asynchronous contact through SMS or the online platform. The best improvement in outcomes, therefore, may be achieved through a blended approach of online intervention and human support. As technology evolves rapidly, future online interventions will be more dynamic, perhaps including real-time therapist input and integrated synchronous crisis support. A promising new development is the use of virtual reality, which has had positive results on children with other neurodevelopmental disorders (29) and a range of other mental health problems (30) but has yet to be explored with individuals with tics. Developers could utilize virtual reality to its full effect and enable a simulated, life-like human therapist to support patients with tics, which would also be more cost effective than a human therapist an area worthy of future pursuit.

Future studies of digital interventions for people with tic disorders must have larger sample sizes to generate greater statistical power and allow for an increase in generalizability. Moreover, there should be a more concerted effort to diversify the inclusion criteria so that the samples are representative of clinical practice. They must also consider including long-term follow-up assessments to evaluate whether effects are maintained over a prolonged period. Only one of the included trials followed up participants beyond 12-months post-randomization (18, 22). Although currently under investigated, a potential strength of digital interventions is the delivery of treatment in geographically distant and economically challenged contexts, such as low- and middle-income countries, where knowledge and application of treatments is reported to be low (31). This area requires further research to define the barriers and benefits. Furthermore, as is known within the digital literature, it is crucial to understand how these complex interventions work and for whom. Thus, future RCTs evaluating DHIs for people with tic disorders should consider conducting a mixed methods process evaluation concurrently with trial delivery, as this would be useful in addressing the intervention's implementation, mechanisms of impact and context. Such findings were crucial in understanding the extent to which ORBIT was both implemented with a high degree of quality (32) and the mechanisms through which it achieved impact (33).

Despite much talk of triggering a revolution in health service delivery and treatment, digital interventions are rarely mainstreamed or sustained (34). This is partly because once a DHI has shown efficacy in an RCT, there is an unclear pathway to implementation. Therefore, the critical next step is to conduct a real-world implementation study to show proof-of-concept of a DHI for children with tic disorders. This could take the form of a process evaluation, effectiveness, and cost-effectiveness study. Furthermore, it would be sensible for any future real-world evaluation to employ an evidence-based implementation science framework to inform planning and evaluation. For instance, the NASSS model (Non-adoption, Abandonment, Scale-up, Spread and Sustain) (35) is a mixed-methods approach that considers the influence on implementation of complexities in key domains, such as target problem, technology, adopters, organization, and broader systems. This will enable policymakers to make decisions on strategies to reduce or address complexity, which may increase the likelihood of effective implementation and adoption in routine healthcare services.

Another promising route to implementation for digital interventions for tic disorders are hybrid implementation-effectiveness trials, which have the potential to be an appropriate design for simultaneously examining clinical and implementation outcomes for DHIs. This would save valuable time, as it would not rely on researchers carrying out efficacy trials entirely separately from implementation research. For example, Lane-Fall et al. (36) have developed a "subway line" of translational research that may be a helpful heuristic for conceptualizing future directions for hybrid implementation-effectiveness trials within the tic-related field. However, this requires a defined care pathway so the routes to accessing these treatments are clear, as that is often a significant barrier. For instance, these interventions would need to be overseen by a clinician with tic experience and knowledge, as it would not fit in with general practitioner's (GP) who do not necessarily have the expertise to deal with tic disorders.

## The human factor

One could argue that there is no need for a therapist and, to cut costs, all these digital therapies could be implemented as self-help programs; however, there is no empirical evidence to support this notion. Moreover, the literature suggests that supported digital interventions are more engaging and efficacious than non-supported interventions (5, 37, 38). Optimizing user experience, which is defined as the extent

to which an intervention is perceived by a person as useful, enjoyable and user friendly, has great potential to address barriers to successful future implementation (39). Increasingly, human-centered designs are being employed in healthcare innovations to enhance user experience, thereby promoting better adherence and efficacy (40). As the adherence and engagement rates were high in all included studies, it is clear that human support played a crucial role in improving user involvement.

Another point of consideration that is specific for children and young people is the extent to which parents or carers should be involved. Most of the interventions in this review had some form of parental involvement, however the level of involvement differed between studies. It does seem that parents play a crucial role in engaging and ensuring the adherence of treatment content within these interventions. Indeed, the ORBIT trial's process evaluation found that parental engagement significantly influenced child's level of engagement (32) and efficacy (33). Several systematic reviews have also noted the crucial role parents have in positive outcomes for children and adolescents across a range of treatments for a variety of conditions (41–43). Parents bring a strong level of commitment, availability and personal expertise of their child that is an invaluable asset to researchers and clinicians so must be utilized in any future roll out. However, it must be noted that not all caregivers have the capacity to assist with the delivery of such interventions given systemic factors and competing demands. Therefore, there may also be value in designing interventions that can be delivered to children and young people whose parents do not have the capacity to engage regularly in treatment. Furthermore, it is worth considering that digital interventions have the potential to provide more equitable access to care for caregivers who have limited capacity to engage in face-to-face interventions (i.e., due to costs, travel, work schedules, busy lives).

## Recommendations for future practice

Face-to-face behavioral therapy is an effective treatment for tic disorders in children and adults, however less than one in five have access in the UK (44). Rates vary across the world but access to non-pharmacological treatments for tic disorders is low in many contexts, even those with good provision of care in other areas of mental health. All the studies in this review show that digital delivery of behavior therapy for tics can be an efficacious, engaging, and safe form of treatment. This could greatly increase access to therapy. With recent European clinical guidelines stating that behavior therapy should be offered as first line treatment option (4), it seems that the digital revolution offers a significant approach in overcoming the lack of access.

Despite this, there is a need to determine the optimum care pathways with respect to sequencing and integration of digital and face-to-face behavioral therapy for tics. For example, a stepped-care approach could be implemented whereby digital therapy is offered first, followed by more intensive face-to-face therapy for those who may require it. Initially, this should be offered to children and adolescents with tic disorders, as the research to date is less robust in adults with tics. Only one study in this review was conducted on adults with tics (20) and thus more research is needed to establish its efficacy before wider implementation.

In terms of what active components may be essential and what this digital therapy may look like in any future roll out in clinical services; this review may be able to shed some light on this. Firstly, based on the available evidence, it appears that either CBIT or ERP are likely to lend themselves to remote delivery. Although CBIT has the largest evidence base of any behavioral therapy in the tic literature (26), ERP is arguably more efficient and less intensive as a digital therapy. For instance, findings from the ORBIT trial, which used ERP as its form of therapy, showed that participants only required their therapists support for around 15 min per week and largely undertook the ERP practices themselves (18, 32). Moreover, therapists involved in the ORBIT study needed very little training and were less experienced than those who may deliver CBIT. Employing therapists with little experience and who are less qualified than a licensed doctoral-level therapist, for example, would also present better value for money for healthcare services, as they could be employed at a lower salary rate. However, caution must be taken with these considerations as none of the studies in this review included a comparison of which intervention and components are best delivered digitally.

Design considerations of DHIs are one of many factors that must be examined before any potential implementation. Firstly, it is essential to include patient and public involvement (PPI) in the process of designing and developing such interventions, as is consistent with user-centered design principles. Such insights from the PPI group involved in the ORBIT trial were pivotal to its successful recruitment and retention of participants (45). Findings from the literature suggest that individuals make credibility judgements about online information (46) and cost-benefit analysis of behavior (47) to determine their projections of continuing, especially in the early stages of treatment. Thus, it appears that developers of future iterations of DHIs for children with tic disorders must consider how to make these engaging and stimulating to facilitate continued usage. This may constitute specific features such as video demonstrations of therapy, animations, the ability to visualize which tics are increasing or decreasing in severity and frequency which may be especially engaging and enjoyable for children. Indeed, these interactive components were identified as key features of the ORBIT intervention and seemed to be used most (32). This

is consistent with evidence that interactive elements, including attractive audio-visual material to be amongst the most highly used features of DHIs as they tend to keep users' interest (48, 49). This would be especially important to younger children whose concentration levels would not be maintained with material that was simply presented in writing, for example. It may also be sensible to include some sort of reward system. This seems to be an effective strategy to engage children and ensure that they maintain their level of commitment with the practices involved in behavioral therapy for tics.

## Conclusion

The available evidence indicates that DHIs have potential to be clinically efficacious in reducing tics as well as being acceptable to patients. Further research is required to determine cost-effectiveness. However, given potential cost-savings and service efficiencies associated with a release of clinical time, it is likely this would be cost-effective. Furthermore, additional research is needed to establish long-term impact and determine DHI in routine care pathways, outside of clinical trials. As all the research to date in this domain have been conducted in tightly controlled and monitored trials, the focus has been on efficacy rather than effectiveness. Digital technology evolves at a rapid pace meaning that as technology changes and interfaces are updated it cannot be certain that a program that was efficacious five or ten years ago would be equally efficacious today. Although RCTs are still the gold standard for which to assess the efficacy of DHIs, they can take many years to establish evidence meaning technology outpaces this. Thus, there is a need for more real-world evaluations to establish effectiveness. A digital intervention that could be deployed to large numbers of patients at a relatively low cost is a much needed and seemingly acceptable means of providing patients with access to evidence-based treatments. It could provide immediate access to these treatments for those who otherwise would not have access due to long waiting lists or their geographical location, which could also potentially free up existing resources and services for those requiring more complex treatment and assessment. Thus, cutting costs and waiting times would be a two-fold benefit for healthcare services and patients alike. There is a need to conduct more robust research in this domain but also an urgency to implement a digital intervention for children with tic disorders in real-world settings.

## Author contributions

KK and CLH outlined the structure, reviewed the literature, and wrote this paper. TM and CH provided critical feedback. All authors contributed to the article and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Open-case series of a remote administration and group setting comprehensive behavioral intervention for tics (RG-CBIT): A pilot trial

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**Purpose:** The comprehensive behavioral intervention for tics (CBIT) is the first-line psychotherapeutic treatment for individuals with tic disorders. However, most patients with tic disorders do not have access to CBIT due to different factors including lack of trained therapists, treatment cost, and travel distance. Such barriers are more prominent in non-English speaking countries. Therefore, the current study assessed the preliminary efficacy, feasibility, and acceptability of remotely administered group CBIT (RG-CBIT) in Japan.

**Methods:** This was an open-case series that adopted the AB design. Three Japanese children aged between 6 and 13 years who were diagnosed with TS were recruited. RG-CBIT was developed based on the published CBIT manual. Videoconference application, slide presentation software, and cloud learning platform were used as appropriate.

**Results:** The Yale Global Tic Severity Scale scores of all participants decreased from baseline to post-treatment. That is, the score reduced by an average of 7.0. Regarding feasibility and acceptability, the attendance rate of participants was 100%, and the process measurement items had favorable scores.

**Conclusions:** RG-CBIT had satisfactory efficacy, feasibility, and acceptability. Hence, it could mitigate the barriers for treatment access.

KEYWORDS

**tic disorders, Tourette syndrome, the comprehensive behavioral intervention for tics (CBIT), group, remote, telehealth**

## Introduction

Tics are sudden, repetitive, non-rhythmic movements (i.e., motor tics) or vocalizations (i.e., vocal tics). Tic disorder is one of the neurodevelopmental disorders characterized by motor and/or vocal tics that begin in childhood. Tics may persist, and the type of tics can change over time. Symptom severity commonly peaks at the early

years of teenage life (1). Chronic tic disorder (CTD) is characterized by tics lasting more than 1 year, and tics may be either motor or vocal, but not both. Tourette's disorder (TD), also known as Tourette syndrome (TS), is characterized by the presence of one or more chronic multiple motor and vocal tics (2). In a previous meta-analysis, the prevalence of TS was 0.77%, and TS is more common in boys (3).

In most cases, tic disorders are mild to moderate, and they do not always require treatment. However, if tics are severe or children experience several psychosocial problems, such as deteriorating relationships with family and friends and interference with school and extracurricular activities, then treatment is required (4). The comprehensive behavioral intervention for tics (CBIT) is the first-line treatment for individuals with tic disorders (5). Woods and colleagues developed CBIT (6), which includes the core therapeutic components of psychoeducation, functional assessments and interventions (FAI), habit reversal training (HRT), and relaxation training (**Figure 1**). CBIT was designed to include eight sessions weekly for 10 weeks, followed by periodic booster session(s) to maintain treatment gains and to learn how to deal with tics that may emerge in the future. The first two sessions last 90 min (combined 180 min), during which patients and their parents receive psychoeducation about tics and learn the basics of the functional assessments/interventions and HRT procedures. The remaining sessions last 60 min and focus on administering core therapeutic components to additional tics and teaching patients and their parents regarding relaxation skills. CBIT was initially tested among children aged 9 years and older. However, a recent study showed that CBIT is effective in young children aged between 5 and 8 years, incorporating enjoyable and ingenious elements of the game called "the opposite game" (7). In this study, the authors highlighted that involving parents in behavioral interventions for young children improves the acceptability, efficacy, and durability.

A controlled clinical study has shown that CBIT, similar to pharmacologic treatment, can improve tics in children and adults without causing significant side effects (8–10). Although CBIT is effective, several children with CTD and TS cannot access CBIT because of several factors including lack of trained therapists, treatment cost, travel distance, and time commitment (11–13). CBIT is not widely available particularly in non-English speaking countries (14). To address these barriers and to promote CBIT dissemination, controlled trials of remote administration, such as telehealth and internet-delivered psychotherapy, have been carried out recently. Himle et al. conducted a small randomized controlled trial (RCT) comparing CBIT delivered using the videoconference system and traditional face-to-face CBIT (15). Results showed that both formats were equally beneficial to children with tic disorders. In addition to CBIT, a large long-term follow-up study of ERP is underway in the United Kingdom. Remote Administration is an emerging and significant topic in behavioral therapy (16).

Group CBIT is another method that can increase treatment accessibility. Zimmerman-Brenner et al. conducted an RCT of group CBIT and group educational intervention. Results showed that group CBIT significantly decreased total and motor tic severity (17).

However, CBIT is not widely available in Japan due to a considerable lack of well-trained therapists. Although there is a Japanese translation of the manual established by Woods et al. (6), which was published in 2018, training opportunities for learning CBIT procedures are limited among therapists. Moreover, CBIT is not covered by public health insurance in Japan; thus, the cost burden on patients is substantial. Therefore, the current study aimed to assess the preliminary efficacy, feasibility, and acceptability of remotely administered group CBIT (RG-CBIT) for reducing tics in children with TS *via* an open-case series.

# Materials and methods

## Study design and ethical considerations

This was an open-case series that utilized the AB design study (two-phase design comprising a baseline and an intervention phase). The recruitment phase was 4 weeks; the baseline phase, 10 weeks; and the intervention phase, 10 weeks. Clinical assessments were performed 5 days before baseline (Ax1 assessment 1) and the first session (Ax2 assessment 2), and 5 days after the end of the sessions (Ax3 assessment 3). Standard care, including medication treatment, was continued (not changed) throughout the study period.

Written informed consents were obtained from the participants. This study was approved by the Ethical Committee of Dokkyo Medical University Saitama Medical Center (21019).

## Participants

The inclusion criteria were as follows: (a) individuals aged between 6 and 15 years, (b) those with a diagnosis of TS based on the DSM-5 criteria (18), (c) those with a score of $\geq$ 14 for the total tic severity score on the Yale Global Tic Severity Scale (YGTSS), and (d) those who are medication free or on a stable medication for the treatment of tics, obsessive-compulsive disorder (OCD), and attention deficit hyperactivity disorder (ADHD) for at least 6 weeks, without planned changes during the study period. The exclusion criteria were as follows: (a) individuals with a diagnosis of other psychiatric disorders except for TS, ADHD, and OCD based on the DSM-5 criteria, (b) those with any serious physical disease, psychosocial, or neurological condition requiring treatment, (c) those with previous behavioral therapy for TS, and (d) those with lack of

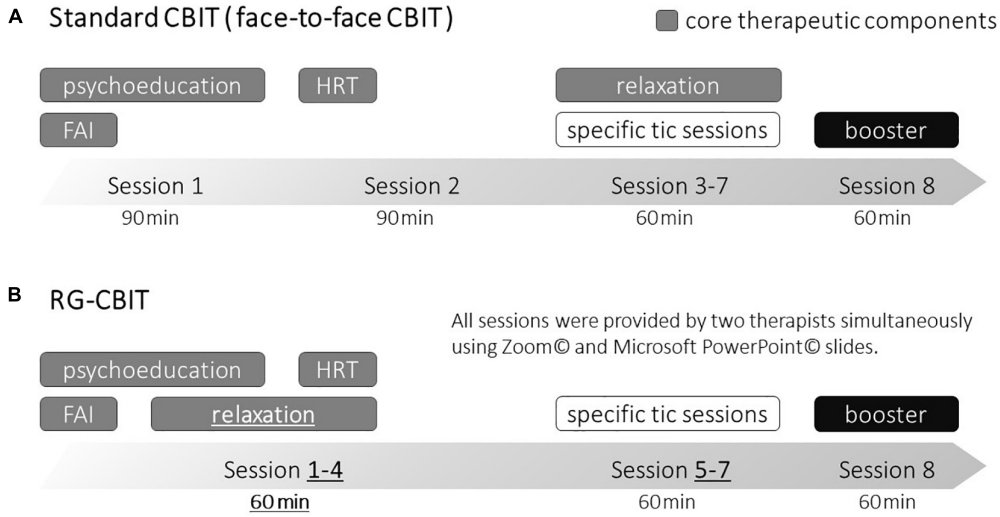


FIGURE 1
Difference between RG-CBIT and standard CBIT. *FAI*, functional assessments and interventions; *HRT*, habit reversal training; *RG-CBIT*, remotely administered group comprehensive behavioral intervention for tics; *CBIT*, comprehensive behavioral intervention for tics. The upper part **(A)** is a schematic diagram of the standard CBIT, and the lower part **(B)** is a schematic diagram of RG-CBIT. The dark gray cells indicate core therapeutic components. There were three primary differences between RG-CBIT and the standard CBIT (underline and bold text). First, the duration of all sessions were changed to 60 min. Second, the learning relaxation components were moved to the first session. Third, the core therapeutic components were trained in the first four sessions (combined 240 min) rather than the first two sessions (combined 180 min).

accessible home computer or tablet device and/or high-speed internet connection.

Three Japanese children aged between 6 and 13 years and diagnosed with TS were recruited from Child Development and Psychosomatic Medicine Center, Dokkyo Medical University Saitama Medical Center, in February 2021. The clinical characteristics were obtained during the recruitment phase (as shown in Table 1).

## Materials

Zoom© (Zoom Video Communications, Inc.), a secure, reliable video platform, was adopted to communicate between participants and therapists. It was chosen because of its high image resolution, availability, and affordability in the general population in Japan. The breakout-room function was another important factor that contributed to the decision to use Zoom©. Microsoft PowerPoint© is a slide presentation software that was used to explain the CBIT session contents. Google docs© and sheets© were used to design homework materials, and Google Classroom© is a cloud-based learning platform used to assign and submit the homework and provide feedback for the homework. Participants and therapists used their home computer or tablet with high-speed internet connection, and a built-in webcam was used to monitor the participant's movements, positioning, and other non-vocal responses (e.g., nodding or raising the hand to indicate that a task is completed) during the meetings. Zoom, or email or cellular phones were used to communicate with participants outside of the RG-CBIT sessions as needed.

## RG-CBIT and procedure

RG-CBIT was developed based on the CBIT manual developed by Woods and colleagues in terms of the number and components of treatment sessions, distribution of CBIT contents, and length of intervention. RG-CBIT was modified by the authors [Takeshi Inoue (TI) who has a Ph.D. degree in Medicine and a Board-Certified Member of the Japanese Society of Child Neurology and who is well experienced in all aspects of TS and CTD, Kohei Togashi (KT) who was a clinical psychologist certified in Japan and a doctoral-level behavior analyst, and Jumpei Iwanami (JI) who was a clinical psychologist certified in Japan and has a master's degree in psychology]. Consultation with Dr. Douglas Woods was performed as needed. There were three primary differences between RG-CBIT and standard CBIT. First, the duration of all sessions was changed to 60 min because duration of 90 min remote session was lengthy for young children. Second, learning relaxation components were moved to the first session since they were easy to teach and perform. Third, the skills required to implement these therapeutic components are complex and we wanted to provide the participants with multiple opportunities to practice them. Thus, core therapeutic components (psychoeducation, FAI,

TABLE 1 Clinical characteristic details.

| | Age | Sex | Diagnosis | Age of TS onset | Comorbidity | Medication | ADHD RS-IV | CY-BOCS |
|---|---|---|---|---|---|---|---|---|
| Case 1 | 6 | M | TS | 4 | ADHD | - | 22 | 0 |
| Case 2 | 9 | M | TS | 6 | ADHD | Guanfacine 3 mg/d | 25 | 0 |
| Case 3 | 13 | F | TS | 4 | ADHD OCD | Guanfacine 4 mg/d Atomoxetine 50 mg/d | 25 | 11 |

TS, Tourette syndrome; ADHD RS-IV, attention deficit hyperactivity disorder rating scale IV; CY-BOCS, children's Yale-Brown obsessive compulsive scale.

TABLE 2 Schedule of assessments.

| | Ax 1 | Baseline 10 weeks | Ax 2 | RG-CBIT 10 weeks | Ax 3 |
|---|---|---|---|---|---|
| YGTSS | x | | x | | x |
| CGI-S | x | | x | | x |
| CGI-I | | | x | | x |
| PUTS | x | | x | | x |
| SDQ | x | | x | | x |
| CSQ-8J | | | | | x |
| J-WAI-SR | | | | | x |
| Modified-TEI | | | | | x |

Ax, assessment; YGTSS, Yale Global Tic Severity Scale; CGI-S, The Clinical Global Impression-severity score; CGI-I, The Clinical Global Impression-Improvement scale; PUTS, The Premonitory Urge of Tics Scale; SDQ, The Strength and Difficulties Questionnaire; CSQ-8J, The Japanese version of the Client Satisfaction Questionnaire-8; J-WAI-SR, The Japanese version of the Working Alliance Inventory-Short Revised; Modified-TEI, Modified version of the Treatment Evaluation Inventory.

HRT, and relaxation training) were trained in the first four sessions (combined 240 min) rather than the first two sessions (combined 180 min) (Figure 1).

All sessions were facilitated simultaneously by the two qualified clinical psychologists in one group. Educational slides were basically adopted strictly from the handbook. The slides were designed familiar and ingenious including illustrations, videos, and quizzes, to be enjoyable and approachable for even young children. The video contents included scenes about tic maintained by attention (social positive reinforcement), escape/avoidance (social negative reinforcement), and automatic reinforcement. KT was in charge of administering the core therapeutic components, and JI provided technical support as needed during the first four sessions (core therapeutic sessions). A lecture on social support, or how to give appropriate praise and reminder for the competing response (a specific action that makes the tic more difficult to emerge), was given at the end of the core therapeutic sessions to parents. Besides, the parents were involved throughout the sessions. For instance, helping the children with selecting appropriate competing responses, conducting homework with the children, and monitoring and recording the children's tics.

In sessions 5–7, which focused on a specific individual tic (specific tic sessions), HRT was provided in group settings according to each participant's tic. If one participant (child–parent dyads) participated in the HRT, other participants observed the training. FAI was conducted separately (one on one) using the breakout-room function of Zoom© with KT. We created opportunities for participants to talk with the therapist individually. Hence, they could discuss issues that they may not be comfortable sharing with the group. A booster session was provided to review the topics covered in the previous sessions and treatment gains, and to learn how to deal with newly emerging tics in the future (as shown in Figure 1).

The core therapeutic sessions and specific tic sessions (the first seven sessions) were held weekly. A booster session was held 4 weeks after the last specific tic session to promote skill maintenance. The duration of the entire treatment program was 10 weeks. Consistent with the manual, a weekly homework was created using Google docs© and sheets©, which was assigned and submitted *via* Google Classroom©. KT checked and provided feedback weekly and individually *via* Google Classroom©.

## Assessment measures

Clinical assessments were performed 5 days before the baseline (Ax1 assessment 1) and the first session (Ax2 assessment 2), and 5 days after the end of the sessions (Ax3 assessment 3). Table 2 depicts the detailed assessment schedule. Questionnaire-based assessments were mailed to the participants, and interview-based assessments were conducted by an experienced medical doctor (non-therapist) *via* Zoom©.

### Yale global tic severity scale (19)

The YGTSS result was the primary outcome measure for evaluating the preliminary efficacy of the intervention for reducing tics. YGTSS is a semi-structured interview that is the gold standard for tic assessment. It yields two separate 0–50-point scales. The Total Tic Severity scale can be used to assess the severity of motor and vocal tic symptoms across the domains of tic number, frequency, intensity, complexity, and interference. The Tic Impairment scale assesses the extent to which the tics lead to impairment in the child's daily life and activities (impairment scale score: 0–50). In both scales, higher scores indicate more severe tic symptoms or impairment.

### Clinical global impression (20)

The Clinical Global Impression (CGI) rating scale is one of the most widely used assessment scales for assessing

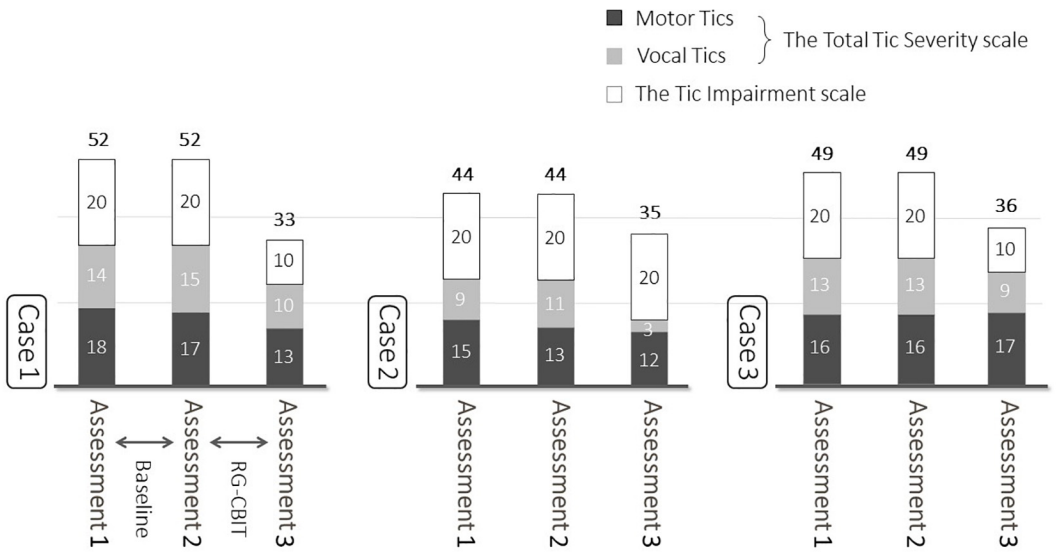


FIGURE 2
Baseline and post-treatment YGTSS. At baseline, the Total Tic Severity scale score did not change. However, after the intervention, those scores decreased by 9, 9, and 3 points for cases 1, 2, and 3, respectively. The score reduced by an average of 7.0.

TABLE 3 Clinical outcomes (CGI and PUTS).

| | Ax 1 | Baseline 10 weeks | Ax 2 | RG-CBIT 10 weeks | Ax 3 |
|---|---|---|---|---|---|
| CGI-S | | | | | |
| Case 1 | 5 | | 5 | | 3 |
| Case 2 | 4 | | 4 | | 4 |
| Case 3 | 3 | | 5 | | 4 |
| CGI-I | | | | | |
| Case 1 | NA | | 4 | | 2 |
| Case 2 | NA | | 4 | | 4 |
| Case 3 | NA | | 5 | | 3 |
| PUTS | | | | | |
| Case 1 | 20 | | 13 | | 29 |
| Case 2 | 24 | | 26 | | 23 |
| Case 3 | 21 | | 21 | | 19 |

Ax, Assessment; NA, not available; CGI-S, The Clinical Global Impression-severity score; CGI-I, The Clinical Global Impression-Improvement scale; PUTS, The Premonitory Urge of Tics Scale.

symptom severity and treatment response in intervention studies of patients with mental disorders. The CGI Severity score (CGI-S) is an observer-rated seven-point scale for evaluating illness severity at the time of assessment (scored between 1: normal, not at all ill and 7: among the most extremely ill patients). The seven-point CGI Improvement scale (CGI-I) rates improvement from 1 (very much improved) and 7 (very much worse due to intervention). A rating of 4 indicates that a patient did not experience any improvement after the intervention.

## Premonitory urge of tics scale (21, 22)

Premonitory Urge of Tics Scale (PUTS) is a 9-item self-reported questionnaire scored from 1 to 4 (with a total score of 9–36), which is commonly used to assess premonitory urge strength. The Japanese version was designed using rigid methods, including translation and back translation, and with sufficient internal and concurrent validity.

## Strength and difficulties questionnaire (23, 24)

Strength and Difficulties Questionnaire (SDQ) is a 25-item questionnaire that is used to assess the emotional and behavioral perspective of children. It was answered by the parents in this study. These items comprise five scales, which are as follows: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationships problem, and prosocial behavior. The previous four subscales were added together to generate the total difficulty score (range: 0–40) (based on 20 items), with higher scores indicating more severe conditions.

## Japanese version of the client satisfaction questionnaire-8 (25, 26)

Client Satisfaction Questionnaire-8 (CSQ-8) is an 8-item self-report questionnaire providing comprehensive measures of patient or client satisfaction with services in the medical and mental health primary care. Each item was scored from 1 to 4 (with a total score of 8–32), with higher scores representing higher satisfaction.

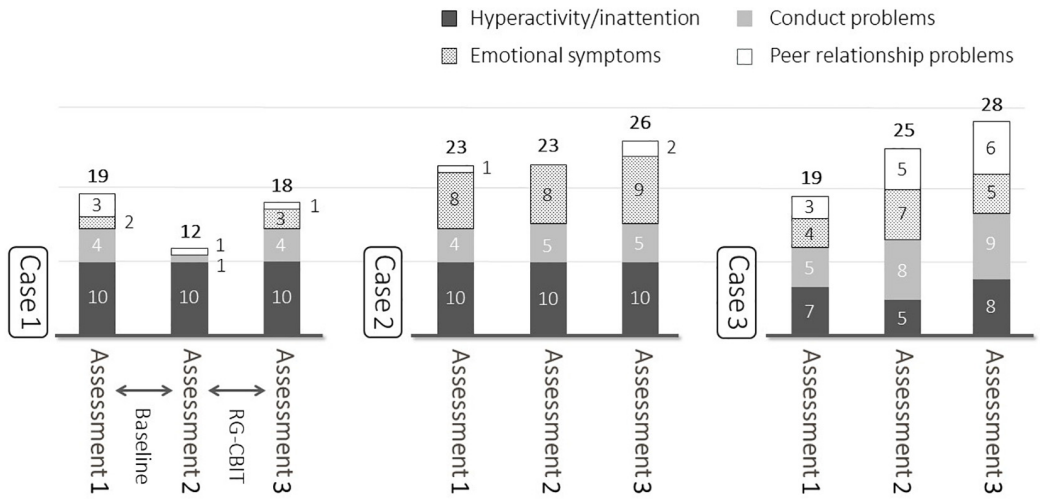


FIGURE 3
Baseline and post-treatment SDQ. After the intervention, the total SDQ scores increased by 6, 3, and 3 points for cases 1, 2, and 3, respectively.

### Japanese version of the working alliance inventory-short revised (27, 28)

Working Alliance Inventory-Short Revised (WAI-SR) is a recently refined self-reported questionnaire evaluating the therapeutic alliance that assesses three key aspects: agreement on the tasks of therapy, agreement on the goals of therapy, and development of an affective bond. It contains 12 questions according to the 7-point Likert scale (with a total score of 12–84), with higher scores indicating good alliance.

### Modified version of the treatment evaluation inventory (29, 30)

Treatment Evaluation Inventory (TEI) is a commonly used measure of treatment acceptability. Modified TEI contains 11 items divided into two subscales: (a) general acceptability scale (8 items) and (b) negative aspect subscale (3 items). Each item is seven-point Likert scale (with a total score of 11–77). A score of 44 indicates moderately favorable attitudes toward the treatment, with higher scores representing favorable treatment.

## Results

Three participants attended all the sessions and completed all assessments.

Figure 2 shows the YGTSS scores. During baseline (between Ax1 and Ax 2), the Total Tic Severity scale score did not change. However, after the intervention, the scores decreased by 9, 9, and 3 points for cases 1, 2, and 3, respectively. The score reduced by an average of 7.0. The Tic Impairment scale score did not change at baseline. However, it decreased by 10, 0, and 10 points for cases 1, 2, and 3, respectively, after the intervention.

TABLE 4 Process measures (CSQ-8J, J-WAI-SR and TEI-R).

| Measure | Scores range | Case 1 | Case 2 | Case 3 | Average |
|---|---|---|---|---|---|
| CSQ-8J | 8–32 | 29 | 30 | 25 | 28.0 |
| J-WAI-SR | 12–84 | 84 | 75 | 66 | 75.0 |
| Modified-TEI | 11–77 | 67 | 69 | 60 | 65.3 |

CSQ-8J, The Japanese version of the Client Satisfaction Questionnaire-8; J WAI-SR, The Japanese version of the Working Alliance Inventory-Short Revised; Modified-TEI, Modified version of the Treatment Evaluation Inventory.

Table 3 depicts the CGI and PUTS scores. The CGI-S and CGI-I score showed no change or worsened at baseline. Nevertheless, they showed improvement in two cases after the intervention (Table 3). Figure 3 shows the SDQ scores. After the intervention, the total SDQ scores increased by 6, 3, and 3 points for cases, respectively.

Table 4 shows the process measures (CSQ-8J, J-WAI-SR, and Modified-TEI). The average CSQ-8J, J-WAI-SR, and Modified-TEI were 28.0, 75.0, and 65.3, respectively.

## Discussion

Using the Bayesian network meta-analysis methods, Liang et al. showed that CBIT is an effective treatment for patients with TS (31). However, most children and adolescents with TS, particularly in non-English speaking countries, do not have access to CBIT because of several barriers. Thus, we developed RG-CBIT to eliminate barriers such as lack of trained therapists, treatment cost, and travel distance. The current study aimed to evaluate the preliminary efficacy, feasibility, and acceptability of RG-CBIT *via* an open case series.

Tic severity and impairment reduced from baseline to post-intervention in this study. Tic severity and tic-related impairment reduced based on the assessment using YGTSS. Piacentini et al. performed a large RCT examining the efficacy of individual face-to-face CBIT. Results showed that the total tic severity score decreased by an average of 7.6 points (8). The current study showed a similar improvement. That is, the total tic severity score decreased by 7.0 points even though remote administration and group format were applied. A 6-7 point decrease in the total tic severity score is an indicator of treatment response (32), and we believe that our trial was clinically effective. Impairment scores on YGTSS were not high from baseline for all 3 participants, this is probably because they had previously attended our facility, received psycho-education as usual medical care, and consulted with the school.

Moreover, improvement was also observed based on CGI, and this finding supports the efficacy of RG-CBIT. Even though the number of sessions specifically focused on tics, it was less than that specified in the original CBIT manual (**Figure 1**), and the results of the current study were comparable to that of previous ones. One potential explanation is that HRT was provided in groups. Thus, the participants could also learn to deal with the tic symptoms of other patients. Another reason is that the four separate core therapeutic components sessions may have a positive impact on the retention of knowledge and skills.

Despite the explicit teaching about awareness to the perception of premonitory urges and instruction of voluntary competing response in HRT contents, the PUTS score did not improve with RG-CBIT. Previous studies have reported similar results (8, 10, 33).

Strength and difficulties questionnaire was used to assess the impact of RG-CBIT on the QOL of patients. Results showed that the QOL increased after the intervention. SDQ is affected by different factors including school life and family relationships. Thus, it might have been influenced by other factors other than the intervention in this study (23, 34).

Regarding the feasibility and acceptability of RG-CBIT, the attendance rate of participants was 100%, and the patients had strong treatment satisfaction and therapeutic alliance based on the process measures (CSQ-8J, J-WAI-SR, and TEI-R) (**Table 4**). The CSQ-8J and J-WAI-SR findings were similar to those reported by Ricketts et al. (35) and Himle et al. (15). This finding is particularly significant, as doing group remote therapy has become even more important during the coronavirus disease 2019 pandemic. The average scores were favorable. However, these scores were lower in case 3. In this open case series, the participants were aged 6, 9, and 13 years. Case 3 was the oldest among the three participants and was only a junior high school student. Group sessions were conducted using methods that can help the youngest participant understand instructions and maintain attention during the session, therefore, 13 years-girl may have felt a little bored. The age difference might have affected the process measures of case 3, and the inclusion of matching age groups may enhance the acceptability of this treatment. Additionally, homework wasn't submitted in Case 3, occasionally. It is also important to devise ways to enhance the submission of homework.

Regarding materials, Zoom© was a reliable video platform. We can observe their facial expression and fine motor tics even eye blinking, lip cramp, and so on. The breakout-room was useful for private consultations in FAI as intended, except that it is a bit complicated to operate. The participants were asked to keep their video cameras on throughout the sessions so the therapist could monitor their responses. As for Google Classroom©, it was a favorable way to provide feedback for the homework, however, trouble occurred occasionally with sharing files between participants and the therapist. The current study had several limitations. That is, the research design was not controlled, and a small sample size was included. Moreover, RG-CBIT was delivered during the circumstances of a COVID-19 pandemic. The repeated lockdowns and restrictions on school life might have affected the mental health of all children, and may have had no small impact on the participants in this study. Finally, follow-up assessment was not conducted. Thus, whether gains were maintained is unknown. In the near future, we plan to conduct an assessor-blind RCT of RG-CBIT on children with tic disorders that can address these limitations.

In conclusion, RG-CBIT had satisfactory efficacy and adequate feasibility and acceptability. Although further studies are required, the current research supported previous notions showing that RG-CBIT is effective for reducing tic severity and impairment. Moreover, remote administration and group setting could mitigate barriers for accessing CBIT such as lack of experienced psychotherapists, treatment cost, and travel distance.

## Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving human participants were reviewed and approved by the ethical committee of Dokkyo Medical University Saitama Medical Center (21019). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## Author contributions

TI, KT, and JI collected patient's data. KT and JI facilitated the sessions. TI, KT, and DW compiled the manuscript. TI, KT, and RS participated in the design of this study. DW and RS supervised this research. All authors reviewed the manuscript and approved it in its current form and have approved the ordering of authorship.

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## Conflict of interest

DW was received book royalties on the CBIT manual from Oxford University Press.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note



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# Tourettic OCD: Current understanding and treatment challenges of a unique endophenotype

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Obsessive compulsive disorder (OCD) and chronic tic disorders (CTD) including Tourette Syndrome (TS) are often comorbid conditions. While some patients present with distinct symptoms of CTD and/or OCD, a subset of patients demonstrate a unique overlap of symptoms, known as Tourettic OCD (TOCD), in which tics, compulsions, and their preceding premonitory urges are overlapping and tightly intertwined. The specific behaviors seen in TOCD are typically complex tic-like behaviors although with a compulsive and partially anxious nature reminiscent of OCD. TOCD is not classified within the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) as an independent diagnostic entity, but mounting evidence suggests that TOCD is an intermediate neuropsychiatric disorder distinct from either TS or OCD alone and as such represents a unique phenomenology. In this review of TOCD we discuss clinical, genetic, environmental, neurodevelopmental, and neurocircuit-based research to better characterize our current understanding of this disorder. TOCD is characterized by earlier age of onset, male predominance, and specific symptom clusters such as lower tendency toward compulsions related to checking, cleaning, and reassurance seeking and higher tendency toward compulsions such as rubbing, tapping, or touching associated with symmetry concerns or thoughts of exactness. Functional magnetic resonance imaging (fMRI) imaging suggests that TOCD symptoms may arise from involvement of an intermediate neurocircuitry distinct from classic OCD or classic CTD. Small cumulative contributions from multiple genetic loci have been implicated, as have environmental factors such as infection and perinatal trauma. In addition, this review addresses the treatment of TOCD which is especially complex and often treatment resistant and requires pharmacology and behavioral therapy in multiple modalities. Given the distressing impact of TOCD on patients' functioning, the goal of this review is to raise awareness of this distinct entity toward the goal of improving standards of care.

KEYWORDS

**Tourette syndrome, obsessive-compulsive disorder, OCD, TOCD, Tourettic OCD**

## Introduction

Obsessive compulsive disorder (OCD) and tic disorders such as Tourette Syndrome (TS) are well established entities within the pediatric population that can occur independently, but are often comorbid within the same individual. Over the last 10–15 years, there has been increasing awareness of the overlapping neurocircuitry of tics and OCD and the existence of an intermediate phenotype, known as Tourettic OCD (TOCD), in which symptoms are influenced by features of both OCD and TS and differ from either disorder alone (1). Patients with TOCD present with thoughts, sensations, and behavioral urges at the interface of compulsions and tics that may pose challenges to assessment, diagnosis, and treatment. Given that treatment differs for TS and OCD, combined therapy is typically required for full remission of TOCD symptoms.

Unlike the DSM-4, which classified OCD within the spectrum of anxiety disorders, DSM-5 delineates a distinct diagnostic classification of Obsessive-Compulsive and Related Disorders which encompasses OCD as well as body dysmorphic disorder, trichotillomania, hoarding disorder, and excoriation disorders (2). Despite this new classification, TOCD is not recognized as an independent diagnostic entity within DSM-5. Instead, a qualifying specification of "Tic-related" OCD is suggested, although this qualifier simply indicates any current or past history of a tic disorder but does not illuminate the unique nature of TOCD symptoms. This distinction is important as the symptoms of TOCD do not equate to simply having a comorbid tic disorder and OCD.

The goal of this review is to expand upon the original framework of TOCD (1) as an independent diagnosis with updated clinical, genetic, neurodevelopmental, and neurocircuit-based research as they have evolved over the past 15 years since the original conceptualization of TOCD. As tics are typically childhood onset disorders, tic-related OCD and TOCD are predominantly pediatric diagnoses and may represent developmentally unique subtypes of pediatric OCD. The overlapping neurocircuitry of tics and OCD during key developmental stages argues toward an intermediary neuropsychiatric disorder that may later resolve as brain architecture matures and tics are often outgrown, leading to changes in the nature of OCD symptoms as patients age.

## Symptom presentation

To understand the unique nature of TOCD symptoms it is helpful to first elucidate the symptoms of TS or OCD alone.

Tics are sudden, stereotyped movements, typically repetitive, that wax and wane in severity and intensity. Typically involuntary, they are at times associated with a preceding somatic sensation, often described as a physical or sensory urge that is relieved by engaging in either a motor movement or phonic vocalization. Examples of classic tics may include but are not limited to: facial grimacing, shoulder shrugging, tapping, touching, blinking, neck jerking, or vocalizations such as throat clearing, coughing, whistling, grunting, or yelling words out of context.

In contrast, OCD is categorized by the presence of intrusive, ego-dystonic thoughts, known as *obsessions* that are distressing to the individual and cause heightened anxiety. These are commonly followed by *compulsions*, which are repetitive ritualized actions intended to alleviate the anxiety. A classic example would be contamination fears that lead to compulsive washing behaviors. Obsessions typically recur throughout the day and lead to compulsions which can last for hours and interfere with functioning in multiple domains including academic, social, emotional, or physical. In more severe cases, compulsions may interfere with self-care and activities of daily living, such as washing one's hands to the point of pain, skin breakdown, or infection. Subtypes of OCD are often classified by the nature of the obsessional thoughts, such as contamination obsessions with cleaning compulsions, waste-related obsessions with hoarding compulsions, symmetry obsessions with ordering compulsions, religious obsessions with ritual-based compulsions, harm obsessions with checking compulsions, and ethical obsessions with reassurance-seeking compulsions. Some patients may experience obsessional thoughts without visible compulsions, such as intrusive thoughts of a violent or sexual nature or moralistic concerns. Newer theories suggest that compulsions may actually *precede* and trigger anxiety or obsessions (3) although by all accounts the cycle of obsessions and compulsions are hallmark features of OCD regardless of the order of occurrence.

Both OCD and TS are accompanied by a feeling of discomfort that precedes the behavior. In OCD the discomfort is emotional – anxiety related – whereas in TS the discomfort is a physical or sensory premonitory urge. Both conditions share the drive to engage in repetitive behavior; however, tics are classically considered involuntary and able to be suppressed only with effort whereas compulsions require higher order cognitive volition and awareness. The neurocircuitry behind TS and OCD share commonalities. As widely reported in the literature (4) the cortico-striatal-thalamo-cortical (CSTC) pathway is involved in both TS and OCD. The specific brain regions thought to be involved in this pathway include the Ventromedial Prefrontal Cortex, Anterior Cingulate Cortex, Orbitofrontal Cortex, and Parietal and Somatosensory Cortex. These are regions that are often associated with "action selection, performance, monitoring, response inhibition, and goal-directed behaviors" (3), behaviors often implicated in both TS and OCD.

Patients with TOCD present with overlapping symptomatology (**Table 1**). Unlike in OCD, patients with TOCD rarely describe obsessional thoughts but rather a feeling

TABLE 1 Comparative characteristics of OCD, Tourette's syndrome, and Tourettic OCD.

| | OCD | Tourette's syndrome | Tourettic OCD |
|---|---|---|---|
| Age of onset | 11–15 years | Age 6–9 years | Age 7–13 |
| Heritability | 37–47% (95) | 58–77% | Unknown |
| Prevalence | 1–3% (96–98) | ∼0.85–1% (4) | Unknown |
| Symptom course | Waxing and waning throughout life, typically persists if untreated | 60–75% resolution by adulthood | Unknown |
| Symptom characteristics | Internalizing | Externalizing | Both |
| Precipitating cause | Provoked by intrusive anxious thoughts | Provoked by somatic sensations/premonitory urge | Provoked by somatic premonitory urge often with an associated cognition of something being "Not right" or needing to be "just so" |
| Content of behaviors | Repetitive behaviors, often involving volitional multi-step compulsions | Repetitive motor movements typically involving one muscle group or body part | Repetitive complex motor movements often with several steps including tapping, arranging, adhering to certain numbers of repetitions |
| Consequences | Anxious thoughts are briefly alleviated | Premonitory urge is briefly alleviated | Premonitory urge is briefly alleviated if tics are performed "just right" |
| Suppressable? | Yes, with effort | Yes, with effort | More difficult to suppress than OCD or TD alone |
| Behavioral therapy | ERP, CBT | CBIT | ERP/CBIT/CBT |

of intense physical discomfort, more akin to tic disorders, that drives compulsive behaviors. However, although this sensation is not initially driven by anxiety, it can become intolerable and anxiety provoking if not mitigated by engaging in the desired behavior. Similarly, the compulsions of TOCD have components of both OCD and TS. Movements are typically complex rather than simple tics and may involve tapping or touching things in a specific way, vocalizing phrases rather than simple sounds, or a multistep progression of movements, for example, a sequence of several different hand or body movements, rather than a single motor movement. Patients with TOCD often need to repeat the behaviors a number of times until they feel "right" and the discomforting premonitory sensation has passed. In this way, TOCD is both an externalizing and an internalizing disorder. It conflates the externalizing disinhibited movements of TS in parallel with internalized distress reminiscent of OCD when the behaviors are not completed "just so." These behaviors have been termed "impulsions," rather than compulsions, to help denote their particular phenomenology (5). While impulsions share some common features with compulsions, impulsions tend not to be driven by classic anxiety and so are not goal directed like classic OCD compulsions.

The lack of clarity over the etiology of the patient's discomfort as well as the nature of the repetitive behavior can cloud diagnostic clarification and treatment decisions and patients can be miscategorized as having only a tic disorder or only OCD. Categorization is particularly complicated and relevant as the treatment for tic disorders differs widely from that of OCD. Additionally, children can have comorbid classic tics and OCD, known as tic-related OCD, but may not possess the unique blend of symptoms required for TOCD; this can further confound the diagnosis of TOCD which is a clinical diagnosis. While many mental health disorders are clinical diagnoses, the unique challenges in TOCD are that the diagnostic entity itself is not as well-known as tics or OCD alone, and TOCD does not have clear diagnostic parameters in DSM-5 as do tic- and obsessive-compulsive related disorders. Therefore, the diagnosis of TOCD may be overlooked even by psychiatrists and neurologists.

The medical literature that evaluates tic-related OCD is also muddied; it can be difficult to interpret the nature of the population being studied as TOCD may not be explicitly distinguished within the study population. Many of the studies included in this article address tic-related OCD and we have attempted to extrapolate from this data to the extent possible. Focused studies on TOCD, of which there are currently few, are needed.

## Epidemiology, genetics, and epigenetics

Obsessive compulsive disorder presents in a bimodal distribution, with the first mean age of onset around 9–10 years (SD ± 2.5 years) and a second wave of new cases with mean onset in the early 20's (6, 7). In contrast to OCD alone, tic-related OCD is characterized by earlier, pre-pubertal age of onset, and male predominance. Individuals with tic-related OCD have specific symptom clusters such as lower tendency toward compulsions related to checking, cleaning, and reassurance seeking and higher tendency toward compulsions such as rubbing, tapping, or touching associated with symmetry concerns or thoughts of exactness (8). The studies in tic-related

OCD have shown mixed results in youth, with some reporting that tic-related OCD may present with intrusive thoughts of a violent or sexual nature that are not accompanied by a particular compulsion (9, 10). Other groups showed that individuals with tic-related OCD were more likely to experience washing and cleaning compulsions, hoarding, and ordering (11, 12).

## Genetics

Tourette syndrome is inherited in 70–80% of cases (13) making it one of the most heritable childhood-onset neuropsychiatric disorders (14), which has been widely reproduced in the literature (15, 16). Various approaches have been undertaken to evaluate the genetic architecture of TS including candidate gene studies, segregation analysis, linkage analysis, cytogenetics, copy number variants (CNV), studies of rare variations, genome-wide association studies (GWAS), and whole exome sequencing (WES). The Tourette Syndrome Association International Consortium for Genetics (TSAICG) and others investigated various susceptibility genes in the dopaminergic, serotonergic and glutamatergic pathways, such as the receptors and transporters *DRD2*, *DAT1* (*SLC6A3*), *HTR2A*, and *EAAT1* but later switched to GWAS and CNV studies (16). TSAICG contributed to the creation of the Psychiatric Genomics Consortium for Tourette Syndrome, which undertook the first genome-wide association study (GWAS) of TS. It found that no single nucleotide polymorphisms (SNP) reached genome-wide significance, but the top-ranking variants were enriched for genes that affect gene expression and methylation in the fronto-striatal circuitry, which is in line with current working models of TS neurocircuitry (17). A similar study done by the Tourette International Collaborative Genetics Study (TIC GENETICS), analyzed WES in families with TS and found that histaminergic pathway genes were highly enriched in TS etiology (L-histidine Decarboxylase- *HDC* enzyme that converts L-histidine to histamine) (18–20), again in line with current models of TS pathophysiology, which involve neurotransmission, inflammation, and smooth muscle tone.

In parallel, the genetic architecture of OCD has been analyzed by other large multicenter collaborations including the International Obsessive-Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC) and the OCD Collaborative Genetics Association Study (OCGAS). The meta-analysis from the two consortia of 2,688 individuals with OCD and 7,037 matched controls found that no SNPs reached genome-wide significance (21) but several glutaminergic system genes have been implicated (e.g., *GRID2*, *DLGAP1*). Genome-wide association studies (GWAS) have estimated the genetic heritability for OCD at approximately 0.37 in adults with OCD and 0.43 in childhood onset OCD (22). The age of onset of OCD is strongly linked to familial genetic loading. In pediatric OCD, individuals have a two-fold higher risk of having a first-degree relative with OCD as compared to adult-onset cases. The current understanding of the genetics of OCD has been extensively reviewed in the literature (23).

Previous data suggests that OCD and TS share some genetic blueprint. Among pediatric patients with OCD, greater than 50% exhibit tics. Likewise, an estimated 30–60% of patients with TS manifest symptoms of OCD (24). Patients with TS or OCD are also more likely to have a first-degree relative with either of these disorders (25). Additionally, biological relatives of probands with TS are more likely to develop OCD as compared to adoptive relatives of the same probands (26). This cross-disorder prevalence both within patients and within families suggests shared genetic underpinnings. Genome-wide associations in a combined sample of OCD and TS patients did not show overlapping polygenic scores for both disorders (27) although a genetic correlation between TS and OCD was estimated at 0.41 using genome wide complex trait analysis (22). These varying studies suggest a complex genetic background to each disorder, with small cumulative contributions from multiple genetic loci. Genetic studies in monozygotic twins show only 50% concordance rates in tic-related OCD/TOCD (28) highlighting the complex nature of heritability in these disorders.

The genetic architecture for TOCD is still unknown. Given that TOCD manifests with components of both TS and OCD, it is postulated to share genetic similarities to both disorders. Coffey et al. suggest that TOCD is more genetically similar to TS than to OCD because patients with TS and TOCD have higher rates of comorbid ADHD compared to patients with OCD (29). Ironically, newer advent technologies, designed to shed light on these questions, have in fact made the data even more disparate as the increased numbers of genetic studies yield conflicting results. Given the lack of clarity in both OCD and TS, it is no surprise that even less is known about TOCD. By extrapolation we presume that genes in the dopaminergic, serotonergic, glutaminergic and histaminergic pathways along the CTSC circuit are implicated. Epigenetic factors likely also contribute to variability in clinical presentation including age of onset, symptom severity, and symptom characteristics, although large population studies are needed.

## Environmental factors

It is widely known in the literature that environmental factors exacerbate tic/OCD symptoms. In addition to the known tendency of environmental stressors to exacerbate existing symptoms within an individual, prospective studies are elucidating a potential link between environmental factors and the onset of tics or OCD in individuals with no personal prior diagnosis but with a first degree relative with a CTD (30). While multiple environmental stressors are being considered,

three in particular have been elucidated: (1) infection or inflammation, (2) perinatal complications, and (3) chronic childhood psychosocial stress.

## Infectious or inflammatory processes

A variety of neuropsychiatric disorders that include pre-existing tic, OCD, and TOCD symptoms are known to increase during infectious or inflammatory processes, suggesting immune-mediated mechanisms for these symptoms (31). Not only has active inflammation been shown in the neurocircuits underlying OCD symptoms (and by extension, the neurocircuitry of tics as these are overlapping networks in the brain) (32), but even a history of infection has been implicated in increased incidence of mental health disorders that include tics and OCD. A Danish study of over one million youth aged birth-17 years evaluated patient records in a period of up to 17 years following documented infection and found that a remote history of both streptococcal and non-streptococcal infection increased the risk of both tic and OCD symptoms (33). Interestingly, streptococcal infection in particular was linked to later development of tic disorders, while OCD arose from all-cause infectious etiologies (33).

The possibility of a specific connection between streptococcal infection and tic/OCD symptoms has been widely debated in the literature. While some studies have shown a link, others have failed to corroborate these results. A very recent European study did not confirm this specific association between tics and streptococcal infection (34). The prospective European Multicentre Tics in Children Study (EMTICS) across 16 European centers followed a cohort of 259 children aged 3–10 years with no prior history of tics but a first degree relative with CTD, to assess the presence of Group A Streptococcal (GAS) infection using throat swabs, serum Anti-streptolysin O titers (ASOT) and Anti-DNAse B (ADB) titers whether they had pharyngitis symptoms or not. Sixty-one children (23.6%) had new onset tics over a 1-year follow up with a strong association with male sex, but no statistical correlation linked those who developed tics with evidence of a prior GAS infection. Based on what is known about genetic heritability of tic disorders, the 23.6% of children who developed tics would fall within the expected range based on genetic heritability alone, suggesting little contribution from a prior GAS-related etiology.

The hotly debated connection between GAS infection and tic/OCD symptoms is disputed not only as it relates to symptom flares in diagnosed patients, but also the potential for GAS to trigger abrupt onset CTD or OCD in previously healthy children. The diagnostic term PANDAS – Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus – was introduced in 1998 to describe a presumed subset of acute onset OCD and tic disorders that occur spontaneously in response to GAS infections, primarily in children (35, 36). This relationship has since been expanded to include non-streptococcal infections as well, under the umbrella term PANS – Pediatric Acute-onset Neuropsychiatric Syndrome, a fairly vague and inclusive term that may have led to high rates of over-diagnosis, although a small subset of true cases is probable. One of the key diagnostic criteria for both PANS and PANDAS is the abrupt onset of OCD and/or tic-like behaviors. A suggested mechanism is cross reactivity of anti-strep or other antigen-specific antibodies that affect neural circuits in the basal ganglia, a structure implicated in the neurocircuitry of both tics and OCD (37). However, the evidence to support this mechanism is insufficient as no specific antigen-antibody interactions have been experimentally demonstrated in cases of PANDAS, nor have specific biomarkers been elucidated. Instead, the proposed mechanism is borrowed from what is known from Sydenham's chorea, a similar disorder that is precipitated by GAS infection and associated with basal ganglia dysfunction (37) and for which antigen-antibody interactions in the basal ganglia have been demonstrated. Both PANDAS and PANS remain widely debated in the literature because it is often unclear if pre-existing mild tic or OCD symptoms were escalated by infection to the level of clinical concern, or whether the symptoms are truly abrupt onset and directly caused by infectious processes. To the extent to which infection either exacerbates or gives rise to abrupt onset tic or OCD symptoms, TOCD is likely equally exacerbated by this phenomenon, and the complex and atypical tics described in the literature may indicate TOCD symptoms.

In a timely example of the effects of infections, both tic and OCD symptoms have been shown to sometimes increase in relation to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen behind COVID-19. This increase is thought to be related to both the infectious agent itself as well as to increased environmental stress of quarantining and the effect of social protocols that may encourage compulsions such as cleaning, checking, and hand washing (38).

## Perinatal complications

A 2016 study examining 1,113 patients from the Tourette International Collaborative Genetics Study evaluated 586 patients with CTD and 527 healthy family controls and found that pre- and perinatal complications result in increased incidence of CTD and OCD (39). These complications included premature birth (OR = 1.72), severe hyperemesis gravidarum (OR = 2.57), and problems during delivery (OR = 1.49), suggesting that early adverse events predispose to later development of tics and OCD, and by extrapolation likely to TOCD. Interestingly, prenatal complications were more closely associated with development of CTD while problems during delivery and immediately post-natal were more closely

linked to OCD. A parallel similar study comparing perinatal history of 130 youths with OCD compared to 49 age-matched controls found that history of maternal prenatal illness and higher rates of difficulties during labor such as induction, use of forceps, prolonged labor, and conversion to Cesarean-section were correlated with earlier age of OCD, greater symptoms severity, and higher incidence of comorbid tic disorders/TOCD (40). Similar studies have reinforced the increased incidence of tic-related OCD vs. TOCD in cases of prenatal and perinatal complications (41). The increased incidence of early adverse events suggests environmental or epigenetic contributions that may occur during key critical periods of pre- and perinatal neuronal development. Much remains to be understood regarding the timing of injury as it relates to downstream development of CTD or OCD. The discrepancy in the timing of pre- vs. post-natal injury correlating to later onset CTD vs. OCD suggests that CTD, OCD, and TOCD may lie along a developmental spectrum, such that proximal injury at different stages of development affects distal symptom characteristics.

## Psychosocial stress

Psychosocial stress has been linked to the development of CTD and OCD as well as to symptom severity, suggesting that the same is true in TOCD patients (42–44). Lin et al. demonstrated that children with OCD scored significantly higher on self- and parent-rating scales of perceived stress, and that higher levels of stress correlated with later symptom severity as well as later depressive episodes (45). Similarly, in a survey completed by patients with TS, 96.8% of patients identified psychosocial stressors as a major precipitant for tic symptom severity (46). This correlation has been exemplified by the stressors endured during the recent COVID-19 pandemic, which was shown to have increased OCD severity across all symptom dimensions (43). In a population of patients with OCD, over 60% reported at least one stressful life event prior to the onset of symptoms, and of those over 1/3 rated the stressful event as severe (i.e., death of a family member, major illness, etc.) (42). Other studies suggest that children and adolescents with TS and OCD tend to experience significantly more psychosocial stress than children without these conditions, including a higher number of daily stressful events as well as major life stressors of a chronic nature (47).

## Limitations of current knowledge

Taken together, genetic, epigenetic, and environmental factors play a role in driving both tic and OCD symptoms as described above. The strong familial tendency for first degree relatives with a shared family history to develop *either* OCD or CTD, confirms that these disorders do not follow simple inheritance patterns, nor are they likely to be exclusively determined by genetic factors. Clinically, we have observed that CTD are prevalent among patients with a parent with CTD *or* OCD and vice versa, as compared to the general population. Likewise, it is common for one sibling within the family to develop a CTD, while another sibling may develop OCD suggesting epigenetic or environmental contributions to an underlying genetic predisposition. Unfortunately, no definitive data has yet elucidated why one family member may develop a CTD while another may develop OCD or TOCD. This remains an important and outstanding question that requires further study.

# Neurocircuitry

The overlapping symptomatology of OCD and TS suggests similar mechanisms for reduced cognitive control over motor and behavioral inhibition. Therefore, it is not surprising that ADHD and ASD run comorbid with TOCD because ADHD and ASD both arguably manifest with difficulties of inhibition indicated by impulsivity (ADHD) and repetitive, stereotyped behaviors (ASD).

The neurocircuitry of tic disorders and OCD are among the best characterized within neuropsychiatric disorders. In recent years, studies have implicated up to five circuits that play critical roles in the neurocircuitry of OCD and may explain some of the heterogeneity of this disorder (3, 48). Multiple neuroanatomical regions have been implicated including the amygdala and hippocampus (49), as well as frontoparietal and cerebellar structures (48, 50). However, the most heavily implicated and replicated region on fMRI imaging of both tic and OCD disorders is the cortico-striatal-thalamo-cortical (CSTC) loop. This network connects the prefrontal cortex (PFC), basal ganglia (including the caudate nucleus, putamen, nucleus accumbens, internal and external segments of the globus pallidus, subthalamic nuclei, and substantia nigra), and the thalamus, then returning to the PFC. Multiple reports of disruption to these networks, such as due to trauma or infection of the PFC or basal ganglia result in OCD and tic behaviors (35, 51–53).

The CSTC circuit is comprised of three primary sub-loops as described below. A full description of these circuits can be found in the medical literature (3, 48).

1. The *Motor Circuit* connects the sensorimotor and premotor cortices to the basal ganglia via the posterior-lateral putamen which in turn projects to the globus pallidus externus (GPe), the globus pallidus internus (GPi), and the subthalamic nuclei (STN). The GPi outputs to the ventrolateral thalamus en route back to the cortex.

This loop is involved in habit formation and top-down motor control.

2. The *Associative Circuit* (also known as the Dorsal and Ventral Cognitive Circuits) involves circuits from the dorsolateral prefrontal and lateral orbitofrontal cortices, which project through the caudate nucleus to the other basal ganglia structures described above. This circuit is thought to play a role in goal-directed behavior.
3. The *Limbic Circuit* involves the orbitofrontal and anterior cingulate cortices, which project to the caudate nucleus (CN), putamen, GPe, GPi, and STN and thalamus before returning to the cortex. This circuit is involved in motivation and reward.

Relative upregulation and downregulation of the CSTC network —the motor circuit, the associative circuit, and the limbic circuit —are postulated to underlie the neurophysiology of both tics and OCD. In both conditions, patients experience a loss of top-down control in which anxious stimuli or sensory perceptions lose their rational salience and become overly discomforting. This triggers repetitive behaviors by means of the associative circuit and basal ganglia activation, resulting in reward feedback that diminishes the anxious (intrusive thoughts) or somatic (premonitory urge) triggers. However, the relative *balance* of these loops has been postulated to differ between TS and OCD. While both symptom clusters involve the associative circuit, OCD is thought to more heavily involve the limbic-associative circuits (associated with anxious distress), while TS involves the motor-associative circuits (associated with a somatic premonitory urge) (54, 55). As Shephard et al. have pointed out, both tics and OCD involve an "intolerance of uncertainty. . . a tendency to perceive and interpret uncertain situations as negative or threatening" (56). Such intolerance leads individuals to develop motor or behavioral responses that minimize their anxiety or discomfort.

These findings have been supported by fMRI and Positron Emission Tomography (PET) in separate studies of patients with tics or OCD. In a study of four patients with OCD exposed to progressively more distressing triggers, McGuire et al. (57) correlated symptom intensity of obsessive thoughts and desire to perform compulsions with increased blood flow in the right inferior frontal gyrus, caudate nucleus, putamen, globus pallidus, thalamus, left hippocampus, and cingulate gyrus. Notably, the premotor cortex and sensorimotor cortex were not heavily implicated, in keeping with the notion that OCD relies more heavily on limbic-associative circuits. Analogously, fMRI imaging of 13 patients with TS with spontaneous tics compared to 21 healthy controls with volitional tic-like movements (58) corroborated previous findings of elevated activity in all portions of the motor pathway including the sensorimotor cortex and basal ganglia. This finding supports the notion that dysregulation of the motor-associative circuit causes a lack of control over tic behaviors. Furthermore, the severity of tic symptoms was also positively correlated with increased neural activity in the amygdala/hippocampus complex, and was heightened in TS patients with spontaneous tics as compared to voluntary "tics" among healthy controls. This suggests that these regions may be involved in generating the premonitory urges of CTD which distinguish them from volitional movements. In contrast, the TS group had weaker activity in the caudate and anterior cingulate cortex, which exert top-down control over motor pathways though may fail to do so in patients with CTD. Activity in these regions negatively correlated with increased tic severity (58).

Although further studies are required, preliminary data suggest that TOCD symptoms may arise from involvement of all three sub-loops as part of an "intermediate" neurocircuitry that lies along the "impulsive-compulsive spectrum" (59). Indeed, studies among a clinically heterogeneous population of TS patients have postulated that while simple tics are most closely associated with changes in the motor circuit, complex tics (more reminiscent of TOCD behaviors) are associated with changes in the associative circuit, and frank OC behaviors in patients with TS are associated with greater dysregulation of the limbic circuit (54, 55). Regional brain involvement of the associative and limbic circuits in patients with complex tics or OC behaviors is more similar to OCD neurocircuitry in which the limbic-associative circuits are more heavily implicated than in simple tics alone. This heightened dysregulation of the associative-limbic circuit, in addition to the motor circuit, may yield a loss of top-down executive control, resulting in an inability to rationally analyze the accuracy of one's emotions, control their motor responses, or inhibit reward learning and habit formation. Phenotypically, the imbalanced network drives complex tic-like behaviors of a compulsive and partially anxious nature, commensurate with TOCD. Few neuroimaging data exists to confirm the specific circuits or neuroanatomical regions involved in TOCD specifically as compared to OCD and CTD, and further studies are warranted.

In an attempt to modulate the neurocircuitry for purposes of treatment, deep brain stimulation (DBS) has been used for adults with treatment-refractory Tourette syndrome (TS) since the late 1990s. Several different nuclei within the CSTC network have been explored as potential targets for DBS (60–62). Four targets within the basal ganglia have been most commonly used: the centromedian nucleus–nucleus ventrooralis internus complex of the thalamus (CM-Voi), the centromedian nucleus–parafascicular (CM-Pf) complex of the thalamus, the posteroventrolateral (pvIGPi), and the anteromedial portion of the globus pallidus internus (amGPi). A recent review on DBS in TS (63) analyzed 65 studies and included 376 patients. Overall, nearly 70% of the patients had >50 reduction on Yale Global Tic Severity Scale (YGTSS) scores regardless of these different targets. Interestingly, in tic patients with comorbid OCD, DBS in CM-Pf nucleus resulted in a reduction in OCD symptoms as measured by the Yale Brown

Obsessive Compulsive Scale (Y-BOCS) scores. For treatment-refractory OCD, the most widely used DBS targets have been the nucleus accumbens and the anterior limb of the internal capsule (NA/ALIC) (64–66). DBS targeting NA/ALIC has also been successfully used in patients with TS (67) again proving the structural and functional interconnectivity between these two disorders (67, 68). DBS therapy is invasive, may have side effects and has not been approved for use in the pediatric population. In addition, the optimal targets for symptom control may need to be individualized. Future efforts of combining fMRI with stereotactic surgery may help determine the best targets for patients with TOCD (64–66, 69).

## Pharmacological treatment

Unfortunately, as described above, TOCD is not independently classified within the DSM-5. It is best but inadequately captured under the diagnostic specifier of "tic-related OCD," defined as an OCD "diagnostic subtype based on whether the individual has a past or current tic disorder." As a result, pharmacological treatment for these patients may mistakenly concentrate on medication specific solely to OCD, which is often inadequate for remission of TOCD symptoms. To better account for TOCD holistically when considering the best treatment, clinicians should consider their condition as a case of comorbid OCD and tics disorder rather than a tic-related subtype of OCD (1).

First line agents differ between CTD and OCD (**Figure 1**). OCD and anxiety spectrum disorders are treated with strong serotonergic agents such as Selective Serotonin Reuptake Inhibitors (SSRIs) or Selective Serotonin and Norepinephrine Reuptake inhibitors (SSNRIs) (70). These agents work by blocking serotonin reuptake and therefore increasing serotonin availability at the synapse. Four SSRIs: fluvoxamine, paroxetine, fluoxetine, and sertraline, are FDA approved for the treatment of OCD in adults and may be utilized in children. These medications can address the somatic experience of anxiety including headache, fatigue, muscle pain, and GI upset in addition to treating mental anxiety. Tricyclic antidepressants (TCAs), which increase the availability of all monoamines including serotonin, norepinephrine, and dopamine, are equally effective though are less favored due to higher side effect profile compared to SSRIs. Side effects include dry mouth, blurry vision, constipation, and fatigue among others. One TCA, clomipramine, has been FDA approved to treat OCD. 40–60% of patients do not remit with SSRIs alone and have been shown to benefit from augmentation with antipsychotics. Either first- or second-generation antipsychotics are considered highly effective but are avoided as first line agents due to the high side effect profile including metabolic side effects, cognitive dulling, sedation, and extra-pyramidal side effects. Common antipsychotics used for this purpose include haloperidol (first generation), aripiprazole (second generation), or risperidone (second generation). Augmentation is implemented if SSRIs or TCAs fail to show response following 3 months of therapy at a therapeutic dose. As a general rule, "failure to respond" is defined as less than a 25–35% reduction on the Child Yale Brown Obsessive Compulsive Scale (71).

Like with OCD, tic disorders are felt to respond well to antipsychotic medications but have high risk of side effects. Two in particular, haloperidol and pimozide, are FDA approved for this purpose but are typically deferred until first line agents, the alpha agonists, have been tried. Alpha agonists, such as clonidine and guanfacine, are considered first line agents for tic disorders including Tourette syndrome and act by stimulating the post-synaptic alpha-2A receptors in prefrontal cortical pyramidal cells which may stimulates the frontal cortex to regulate attention and thus suppress tics. They may also decrease arousal. Although generally recognized as less effective than antipsychotic medications, they are favored as first line agents due to their lower side effect profile which can include hypotension and sedation. Children with TOCD often require combined treatment due to their overlapping symptomatology. They are more likely to require polypharmacy and higher dosing regimens (**Figure 2**).

A previous meta-analysis reviewing 15 clinical studies noted that tic symptoms in OCD patients are a substantial indicator of treatment-refractory response following SSRI monotherapy and that augmentation of SSRIs with antipsychotics allows for more sustained improvement in patients with comorbid TS and OCD (72, 73). Similarly, among tic-related OCD patients who were treatment refractory to a 12-week SSRI trial, addition of either risperidone or aripiprazole to an SSRI improved OCD symptoms in 56.5% of patients, tic symptoms in 68.1% of patients, and both OCD and tic symptoms in 50% of patients, with high likelihood of capturing TOCD patients within this population (74). One possible mechanism behind the SSRI-antipsychotic co-administration suggests that the SSRI targets OCD symptoms, while antipsychotics reduce tic symptomology in tic-related OCD and TOCD patients. Equally likely is that TOCD (and likely CTD and OCD) involves a combination of serotonergic and dopaminergic signaling, such that conjoint SSRI-antipsychotic administration modulates both of these neurotransmitter pathways and either treatment alone is insufficient. Since SSRI monotherapy generally serves as the first-line treatment in OCD patients, and antipsychotics are among the primary treatments for TS, adjunctive therapy with both medications allows for more effective pharmacological treatment of TOCD (**Figure 1**).

In addition, pharmacologic treatment of comorbid ADHD with alpha-agonists, atomoxetine or stimulants can help control the disinhibition and impulsivity that is common with TOCD patients. Historically, stimulants have been avoided in patients with tics; however, a recent Cochrane review analyzing eight studies with 510 participants with comorbid tics and ADHD

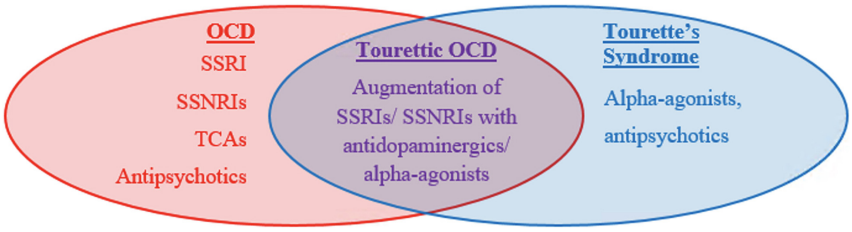


FIGURE 1
Similarities and differences in the pharmacologic management of tic disorders and OCD.

discredited this cause of concern. It showed that symptoms of ADHD and tics, including impulsivity, actually improved when several stimulant and non-stimulant medications were used, including methylphenidate, guanfacine, clonidine, and a combination of methylphenidate and clonidine. The single exception to this was one study of 3 weeks duration that found exacerbation of tics when using high dose dextroamphetamine (75). As always, an individualized approach to the choice of medication, means of delivery (short release vs. extended release vs. patch) and dose adjustment should be taken into consideration.

First line agents differ between these disorders. OCD is treated with SSRIs, SSNRIs, and less commonly with TCAs as first line agents. CTD are treated initially with alpha agonists. In both disorders, antipsychotics can be used for augmentation or as primary agents for children who do not respond or cannot tolerate first line agents. TOCD often warrants combined treatment as well as higher dosing regimens due to overlapping symptomatology. Management with antipsychotics is required more often as compared to CTD or OCD alone.

## Behavioral treatment modalities for patients with Tourettic obsessive compulsive disorder

Various psychological and behavioral therapies are used as monotherapy or in conjunction with pharmacologic therapy for OCD or TS depending on the patient's underlying symptoms (**Figure 2**). Cognitive Behavioral Therapy (CBT) and Exposure-Response Prevention Therapy (ERPT) are widely accepted as first-line behavioral interventions for OCD related symptoms, while Comprehensive Behavioral Intervention for Tics (CBIT) is a widely accepted behavioral treatment for tic disorders. The American Academy of Neurology 2019 Practice guidelines support CBIT as the first line treatment for tics, preceding medication (76). Each of the therapy modalities described here have been shown to be highly effective even in the absence of medication management, although a major barrier is the lack of access to trained providers.

The focus of these therapies differs based on the identified disorder and the symptoms being treated. CBT and ERPT start by identifying obsessional thinking patterns, and slowly train a patient to tolerate increasing levels of anxious distress while suppressing the desired compulsions. CBIT is arguably more behaviorally focused on learning to recognize premonitory urges and the occurrence of tics which are often out of a patient's conscious awareness. It considers the circumstances that trigger tics and seeks ways of diminishing these triggers. The emphasis is on finding the best competing response for each individual tic, focusing on one discrete tic at a time. Unfortunately, because tic disorders and OCD are often conceived of as distinct diagnoses, patients are often referred to only one therapeutic modality.

Utilizing behavioral therapy in addition to medication management has been shown to have higher rates of symptom remission in tics and in OCD alone (77). CBIT was shown to be efficacious for youth aged 9–17 years with CTD or TS (78). In a combined population of children with tic-related OCD, The Pediatric OCD Treatment Study (POTS II) (79) examined the efficacy of CBT augmentation strategies for youth who had only partially responded to SSRI treatment. Those receiving combination therapy in the form of medication management *and* traditional Cognitive Behavioral Therapy (CBT) had significantly greater reduction of OCD symptoms compared to medication alone (ES = 0.85). Because TOCD is even more nuanced than tic-related OCD, not only can its pharmacologic management be challenging but also the type of behavioral therapy employed. Similar to the need for combined medication management of both tic and OCD symptoms, we postulate and have found in our own clinical practice that TOCD responds best to adjunctive behavioral interventions targeting *both* tic and OCD symptoms. In light of the complex neurobehavioral presentation of TOCD, outcomes are significantly improved by focusing on the anxious-somatic distress of OCD through either CBT or ERPT in addition to targeted behavioral interventions for tics using CBIT. The emphasis on unhelpful thinking styles in CBT or ERPT can decrease the anxiety that triggers tics and repetitive behaviors and help develop strategies for coping with the debilitating nature of TOCD (80). In parallel, CBIT may help train the patient to perform a competing behavior when they feel the urge to tic, which over time lessens the premonitory urge.

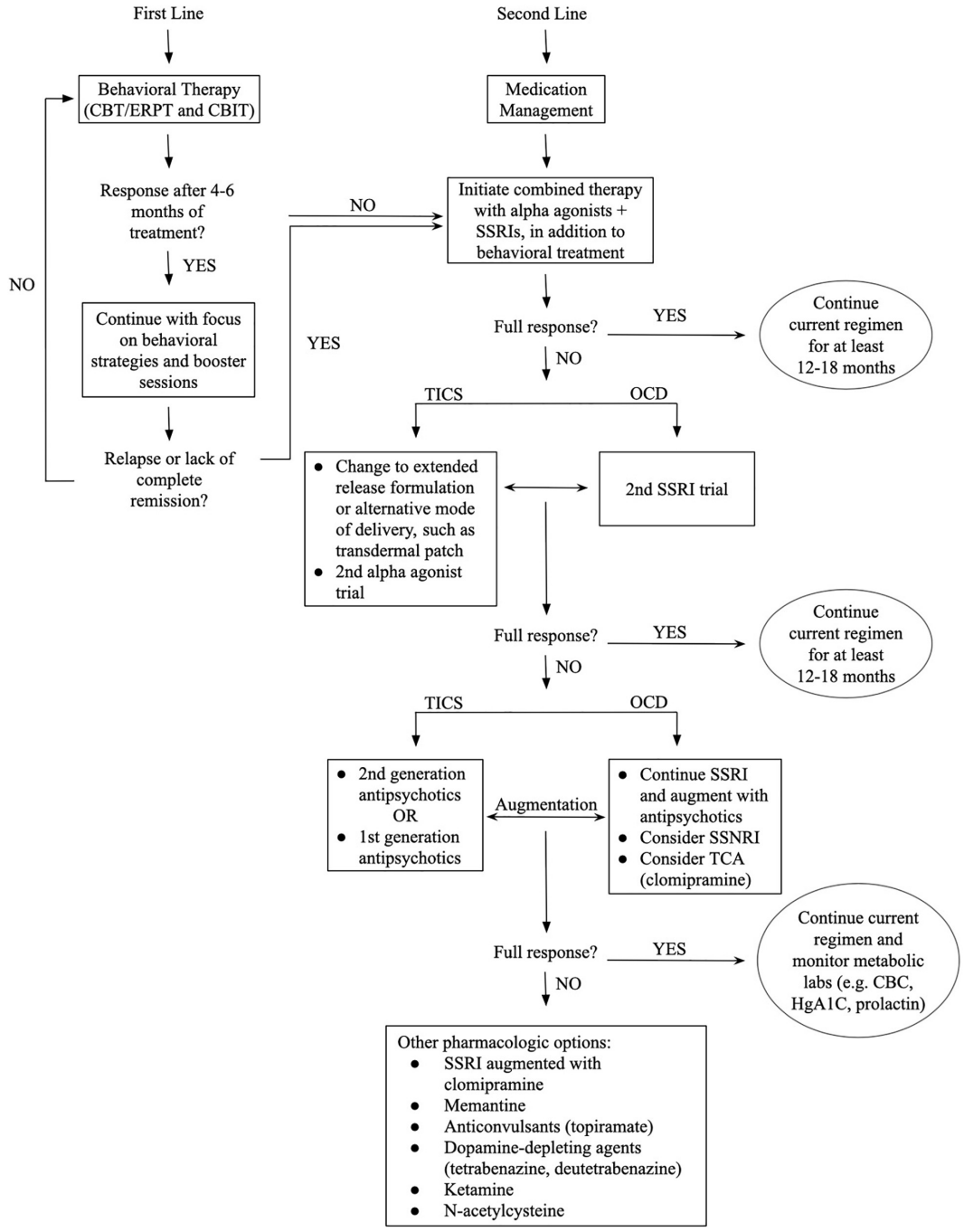


FIGURE 2
Proposed treatment algorithm for patients with TOCD.

To date, no singular behavioral monotherapy exists exclusively targeted to TOCD. A re-imagined version of CBT, ERPT, or CBIT could address the unique nature of TOCD including the anxious-somatic premonitory sense that precedes TOCD impulsions. For example, clinicians trained in both CBT for OCD (77) and CBIT may be able to blend these therapies to expose patients to core obsessional fears, as in CBT, while using competing responses to target the tic component of the symptoms, as in CBIT (81). Similarly, a classic tool used in ERPT is the fear hierarchy ladder, in which patients identify increasingly stressful situations in ascending order from least stressful to most stressful and then work to mitigate their anxiety and suppress compulsions while tolerating increased levels of exposure to the identified stressor. In a TOCD-specific

version of this ladder, therapists might help patients learn to tolerate their tics, first by continuing to engage in their tics without repeating them "just so" (i.e., tolerate doing the tics "imperfectly"), which could then progress higher up the ladder to full suppression of tics altogether.

Behavioral therapies are suggested to be the first line of treatment and medication management can be introduced as a second line treatment though medications are often required. Depending on the response to the initial intervention the next steps are outlined from the top to bottom. Patients with TOCD require treatment of both tic and OCD symptoms in parallel, typically requiring polypharmacy as well as behavioral interventions of more than one modality. Monitoring of both tic and OCD symptoms is essential as patients may have improvement in one domain while having ongoing symptoms in the other. This is denoted above by the bidirectional arrows to indicate the need for attention to both sets of symptom clusters which may be independent or wax and wane in parallel. Of note, while the first line agents for these disorders differ, there is overlap in second line agents which can be useful. Specifically, first or second-generation antipsychotics are helpful second line agents for both tic and OCD symptoms and can be used as monotherapy or as augmentation to SSRIs or alpha agonists. Similarly, SSRIs, which are first line for OCD, can also be added as second line agents to augment alpha agonists or antipsychotics for management of tics. In reality, the "full response" is rarely encountered, and an individualized approach to treatment has to be taken.

## Special considerations in the pediatric population

Tourettic OCD symptoms often initially present with tics around age 7–9 and later evolve into more complex tics with obsessional features as children approach adolescence. These are very important years for a child's psychosocial development. For most children, the peak of TOCD symptoms coincides with middle school, when patients are often more aware of their difficulties and their presentation has stronger implications for social, emotional, and academic functioning.

At home, the family may be affected in multiple ways. Many parents of children with OCD report irritability in their children (82) that affects family dynamics. Parents may accommodate the TOCD behaviors in order to avoid frustrations or tantrums (12), or may lack insight and try to rationalize or minimize their child's behavior, and provide frequent reassurance which then enables the behavior and may delay treatment (80). Some situations in which the child needs to perform their ritualized behaviors "just right," may involve other family members who are asked to participate in a sequence of behaviors that can interfere with family schedules and lead to frustration and distress by all involved (83). The parents' own mounting frustration and anxiety is often projected onto patients with TOCD, creating a difficult and vicious behavioral cycle. Moreover, the treatment-resistant nature of TOCD as well as polypharmacy with various potential side effects exacerbates distress in both patients and parents.

At school, behaviors may interfere with academic functioning or lead to disciplinary action, especially when tics involve yelling of inappropriate phrases, complex movements during class, or behaviors misinterpreted as aggression such as throwing objects or exposing parts of one's body to peers (such as pulling down one's pants). The risk of bullying, social anxiety and fear of being different from peers can be very real. Children with TOCD often work hard to suppress tics at school to the extent possible, although this may cause them to avoid social activities, become temperamentally more withdrawn, and in some cases worsen anxiety, which has the paradoxical effect of exacerbating their behaviors. Friendships and age-appropriate social development are impeded. Shame and embarrassment may cause children to become withdrawn and decline to share their struggles with parents and providers, exacerbating academic decline and delaying treatment. Children with tics/OCD/TOCD are at increased risk of developing additional disorders such as ADHD, anxiety or depression, which further impede social, emotional, and academic development (84).

It is important for the medical professionals taking care of children with tics, OCD, or TOCD to provide them not only with the right pharmacotherapy and psychotherapy but to provide support for the school and family settings. Family guidance, individual therapy for the child, family therapy (taking into account the needs of siblings as well), adequate contact with the school nurse, psychologist, teachers, and coaches can be very beneficial (**Figure 3**).

For patients with TOCD, it is important to encourage physical activity rather than the use of electronics given the known worsening effect of screen time on the prevalence of tics (85). Vigorous physical activity for at least 1–2 h every day is encouraged as there may be some benefit for patients with tics and/or compulsions, making it a promising tool to reduce symptoms as an adjunct to medication and behavioral interventions though the full extent of benefit is not entirely clear (86–88). Exercise is also known, however, to be protective against development of anxiety disorders as well as to significantly reduce anxiety among sufferers (89). The combined effect on tics, compulsions, and anxiety suggests benefit for TOCD. Some examples of activities that can be helpful include swimming, skating, riding a bicycle, soccer, and long-distance running.

In addition, there is evidence that sufficient sleep and a good sleep-wake cycle can decrease anxiety and other mood-related comorbidities (90). We therefore encourage adherence to a good sleep schedule and we generally discourage the intake of caffeine in adolescent patients as it may interfere with their sleep-wake cycle. There are currently no clear dietary recommendations

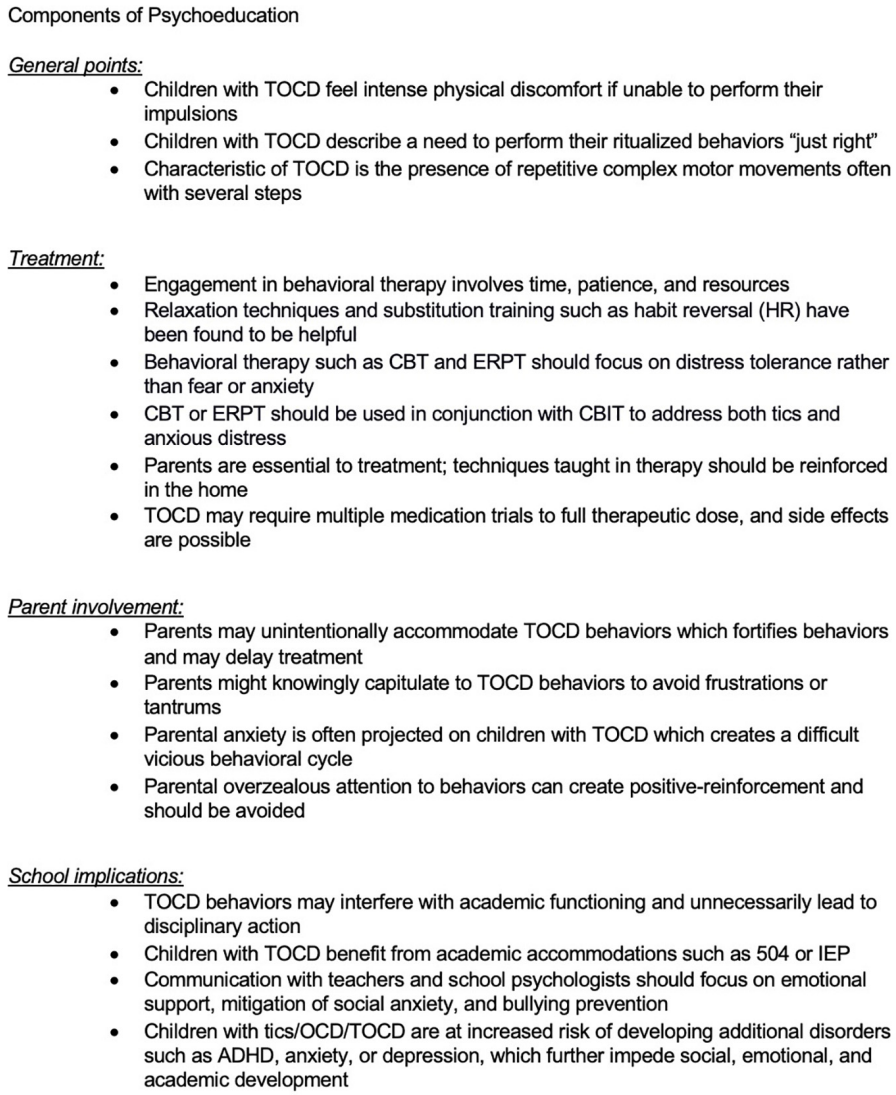


FIGURE 3
Components of psychoeducation for children with TOCD.

for patients with tics or OCD, or for that matter TOCD, except one small pilot study suggesting some benefits from a gluten-free diet for children with tics and comorbid OCD (91). Further research is currently being done on the effect of diet on CTD, OCD, and TOCD.

Tourettic OCD is less commonly recognized as a diagnostic entity compared to OCD or tics alone and often necessitates a broad treatment approach and psychoeducation for all involved. Even some mental health clinicians may not be familiar with the unique treatment needs of TOCD. Medication management typically requires polypharmacy, while therapy may require more than one modality such as Exposure Response Prevention Therapy (ERPT) for OCD with concurrent Cognitive Behavioral Intervention for Tics (CBIT). Close communication between parents, clinicians, and schools is beneficial. Furthermore, educating peers, neighbors, coaches, and even non-mental health clinicians who may be caring for the child can be illuminating and may decrease ostracization, bullying, and can increase a child's functioning by providing a more supportive environment.

## Discussion

Since the initial characterization of TOCD (1) there has been a better appreciation of this particular subtype of patients. Given the lack of precise diagnostic parameters, however, very few studies specifically address this population. Thus, prudence is warranted when discussing TOCD or extrapolating from the existing literature on TS and tic-related OCD. Many studies

address tic-related OCD, and while patients with TOCD are likely broadly included in this category, the specific nature of TOCD is narrower and patients' symptoms are more intertwined. It is important that TOCD be distinguished as a separate, well-defined syndrome because these patients often require different management than other patients on the tic and OCD spectrum. Our current understanding of TOCD supports an endophenotype that shares commonalities with TS and OCD in the brain CSTC circuitry as well as genetic traits, and yet is unique and even more complex than TS or OCD alone.

Tourettic OCD has a later age of onset than classic tic disorders although tics may be the first presentation of TOCD prior to the onset of OCD features. Part of the challenge with TOCD is that symptoms not only wax and wane over time, similar to OCD and TS flares, but that the central nature of the behaviors also evolves over time. Specifically, patients may first present with classic simple tics which morph into complex tics, and later take on the impulsive-obsessional quality of complex repetitive movements that need to be done "just right." For example, vocal tics may begin as a single vocalization that over time becomes a word, then a phrase, then eventually the need to repeat the phrase multiple times in a particular way. The later tendency to repeat complex behaviors in a specific way, although seemingly akin to compulsions, is distinguished from classic OCD in that the behaviors of TOCD are driven by a somatic urge or feeling of somatic distress rather than anxious, intrusive, obsessional thoughts. Behaviors characteristic of TOCD involve repetitive complex motor movements often with several steps, including tapping, arranging, adhering to certain numbers of repetitions. Patients report that their mixed behaviors are more difficult to suppress than OCD or TS alone.

This moving target of symptoms poses diagnostic challenges even to providers familiar with OCD and Tourette patients. The established way of conceptualizing mental health disorders is to put them into specific taxonomic systems (92), categorized as distinct neurological or psychiatric disorders based on clinical presentation. The Diagnostic and Statistical Manual of Mental Disorders (2) and the International Classification of Diseases (ICD) (93) are long-established and well respected diagnostic compendiums used for practical reasons to describe various psychiatric entities, and are based on distinguishing disorders from one another using clearly delineated symptom parameters.

There is a newer trend, however, to think about these disorders as overlapping or spreading across the continuum of clinical presentations. The modern transdiagnostic approaches to neuropsychiatric disorders challenge researchers and providers to think about mental health disorders more

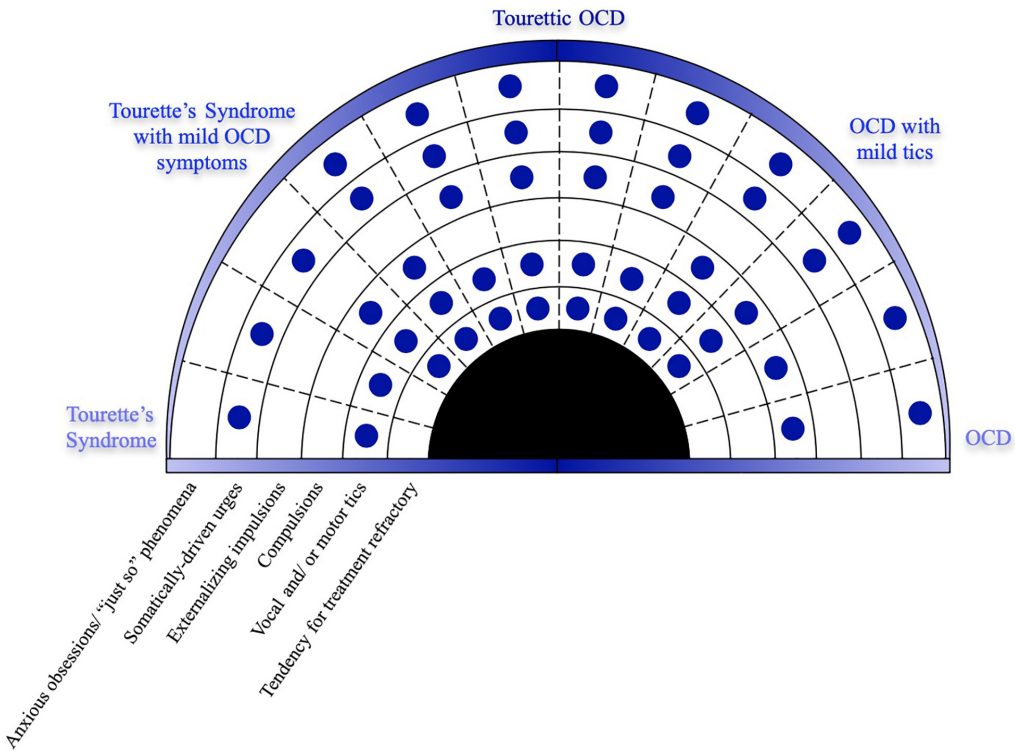


FIGURE 4
TOCD may represent a unique endophenotype along a clinical spectrum of OCD and tic disorders.

broadly than categorizing them into specific symptoms and cause driven nosologies. The interplay between biological, behavioral, psychosocial and cultural processes are not limited to established diagnostic boundaries (94). Given the overlapping neurocircuitry, somewhat overlapping genetics, and high frequency of comorbidity, it is possible that tics and OCD exist within the same larger syndrome. We can conceptualize that tics and OCD lie on two ends of the same diagnostic spectrum on which TOCD can be found somewhere in the middle, sharing characteristics of both (**Figure 4**). Conceptualized slightly differently, given that TOCD tends to be treatment refractory, it may instead represent the severe end of the spectrum, with tic disorders and OCD existing along a developmental gradient of which TOCD is the most severe presentation. We proffer that TOCD deserves validation as a novel diagnostic entity within this continuum.

Transdiagnostic approaches help us describe and understand cases that share characteristics of both disorders and do not care if they fall into the specific realm of psychiatry or neurology. We are trying to describe processes within one brain comprised of millions of synaptic connections. These neuropsychiatric symptoms do not exist in discrete silos but rather may arise from overlapping neuropsychiatric circuits. Genetics plays an important role in defining the predisposition to OCD or tic behaviors, but epigenetic and environmental factors might determine the varying presentation in different individuals. Environmental factors potentially include dietary habits, the status of gut microbiome composition, physical exercise, or the type of behavioral conditioning that is present in various families. The individual's socioeconomic status, demographics, family dynamics, access and initiation of pharmacotherapy and behavioral therapy might also contribute to the specific presentations.

This review suggests that TOCD exists on a continuum with TS and OCD that crosses the boundaries of each and presents with specific characteristics of both disorders. We propose that TOCD should be included in the next version of DSM as a specific, separate diagnosis that requires a multifaceted therapeutic approach. Our understanding of why some individuals present with isolated TS, others with tic-related OCD, while others develop TOCD, is still very limited. More research should be directed at understanding if any factors can be modulated in the developing brain, given that the multigenic background cannot be changed. Most patients will first present with waxing and waning motor and vocal tics, then subsequently develop OCD tendencies, and a subset of patients will develop TOCD. Perhaps earlier treatment with multiple pharmacologic agents to encourage synergistic effects might help the diagnostic spectrum not to progress too far. Behavioral therapy should extend beyond the boundaries of current techniques, including "customized" CBT, ERPT, and CBIT techniques. We hope that new research avenues will include detailed genetic analysis combined with imaging studies such as functional MRI or PET to elucidate the pathogenesis of these disorders. Collaborations between clinicians and researchers from diverse fields of expertise including psychiatry, neurology, psychology, genetics, and molecular biology would maximize recruitment of patients for large prospective observational studies and randomized controlled studies for interventions specifically addressing TOCD patients. Our hope is that increased awareness of this clinical entity will yield downstream interventions and quality of life improvements for those suffering from TOCD.

Tourettic OCD is a unique endophenotype that shares features of both Tourette Syndrome (on the left side of the diagram) and OCD (on the right side). The need to perform tics in a complex and precise way, known as the "just right phenomenon," is the hallmark of TOCD and lies at the interface of the premonitory somatic urges of tics and the anxious obsessions of OCD. This diagram highlights the unique symptomatology of TOCD as it manifests symptoms of both CTD and OCD.

## Author contributions

TK and KT contributed equally to this research and writing of the manuscript, including research and new content, and share equal intellectual contribution to this document. JW and TB provided assistance with formatting, literature review, proofreading, creation of figures, and wrote selected sections of the document. GB assisted with research and formatting. All authors contributed to the article and approved the submitted version.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note

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# Mothers' accounts of mealtime and feeding challenges for children with Tourette syndrome or persistent tic disorders

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Parenting a young person with a tic disorder can present daily challenges to families struggling to manage their child's tics and establish routines. Research recognises that tics can be problematic to everyday activities, however no attention has been given to mealtimes, arguably an important family activity closely related to quality of life of the family. The current qualitative study aimed to investigate the mealtime experiences of families with a child with a tic disorder from the perspective of mothers, looking at mealtime challenges, their impact and how these challenges are navigated. Seventeen mothers with children diagnosed with Tourette Syndrome (TS) or a Persistent Tic Disorder (PTD) (aged 3–14) took part in semi-structured interviews. Interpretative phenomenological analysis of 17 semi-structured interviews resulted in seven subthemes which were grouped under two superordinate themes: (1) tics as a barrier to positive mealtime experiences and (2) eating behaviours and other mealtime challenges. The findings highlight tics to create functional mealtime challenges, affecting a young person's ability to eat, drink and be seated, with mothers noting the family dynamic was often intensified and compounded by additional challenges related to their child's tics and comorbidities. Tics also have the power to disrupt the conviviality of mealtimes. For example, eating out-of-home can be especially challenging, with restaurants being high-pressure environments for young people with tics and their families. The cumulative effect of dissatisfaction, stress and additional foodwork can have a diminishing effect on maternal and familial resilience and wellbeing. Mealtime-related interventions need to be considered to help increase confidence and skills in managing mealtimes.

KEYWORDS

**mealtimes, Tourette syndrome, tic disorders, sensory sensitivity, eating behaviour**

## Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder characterised by motor and vocal tics ranging in form, frequency, complexity, and intensity (1). Tourette Syndrome differs from Chronic Motor or Vocal Tic Disorder and Provisional Tic Disorder in two ways: the type of tic and its persistence. For a Chronic Motor or Vocal Tic Disorder diagnosis, an individual only needs to have the presence of a vocal or motor tic for over a year to be eligible for diagnosis; for TS, the individual would require both types of tics for over a year to be eligible for diagnosis. A Provisional Tic Disorder diagnosis would apply when tics have been present for less than a year. In addition to the core characteristics, there is research drawing attention to feeding challenges in children with TS (2–4); however, these studies have yet to adequately capture the impact of feeding difficulties on family mealtimes.

Mealtimes have been described as the cornerstone of family life, with there being no other daily activity that families share together with such regularity, with around 72.8% of school-aged children found to eat dinner with at least one parent every night of the week (5). Mealtimes also provide families an opportunity for a daily structured routine, often supporting larger family goals as well as communication (6). Larson and colleagues (7) have also suggested that family meals are a symbol of family unity. However, while family mealtimes can be a source of joy, they can also be a source of stress and dissatisfaction as mothers struggle to recreate their ideal family mealtimes (8).

Mealtimes can be a general source of tension, yet in families with a selective eater, this stress is magnified [for review, see (9)]. For example, selective eating, also known as fussy eating, whereby children reject a high proportion of familiar and novel food, is common during early childhood (10). However, food selectivity has been shown to be more persistent and severe in children with TS compared to their typically developing peers, presenting beyond the normal developmental stage of 6 years of age (3), with food avoidant behaviours such as food selectivity, food neophobia and restrictive eating remaining into adulthood (4). Moreover, children with TS have been found to show similar levels of food fussiness compared to other neurodiverse children including Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD) (2), even when accounting for levels of comorbidity.

Research addressing the mealtime experiences in neurodiverse families has largely focused on families with a child with ASD, with mealtime barriers revolving around child's selective eating and mealtime behaviours (11–14). For example, a Canadian study by Rogers et al. (15) found that mothers of children with ASD (aged 4 to 11 years) had to contend with sensory aversions, a need for sameness, rigidity, and food jags (repeatedly eating the same meal for an extended period before cycling to another safe meal). Mothers also described their child as engaging in disruptive mealtime behaviours such as constantly getting up from the table, fidgeting, food refusal and attention seeking during mealtimes (16, 17).

Ausderau and Juarez (18) also found mothers described mealtimes as unsatisfactory due to their child's selective eating, disruptive mealtime behaviour and the additional labour they had to undertake to make mealtimes "work" for their families. For example, mothers had to create individualised mealtime routines to accommodate the needs of their child with ASD, however, adaptations came at a cost to other members of the family. Namely, typically developing siblings who needed to be mother's "little helper" and model "good" behaviours, and mothers who had to undertake additional foodwork with little support or understanding from their partners, friends, and relatives. Consequently, mothers often expressed a sense of hopelessness and dissatisfaction at being unable to create the mealtime experiences they desired due to the eating and mealtime behaviour of their child with ASD (17).

The ASD literature highlights the complexity of maternal mealtime stress and may provide some insight in the experiences of TS due to shared traits, characteristics, and comorbidity (19). Important questions remain regarding how mothers of children with TS, navigate mealtimes and what personal costs are associated with adaptations and additional foodwork. This is particularly important to address, given the suggestion that families of children with TS struggle with daily routines and will often change the timing of meals to accommodate their child's tics (20).

To our knowledge this was the first qualitative study addressing mothers of children with tics experiences of mealtimes. Mothers were chosen, not only to be synonymous with the existing ASD literature, but also because mothers typically tend to undertake most domestic foodwork (21); namely meal planning, cooking, and cleaning and often the emotional toll of labour associated with foodwork and feeding (22). Even during the COVID-19 pandemic, when two parents were present within the family home, mothers spent more time than fathers doing foodwork (23).

## Materials and methods

We aimed to understand mealtimes in families with a young child with a tic disorder from a maternal perspective. For this research, a meal was considered a family meal if at least one adult and one child were seated for a meal together, even if one of them was not eating (24). For data collection and analysis, we referred to interpretative phenomenological analysis (IPA) guidelines by Smith et al. (25). This choice is congruent with

our aim to uncover the meaning given by these mothers to their experiences (26).

## Participants

Seventeen white British mothers with children diagnosed with TS ($N = 15$) or a PTD ($N = 2$) took part. Almost all the participants were reported to be diagnosed with more than one comorbidity and or awaiting further diagnoses (see Table 1). The comorbidities reported were as follows: OCD ($n = 9$), Anxiety Disorder ($n = 9$), ADHD ($n = 8$), Sensory Processing Disorder (SPD, $n = 5$), Learning disability ($n = 5$), and ASD ($n = 3$). Several mothers also reported that their child was awaiting further diagnoses including ASD ($n = 4$), ADHD ($n = 1$) and anxiety ($n = 1$). Mothers also reported the following traits in their children that were not diagnosed nor awaiting diagnoses: SPD ($n = 5$), OCD ($n = 1$), and ASD ($n = 2$). This sample is thought to reflect the spectrum of presentations within this population; with TS being a multifaceted condition with complex clinical presentation due to high comorbidity rates. Mothers were predominantly employed, either full-time ($N = 7$) or part-time ($n = 4$), and most mothers lived with their partner ($N = 16$) and had other children living in the household ($n = 13$). Four mothers also reported that someone else in their household had a tic disorder.

Mothers were recruited through a short online advert disseminated *via* Tourette's Action, Tourettes Hero and private Facebook groups which support families with children with TS. Social media channels such as Twitter and Redditt were also used to aid recruitment. Aligning with the principles of IPA, the relevance of findings is dependent on the richness of the narratives as opposed to the sample size (29, 30). We deliberately chose a larger pool of participants than is usually included when using IPA (typically between $N = 3$–15), to explore the breath of mothers' individual experiences but also reflecting the heterogeneity in the symptoms and comorbidity of children presenting with a tic disorder. Mothers who were interested in the study were advised to contact the lead researcher for more information and were then sent an information sheet that detailed the study's aims and objectives and how data would be used and protected. Once a date, time, and location (virtual or in-person) were agreed upon, mothers were sent an overview of the interview schedule to know what type of questions to expect. All participants provided written and verbal consent and were assured of their anonymity and right to withdraw at any stage. Participants also provided consent for their interview to be recorded for transcription purposes. Ethical approval for this research was obtained from the University of Hertfordshire University Ethical Advisory Committee Protocol Number: aHSK/PGT/UH/03340(5) and the research was performed in accordance with the Declaration of Helsinki.

## Data collection

Empirical literature for assessing mealtime challenges in children with neurodevelopmental disorders guided the creation of the interview schedule. The schedule was further verified by a parent of child with TS (not included in the study) alongside members of the research team. The first part of the schedule captured contextual information about participants, their child, and their household. Notably, parental occupation and work pattern; target child's age, sex, and diagnosis; and family structure. The second part of the schedule focused more specifically on mealtimes, asking the following:

- When was the last time you sat down to eat a meal with your family? Can you describe that mealtime for me?
- What types of food and drink does your child like or dislike?
- How, if at all, does your child's Tourette/tics influence your mealtime experiences or their eating behaviour?
- Does your child take any medication? If so, have you noticed any changes to their appetite and weight? If yes, can you talk to me about that?
- When was the last time you ate out as a family? Can you describe it to me?
- Do you have any future concerns about your child's mealtimes?

Interviews were conducted by the lead researcher between October 2018 and August 2020, with only two participants, Jackie and Susan, interviewed during the COVID-19 pandemic. Fourteen interviews were conducted virtually, using an online platform such as Zoom; the remaining three interviews were held face-to-face at participants' home at their request (pre-COVID-19 pandemic). Interviews lasted from 49–182 min. All interviews were recorded for transcription purposes and transcribed verbatim by the researcher.

## Data analysis

The first author read each transcript multiple times, before the data were analysed. In accordance with quality guidelines for IPA, reflexive conversations occurred amongst the four members of the research team (31). For each transcript, emergent themes and interpretations were noted alongside divergent and convergent themes to highlight the unique experience of each participant (31). To ensure further credibility, triangulation occurred through consultations with the research team, and feedback

TABLE 1 Parent, child, and family characteristics.

| Participant characteristics | | | Child characteristics | | | | Household characteristics | |
|---|---|---|---|---|---|---|---|---|
| **Pseudonym** | **Mother's paid employment status** | **Partner's paid employment status** | **Pseudonym** | **Age** | **Diagnoses[a]** | **Medication[a]** | **Immediate relative with TS/PTD** | **Other children in the home** |
| Amy | Full-time employment | Full-time employment | Talia | 13yo | TS plus 2 NDD | None | No | No |
| Caroline | Not in paid employment | Full-time employment | Adam | 3yo | PTD plus 1 LD | None | Partner with TS, youngest suspected PTD | Yes |
| Charlotte | Not in paid employment | Not in paid employment | Thomas | 14yo | TS plus 2 NDD and 1 MHD | Takes antidepressant, antipsychotic, and antihistamine | No | Yes |
| Ciara | Not in paid employment | Full-time employment | Justin | 11yo | TS plus 1 NDD and 1 trait | None | No | Yes |
| Harriet | Not in paid employment | Full-time employment | Max | 8yo | TS plus 1 NDD and 1 trait | None | No | Yes |
| Jackie | Full-time employment | Part-time employment | Ivy | 14yo | TS plus 1 MHD, 1 NDD and awaiting 1 more NDD | None | No | No |
| Jessica | Part-time employment | Full-time employment | Warren | 11yo | TS plus 2 NDD and 1 MHD | Takes antidepressant and melatonin | No | Yes |
| Lauren | Full-time employment | Full-time employment | Finley | 13yo | TS plus 1 NDD and awaiting 1 more NDD diagnosis | Takes stimulant | No | Yes |
| Marisa | Full-time employment | Full-time employment | Lottie | 4yo | PTD | None | Has TS | No |
| Naomi | Not in paid employment | Full-time employment | Oscar | 8yo | TS plus 1 NDD, 2 MHD and 1 LD | None | No | Yes |
| Polly | Full-time employment | N/A[b] | Zack | 14yo | TS plus 1 NDD and 1 MHD | None | No | Yes |
| Rebecca | Part-Time Employment | Full-time employment | Ryan | 13yo | TS plus 1 NDD, 1 MHD and awaiting 2 more NDD diagnoses | Takes antidepressant | No | Yes |
| Rita | Not in paid employment | Full-time employment | Effy | 13yo | TS plus 3 NDD and 1 trait | Takes alpha-agonist hypotensive agent and melatonin | No | Yes |
| Serena | Part-time employment | Full-time employment | Felix | 11yo | TS plus 2 NDD, 1 MHD and 2 traits | Takes stimulant antipsychotic, antidepressant, antidiuretic, and melatonin | Younger child, possible PTD | Yes |
| Sophie | Part-time employment | Full-time employment | Jack | 10yo | TS plus 1 NDD, 1 LD, awaiting 1 NDD and 1 MHD diagnosis and has 1 trait | Takes lpha$_{2A}$-adrenergic receptor agonist | No | Yes |
| Susan | Full-time employment | Full-time employment | Annabelle | 13yo | TS plus 3 NDD, 1MHD and 3 LD | Takes antipsychotic | No | Yes |
| Yasmin | Full-time employment | Full-time employment | Isaac | 12yo | TS plus 2 NDD, 1 MHD and 1 trait | None | Partner has tics | No |

[a]The specific diagnoses of YP and list of medications that they take have not been listed within the table in order to preserve confidentiality. [b]Polly's ex-husband lives separately, so no other caregiver was living in the family household.
LD, learning disability/disabilities; N/A, not applicable; yo, years old; NDD, Neurodevelopmental diagnosis/diagnoses; MHD, mental health diagnosis/diagnoses.
Columns two and three focus on paid employment status; therefore, those who work within the family home as homemakers and carers are classified as "not in paid employment." This does not serve to discredit the value of their invisible domestic labour and is only used to provide context for caregiver work patterns and to classify whether a family is a single- or dual-earner household as both are important factors worth considering when exploring family mealtimes (27, 28).





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TABLE 2 Theme structure for mothers of young people with TS.

| Superordinate themes | Subthemes |
|---|---|
| Tics as a barrier to positive mealtime experiences | Functional challenges |
| | Disruptive tics and fragmented mealtimes |
| | Self-consciousness and anxiety when dining out |
| Eating behaviours and mealtime challenges | Food preferences and feeding practises |
| | Conflicting mealtime expectations |

was also sought from participants of the study, with no changes requested.

## Results

Analysis resulted in five subthemes grouped under two superordinate themes: (1) Tics as a barrier to positive mealtime experiences, and (2) eating behaviours and mealtime challenges, see Table 2. These themes captured mothers' thoughts and feelings surrounding their family mealtime experiences and their child's eating behaviours. Some of the words mothers used to describe mealtimes were stressful, uncomfortable, chaotic, messy, and fragmented. Each theme articulates these descriptors more fully while situating them within the context of distinct behaviours and characteristics associated with tic disorders and comorbidities.

### Tics as a barrier to positive mealtime experiences

Mothers described their child experiencing an assortment of tics, all of which were portrayed to have varying effects on mealtimes. This superordinate theme consists of three subthemes: (1) functional challenges, (2) disruptive tics and fragmented mealtimes, and (3) self-consciousness and anxiety when dining out.

### Functional challenges

On a functional level, mothers reported that tics impaired their child's ability to eat and drink uninterrupted. In most instances, these functional challenges were more impactful on their child's behaviour than the mealtime experience. For example, Jackie noted that their daughter's head and neck tics made it hard for them to eat "*because of the neck jerking, it'll interrupt her from her eating pattern.*" Whereas oral tics were noted by Amy and Polly:

> "When, when she was doing the lip rolling umm, sometimes she would find it difficult eating and the jaw slamming. Sometimes like she'll bite her tongue or the inside of her cheek." (Amy)
>
> "He had one for a while that was like (demonstrates mouth wide open and eyes closed tic) like this, opening his mouth. But he still ate. It was just that he would chew his food and then (mouth open tic) in between." (Polly)

Jessica described how Warren's throat tic sometimes made it difficult for him to finish his meal and left him "*panicked*."

> "He's choked before because umm… it went to the back of his throat, and he tried to clear his throat, but it got stuck so he choked. It scared him a bit. But then because he panicked, his tic heightened so he was doing it constantly so he couldn't eat. He's done that quite a few times." (Jessica)

Others highted how tics usually interacted with what would be considered good table etiquette. For example, Amy related her daughter's tic spillages to her limb tics whereas, in the case of Yasmin, the issue related to her son's distractibility during mealtimes.

> "I have to feed him, not because he's incapable of feeding himself, but because he'll just sit there and be distracted, maybe because he's thinking if he puts the fork in his mouth, he'll, he'll tic." (Yasmin)

### Disruptive tics and fragmented mealtimes

Tics were also described as being disruptive to family mealtimes, although the disruption depended on type of tic and its severity. For example, tic severity was cited as disrupting mealtimes in several ways. One was delaying mealtimes until tics waned whereas the another was the perpetual movement during meals, as children struggled to sit still.

Importantly a few mothers described their child's tics as influencing the timing of their family meals, as children could not sit down for dinner shortly after returning from school due to what mothers perceived to be "tic rebounds." Mothers rationalised that it was more effective to delay dinner than to try and force their child to sit at the table.

> "He'll hold them in and try and suppress them as much as he can […] but eventually when he gets home, it's like taking a lid off a pressure cooker, and all of those tics have to get out. So, at the time he's coming home, umm when you think actually, we should be sitting down and we should be having dinner, uh we can't do that because he needs at least 2-h just to go into his room, have that space on his own, not really have any interaction." (Lauren)

While mothers, such as Lauren, were able to accommodate an increase in tic severity by pushing mealtimes back, this only resolved the challenge of getting their child seated at the table. Many mothers also noted that it was a struggle to then keep them there.

> "It's just utter chaos, he don't sit down at the table, he walks around, he gets upset… uhhh… I don't know. And then everybody gets stressed." (Jessica)

Mothers described being acutely aware of their child's need for movement and often came to understand that movement was a necessity for their child that should not, and could not, be policed. As such, mothers often made concessions for their child, allowing them to move around as needed, but maintained an expectation that their other children stay seated throughout the meal.

> "Like, he's always found it hard to sit still, and he's never been able to sit at the table, but I sort of knew that as a mum just let him bounce around a lot if he needed to." (Ciara)
>
> "He wants to move around […]…it tends to be 3 of us sitting at the table with Oscar bobbing about. Umm… and… I guess… it's sort of the things that goes with the Tourette's I suppose." (Naomi)

Rebecca described her family mealtimes as being negatively impacted by Ryan's spitting tic, explaining it was particularly challenging for her younger son with ASD, Josh, to ignore Ryan's tics.

> "Josh's got a lot of anxiety around sitting at the table where he's likely to be spat at […] he feels sometimes not safe at the table, he didn't feel like he was comfortable eating, so we kind of made a decision that uh he was better off eating and not associating fear with food and not eating at all." (Rebecca)

Rebecca explained that the only way she was able meet her sons' varying needs was to have both eating in separate parts of the house. Rebecca willingly scarified the family meal in favour of her children's long-term wellbeing and future mealtime enjoyment, stating: "*I just hope that one day they'll come back to the table, and we can eat together because they are not anxious about food.*"

This fragmentation of the family meal was also noted by Marisa, but this time it was her daughter Lottie with PTD who ate alone, separate to the rest of the family unit. Marisa explained that she preferred Lottie to eat alone as this shielded Lottie from being reprimanded by her dad for her expulsive tic which drives her dad "nuts." This allowed Lottie to tic freely without feeling "*like she's bothering her dad.*"

Expulsive tics such as *stabbing, hitting, and kicking* tics, were frequently described by the mothers as not only disruptive but also harmful to others. At times, mothers described these tics as being painful and having a negative effect on enjoyment of mealtimes. For example, Ciara described herself as being "*traumatised*" by Justin's tics making it difficult for her to enjoy mealtimes.

> "Just this week, again, I've been starting to get kicked under the table and having to stop that because you just don't want that when you're eating. […] It's, it's hard to say how difficult that is. You know, I think I've actually been quite traumatised over the years from the amount of being jumped on and touched and umm I say kicked, but it's not aggressive, it's just overly boisterous […]." (Ciara)

While Ciara understood that Justin did not intentionally want to hurt her, she nonetheless felt unsafe. For example, Ciara explained that she felt one of the reasons why she "*got ill*" was due to "*the constant bracing yourself because you never know when you're going to be bundled into.*" Fortunately for Susan, her table was able to maintain distance between her and Annabelle, which meant that being hit during mealtimes was no longer a challenge.

> "We've got enough space. We're lucky enough to have six seats at the table. So, we leave a gap in the middle. I used to sit next to Annabelle, but I got stabbed and hit. One mealtime, I got hit on the head with a spoon over 30 times. And it really does hurt." (Susan)

Susan demonstrated her dedication to persevere through the mealtime, being hit and hurt "*over 30 times*", highlighting not only the impact of the tics on others (e.g., "*and it really does hurt*") but the lengths taken by mothers to ensure everyone's needs were considered and met. Moreover, changes were made to accommodate tics at mealtimes as opposed to centring attention on tics and their impact.

## Self-consciousness and anxiety when dining out

Many reported their child's desire not to have attention drawn to them would influence every aspect of dining-out, from the frequency of dining out, to the location and even the time of eating, causing stress for all members of the family.

> "[…] eating out at a restaurant, depending on his mood and where, what his tics are like can vary massively […] some days it's literally like having a bull in a china shop. Trying to get him to sit down, sit still, he's ticking, not throwing his salad bowl across the table umm… but we try to avoid those places to be honest because it's not nice for anyone." (Serena)

Mothers whose children were not overwhelmed by noisy environments tended to opt for child-friendly establishments where their child could assimilate by blending into the background.

> "We go to a family place, you know like Carveries and things like that because they're darker, they're loud anyway, they're busy, so you just blend in." (Serena)

Other mothers preferred to request quiet tables and inform the staff and fellow diners of their child's condition. This was perceived by mothers to help to ease their child's anxiety and minimise staring. Mothers also reported seating preferences. For example, Amy explained that Talia "*she just prefers to be in the corner*" to be less conscious of onlookers.

> "We have to book in advance and ask for special tables, and then all the waiters have to know. Annabelle likes me to tell everybody and people on the tables around us. It makes her feel more comfortable that they have some understanding." (Susan)

In addition to controlling the environment to create less pressurised experiences, mothers also noted that their child would try to suppress their tics. The challenge with this approach was the abrupt end to mealtimes when their child was no longer able to cope and suppress tics. Sometime this resulted in families being unable to go out for a meal if their child had a bad tic day.

> "[. . . ] there will be times where he will say 'mummy can we go home now?' or you know 'I'm getting a headache' or umm he'll say or 'I've got a tummy ache' and that I know that he can't, he needs to release it. And if we're halfway through the meal then I'll say to him 'come on, do you want to come with me to the toilet' and him and me will go off separately, and then he'll just be able to do his own little thing. Tic away and no one else is watching him, and then he feels comfortable to go back to the table." (Sophie)

Charlotte and Lauren were the only mothers whose sons refused to dine out with their family as they were now old enough to decide to stay home. While Lauren and Charlotte appreciated that it was easier, they often felt uncomfortable about leaving them alone and were concerned about their sons' social withdrawal.

> "It's difficult to eat out because he doesn't like attention being brought to him. And umm he'll wear a hoodie and have it over his head umm because that's some type of protection for him that, you know, he's kind of hiding behind. If we do go out, we don't tend to take Finley with us. And he's 13, and he can make that decision. It is not enjoyable for him, which is really/ it's a shame." (Lauren)
>
> "In fact, I can't think of the last time that [he] came out with us for something to eat." (Charlotte)

## Eating behaviours and mealtime challenges

This superordinate theme discusses how mothers viewed their child's eating behaviours and the role sensory sensitivity and rigidity played in making mealtimes stressful and conflictual. This superordinate theme consists of two subthemes: (1) food preferences and feeding practises and (2) conflicting mealtime expectations.

## Food preferences and feeding practises

Several mothers described their child's food preferences as a source of stress, as they felt that their child's food preferences were limited, albeit to varying degrees. Mothers who described their child as a selective eater or having pronounced food preferences tended to attribute their child's dietary range to sensory aversions.

> "He seems to have heightened sense of smell, like he finds certain textures really uncomfortable umm and then he just/ he just tastes things, he only likes really bland things." (Harriet)
>
> "She'll say if it smells wrong or looks wrong, it feels wrong, and there's like an invisible force field, and she just can't do it." (Rita)

Mothers often described instances where it became apparent to them that their child was genuinely struggling with sensory properties and that their refusal was more than merely behavioural.

> "For instance, and he's a good boy, and he tries his hardest, but he tried to eat a piece of sweetcorn, and it took him 15 min. And it was 15 min of crying, you know, at the noise in his ear of crunching it." (Harriet)

Over time, mothers accepted that controlling feeding practises were counterproductive and appeared to feel powerless and defeated. Mothers reported feeling pressurised as their child's meal had to be served in a particular way, most commonly with each meal component separate on the plate.

> "Beans can't touch his food […] so jacket potato and beans, umm they have to go in a cup […] (Serena)
>
> "[…] he doesn't really like bean juice. So, you have to drain the bean juice up the beans so it's not as wet. And he likes the beans separate to the chips." (Lauren)

Rather than feeling defeated and helpless at changing their child's diets, Serena stressed the importance of knowing what was realistically achievable and working with her son's preferences when increasing acceptance of otherwise refused foods.

> "[…] he hates things with two textures. Like you cannot give him yoghourt with fruit in. Or bits in, that's a no, no. […] I learnt from a very young age when he was little that that's just not something I'm going to force him to have." (Serena)

Mothers who did not feel this burden were less likely to perceive their child's dietary preferences as a challenge and were less likely to encounter mealtime battles. For example, Marisa and Caroline both described their children with PTD as selective eaters, yet this did not appear to be a challenge nor source of stress; seemingly because they both were able to alleviate concerns about nutritional deficiencies.

> "[…] she eats breakfast and lunch and snacks at school so… uhh she/ I know that she's having very varied meals there […] so I'm not going to worry about her too much about what she's eating for dinner." (Marisa)

Interestingly, a couple of mothers also noted that the burden to nourish their child felt heavier due to their child's diagnosis.

> "[…] when your child has a chronic condition, and there's no cure and… there's precious little help from the health service, you have to work it out for yourself […] I am giving him as healthy a meal as possible, and I hope that is at least helping things not get worse." (Ciara)

Ciara's desire for Justin to have a healthier diet than he would like often led to mealtime conflict, stating that *"it just feels like a battle all the time."* In the end, mothers often described themselves as feeding their children their preferred foods, so to avoid them missing a meal. For example, Harriet described having to find a balance between *"starving your child"* and making sure they are *"getting proper nourishment"* as being *"extremely stressful."* Even when mothers tried their best to accommodate their child's preferences, they could not always ensure their child would eat the meal as some children's preferences were unpredictable. This was disheartening for mothers like Jackie, who felt that even despite their best efforts to make a meal their child would enjoy, they were still unable to *"get it right."*

> "It can be a bit disheartening after you've spent an hour or more cooking and then [she] doesn't like that, can't eat it. And I couldn't have predicted that outcome." (Jackie)

The levels of accommodation for food varied, as did the impact of this additional labour on mothers' stress levels. A few mothers prepared separate meals for their child. Although, in the case of Lauren, she prepared individual meals for the whole family due to lack of taste synchronicity. Lauren likened her household to a *"café where everyone has a different meal."* While she first cited this as a source of stress, she later recanted and explained that while it *"sounds like it would be stress city […] it does become the norm."* While Lauren had acclimatised to making several meals, the idea of cooking multiple meals was stressful for others. In such cases, mothers opted for meals that could easily be modified to meet everyone's needs.

> "[…] say I was doing a chana masala or something, a chickpea curry, Max would have the chickpeas and the rice but no sauce so it's not really our dinner at all, but that's, that's what he'd eat." (Harriet)
>
> "I give them an option, and we try and come at one we all agree at because I was cooking different meals for everybody. […] I'll do something where Annabelle could have say, chicken in a wrap and Ella will eat a Caesar salad." (Susan)

## Conflicting mealtime expectations

Expectations surrounding family mealtimes appeared to be a notable factor influencing how satisfied mothers were with their family mealtime experiences. Mothers noted two main conflicts, conflict within themselves between what they want and what their reality was, and conflict between their expectations and that of their partners. For example, Caroline held onto an expectation that her family mealtimes could improve but also recognised that despite all her best efforts thus far, mealtimes were still *"crazy."* Both mothers held strongly onto their expectations, although in Caroline's case, her *"micromanaging"* of mealtimes was described as a source of stress for her family.

> "[…] we used to have them as kids, it should be like a social time where everyone is happy, and you're catching up with the day or/ but it's not because Oscar will want to get up or 'that's not right,' 'that's not right.' I think, maybe I sort of sit there and think, 'oh, they're gonna'/ oh I don't know, not like the Waltons but you know be like 'this is lovely, you've

> worked so hard, this is delicious' (laughs). But it rarely ever is [. . . ] it's like a battleground really to sit down as a family [. . . ]." (Naomi)
>
> "Like the number of times that we've been successful at that is so rare that that's really creating stress for my family because I just keep plugging away at it. Like I keep expecting that we'll be able to [. . . ] every day, all day, like our lives revolve around the kitchen. That we're making food, we're cleaning food, we're eating food, like they're just like so over it." (Caroline)

Naomi's quote captured the discrepancy between what she felt mealtimes should be, a wholesome family activity, vs. what they were, a *"battleground." "it's not like relaxing, we all sit there you know. . . it's quite tiring."*

Naomi commented that even when Oscar was a baby, he refused homemade baby food which meant she could not be the *"smug mummy"* she wanted to be. Her motivation to undertake extensive foodwork appeared to be embedded in her desire to derive joy from the pleasure her family experienced when they ate her meals. Similarly, other mothers noted this challenge as they felt their foodwork was not enjoyed, nor appreciated, as they had hoped.

> "I think it's, it's a challenge trying to predict sometimes whether she's going to like what I'm cooking. That can be frustrating, and that could become a challenge if I allowed it. [. . . ]it can be a bit disheartening after you've spent an hour or more cooking and then doesn't like that, can't eat it. And I couldn't have predicted that outcome." (Jackie)
>
> "I want food to be joyful. I want it to be something that can be social, and I [can't] figure out how to do that when other people won't cooperate (laughs)." (Caroline)

For Harriet, neither she nor her family were able to derive joy from the meal that she had tirelessly prepared, with Max's food refusal and "*meltdowns*" created a stressful mealtime atmosphere.

> "[. . . ] there has been times when I have just picked up my plate because I've had a knot in my stomach from the screaming, picked up my plate and had to go to a different room to eat my meal because I might have made something that took me an hour, an hour and a half, and I can't even taste it because my child is screaming because the smell from his plate or even having to do it. Umm, so it can be very stressful." (Harriet)

Notably, maternal identity was heavily tied to what their child ate and as such, it was challenging for mothers to let go of mealtime expectations entirely. Jackie captured this sentiment as she expressed guilt and disappointment tied to Ivy's eating behaviour.

> "I mean, for me as a mum, I have to not be too disappointed if, you know, I can spend quite a lot of time cooking and preparing and think it's going to be fine. And then if she says, 'I can't eat it,' I've then got the guilt of 'well do I have to go back into the kitchen and cook another meal?" (Jackie)

The very few mothers who accepted that they had no control and released all expectations about mealtimes appeared to be the most content. Rebecca and Lauren captured this best. Rebecca accepted her fragmented mealtimes, while Lauren accepted the need for multiple meals.

> "It would be nice to just cook one meal, and everybody eat it [but] we're not that family. So, you've got to adapt." (Lauren)

Rebecca also recognised that while she *"would like everyone to be in the same place"* that this simply was not possible due to her sons' conflicting needs. For Rebecca and Lauren, mealtimes were simply for getting everyone fed.

Another challenge mothers noted was between their expectations and those of their partners. In most cases, mothers reported their partner to be stricter or less understanding than they were. Both expectations and parenting style were noted to have intergenerational influences. In the example below, Jessica described why she believed she was stricter than her husband, Jim.

> "We were brought up differently. Jim didn't [. . . ] sit and eat with his parents, it were always, you know, you . . . you can sit and eat in there. [. . . ] she (Jim's mother) made meals separately for everyone. So, if he didn't want something, he could have something else. Whereas my sort of upbringing were completely different. I, we had a set meal at a set time." (Jessica)

In cases where mothers believed themselves to be less strict and more understanding than their partners, they also felt the need to advocate on their child's behalf. Like Rita, some of these mothers felt caught in the middle as they empathised with both their partner and their child. Rita articulated this well when discussing her husband's reaction to Effy going out with friends the day after she had a *"meltdown and just absconded and went to the car"* during a family meal.

> "He struggles, he struggles with it more than I do. He/ even now so like she had this meltdown in Pizza Hut. I encouraged her the next day, and she went to drama, and he's upset because we rarely go out for family meals or do stuff anymore because of her issues. [. . . ] he thought 'well if she can go out to drama, why can't she go out for a meal

> with us?,' 'If she can do what she wants to do, why can't she do what we want to do as a family?.' And how sort of sad it is, and I totally understand where he's coming from because I felt like that in the past, and even now I do." (Rita)

## Discussion

The study captured maternal perceptions of their family mealtimes, namely the challenges they faced and how they responded to them. Like previous research, barriers to positive family mealtime experiences and sources of maternal mealtime stress tended to focus on selective eating and disruptive mealtime behaviours (8, 32), which were further magnified by the functional and sometimes expulsive nature of the tics. While mothers appeared to understand that sensory sensitivities often underpinned their child's food preferences, they nonetheless desired their child to have a broader diet. When mothers used controlling feeding practises, mealtimes were described to be stressful and conflictual whereas when they were able to see their child as struggling due to sensory sensitivity, it was easier to accommodate their child's food preferences.

Akin to the research in mothers with children with autism, previously described by Suarez et al. (17), the inability to remain seated was cited as being a particular source of annoyance. There was a strong consensus amongst the mothers that tics intensified when they returned home from school, mothers often conceptualised this being a result of tic suppression during the day. However, it is important to note that empirical research does not support a tic rebound effect (33, 34), though these studies only explore rebounds within 40 min of suppression. A plausible reason for this phenomenon could be due to accumulated fatigue and feeling relaxed in their home environment. Regardless of the reason for increased tic severity upon returning from school, the need to delay mealtimes to accommodate the perceived increase in tic severity was noted by several mothers; something which has previously been described in TS (20). While this was disruptive to the family's routine, it was often less disruptive than the presence of certain tics during the meal. For example, mothers depicted an array of disruptive tics including hitting, throwing, and kicking that impacted their child's ability to eat, be seated and stay seated and generally impacted upon other family members' mealtime experiences.

In addition to the practical challenges tics presented, mothers described experiential and emotional challenges. These included affecting the ability of others at the table to relax, and enjoy their meal, as well as self-consciousness when dining-out. Outside of the family home, tics were often an issue, drawing unwanted attention to the family with some families avoiding dining-out regularly. Avoidance of social activities, due to fear of being stared at is a common challenge faced by families with a young person with TS (35, 36), particularly true for socially unacceptable behaviour [e.g., swearing tics (37, 38)]. Families who dined out tended to opt for environments they felt would be more accepting of their child's tics and behaviours; usually family-friendly restaurants where they could blend into the background. While the need for family-friendly environments was also mentioned by mothers of children with ASD, what was deemed suitable varied depending on each child's needs (17). Mothers in the current study preferred louder venues where their child's tics could blend in, whereas mothers in Suarez and colleagues' study required quieter venues to accommodate their child's sensory sensitivity. This finding highlights the varying needs of neurodiverse populations and how environments that might meet the needs of some families may be problematic to others. Finding a suitable environment may be particularly challenging for children presenting with more than one neurodiverse condition (39).

The children's eating behaviours themselves were also noted to be a particular source of mealtime stress. For example, food related challenges included selective eating, food refusal based on sensory sensitivity (taste, texture, and smell) and mealtime behaviour challenges (meltdowns). These eating behaviours were described as creating stressed and strained mealtime interactions, often leading to conflict and additional foodwork. This study supports previous findings highlighting sensory sensitivity to underlie food selectivity in children with TS (2, 3), but reflects the lived experiences and the resulting challenges from these behaviours.

Some mothers frequently used combative language to describe their mealtime interactions with their children, often describing it as a "*battle*." These mothers tended to be concerned by their child's eating behaviour, which motivated them to assert control over their child's food choices (40, 41). However, mothers often described their attempts to control their child's eating behaviours as leading to a battle of wills, which ultimately ended in a "*meltdown*" and consequently conceding to maintain the peace. The repetition of these experiences led to mothers feeling defeated and exhausted, sentiments echoed about mealtimes by mothers of children with ASD (17, 18, 42). While mothers may think that controlling feeding practises will improve their child's selective eating (41), they may unwittingly further entrench selective eating and create negative associations with food [for review, see (43)].

The current findings also highlight the importance mothers place on family mealtimes and their inability to recreate their desired experiences. Dissatisfaction occurred as result of the incongruency between what mothers desired and their reality, and failure to accept their reality. Mothers in this study who internalised notions of good mothering [e.g., the provision of nutritious home-cooked meals, see (44)], were particularly affected as it challenged their identity. For these mothers, mealtimes appeared to be associated with dissatisfaction with their mealtime experiences, grief for what cannot be, guilt for not being able to recreate the mealtimes they had hoped for, as well as sadness.

The cumulative nature of stressful mealtime experiences and having to accommodate preferences took a toll on mothers; some felt hopeless with no other choice but to give up despite not wanting to, while others surrendered to their reality, opting to give in to keep the peace. For example, Thullen and Bonsall (14) found that disruptive mealtime behaviour, food refusal and mealtime rigidity were all independently associated with increased stress in parents of children with ASD. Mothers of children with a tic disorder may also benefit from interventions to reduce mealtime-related stress, however little support is currently available for these challenges (42, 45). Maternal accounts indicated stress/conflict avoidance as the main overarching goal of mealtimes, which has been shown to be the most common mealtime goal in parents of children aged 1–16 years (46). Therefore, any intervention must be aligned with this goal to be successful. Some practical suggestions to manage mealtime expectations include: providing more food at breakfast or lunch and a smaller meal for dinner; accepting that food will spill, messes will happen, and children will not always be hungry; and allowing more time for meals. However, mealtime interventions are complex mainly as there was not just one profile of mealtime concerns. More research addressing feeding and mealtime challenges is vital, as more knowledge of specific feeding issues for children with a tic disorder may help paediatric therapists plan interventions. These interventions are likely to include various sensory- and behaviour-based techniques (47).

While it has been shown some of the daily challenges mothers and their families faced, this study does not seek to imply that these experiences are representative of all families with a young person with a tic disorder, nor would it be reiterated by the fathers' accounts. For example, this is based on a small sample of self-selected mothers who may have taken part because of their difficult mealtime experiences. Notably, some positive experiences were shared, such as the palpable resilience of these mothers and their commitment to their children and families.

The findings of this study should be considered within the context of its design and limitations. Firstly, this study relied on purpose sampling, which may have biassed the sample towards mothers who place an importance on mealtimes, experience mealtime difficulties and or have children with greater tic severity than those who chose not to participate. The mothers also all identified as White British, thus future research would benefit from a more ethnically diverse sample to explore the intersect of race and culture on mealtime experiences within this clinical population. Thirdly, the children's diagnoses were reported by the mothers, with them being asked to confirm their child had a formal diagnosis. As there was no independent assessment, diagnosis status cannot be confirmed. Relatedly, all but two of the children had a primary TS diagnosis, with two of the youngest children (aged 3 and 4 years) both having a PTD. There is some caution about diagnosing TS and PTD in very young children due to the common transitory nature of tics during this developmental period (48). Nevertheless, in both instances, the children in question had a parent diagnosed with TS and considering the genetic basis for TS, it felt important to capture their mother's experiences. Future research may benefit from exploring differences among those with different types of tic disorders and having a more narrowly defined age range to account for developmental differences. Finally, almost all the children had comorbidities which meant it was difficult to differentiate which mealtime difficulties were strictly related to TS, and which were related to comorbidities. While this is a limitation of the study, it is also representative of a TS sample. This sample is thought to reflect the spectrum of presentations within this population, with TS being a multifaceted condition with a complex clinical presentation due to high comorbidity rates (49, 50). Importantly, anomalous eating patterns have been found in children with TS, even when accounting for comorbidities (2), with mothers in the current study, able to shed further light on how their child's symptoms of TS and associated comorbid conditions intersected to make mealtimes complex.

Despite these limitations, this study contributes unique insights by shining a light on some of the hidden challenges mothers may face. This is an essential first step towards designing studies in the future. The hope is that by highlighting the barriers to harmonious and enjoyable mealtimes, practitioners who work with these families may be able to provide mealtime-specific support. The cumulative effect of dissatisfaction, stress and additional foodwork can have a diminishing effect on maternal and familial resilience and wellbeing. In order to provide ongoing care for children with chronic conditions and their families, more emphasis needs to be placed on barriers to meaningful daily activities such as mealtimes. As such, families may benefit from individualised support that can help them create meaningful experiences, be it adjusted mealtimes to accommodate for their challenges or finding alternative bonding activities.

## Data availability statement

Inquiries regarding the data supporting this article can be directed to the corresponding author.

## Ethics statement

The studies involving human participants were reviewed and approved by Ethical approval for this research was obtained from the University of Hertfordshire University Ethical Advisory Committee Protocol Number: aHSK/PGT/UH/03340(5) and the research was performed in accordance with the Declaration of Helsinki. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication

of any potentially identifiable images or data included in this article.

## Author contributions

S-EB conducted the research as part of her PhD, planned research, recruited participants, collected data, transcribed interviews, conducted analysis, revised themes, wrote up the study as a PhD chapter, and drafted the manuscript. AL and WW were the second supervisors of PhD, supported research design, data analysis, and contributed to the writing of the manuscript. SR was the primary supervisor of the PhD, supported research design, data analysis, and contributed to the writing of the manuscript. SR, WW, and AL contributed equally to the drafting of the manuscript. All authors approved the manuscript for submission.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# "I'm in pain and I want help": An online survey investigating the experiences of tic-related pain and use of pain management techniques in people with tics and tic disorders

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**Objectives:** Tic disorders (TDs) are complex neurological conditions characterized by involuntary, persistent vocalizations and motor movements called tics. Tics involve brief muscle movements and can impair many aspects of daily functioning and quality of life in patients – and their physical nature can cause pain. Understanding individuals' experiences of tic-related pain and pain management could help explore this under-researched area and identify additional support needs for this population. The aim of this study was to investigate experiences of pain and use of pain management techniques in people with tic disorders.

**Methods:** An online survey consisting of multiple choice and open-ended questions exploring experiences of tic-related pain, help-seeking behavior for tic-related pain, and use of pain relief techniques for tic-related pain, was circulated online *via* international Tourette syndrome patient associations, and one online support group for Tourette syndrome. The online survey was open to adults (≥16 years) with self-reported tics. Open-ended questions were analyzed using thematic analysis.

**Results:** One hundred eighty-one participants (16–71 years; 58.0% female) from 18 countries completed the online survey. Several aspects of tics were associated with pain, including the physical effort of motor tics ($n$ = 177, 97.8%), repetitive tics ($n$ = 141, 77.9%) and the consequences of tics ($n$ = 131, 72.4%). Nearly two-thirds ($n$ = 118, 64.6%) had sought professional help for tic-related pain. Distraction techniques ($n$ = 126, 69.6%), taking pain relief medication ($n$ = 125, 69.1%) and altering tics ($n$ = 111, 61.3%) were the most commonly-reported methods used to relieve and cope with tic-related pain. Thematic analysis found an interrelated complex relationship between participants' tics, pain, and pain management techniques, reflected in four themes: the "tic-pain" cycle, the impact of pain, the importance of support, and the perceived successfulness of pain management techniques.

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**Conclusions:** Tic-related pain was reported to have a significant physical and psychological impact which impacted aspects of daily living in people with tic disorders. The findings add to limited research suggesting tic-related pain is a dominant issue for individuals with tic disorders, potentially impacting upon their quality of life. Increased understanding of tic-related pain and its influence may be helpful in the long-term management of tic disorders, both in terms of clinical management and patients' self-management.

KEYWORDS

**pain, pain management, quality of life, tic disorders, Tourette syndrome**

## Introduction

Tic disorders (TDs)–such as Tourette syndrome (TS) and chronic motor or vocal tic disorder (CTD)–are complex neurological conditions characterized by tics: these are abrupt, involuntary, and persistent vocalizations and motor movements (1). Tics typically begin in early childhood, with TS having an ∼1% global prevalence rate (1, 2). Motor tics involve a muscle or a group of muscles, which results in movements such as jerking of the neck or shoulders, eye blinking, or twitching. Vocal tics comprise of noises produced by the nose, mouth, or pharynx, such as whistling, throat clearing, and sniffing (3). Tics can be simple or complex in nature, with complex tics becoming more common with increasing age (4). Not all tics may be rapid and clonic: some tics may be dystonic and slower in nature and cause brief abnormal posture, while tonic tics involve brief muscle tensing and contractions (5). Options for treatment and management for tic disorders includes pharmacological medications and psychological interventions (e.g., behavioral therapy) (2, 6). Many individuals with tics also experience a premonitory urge–a physical feeling or sensation–before tics are expressed. Through awareness of this premonitory urge, tics can be suppressed–which many patients describe as uncomfortable (7). Tics are known to fluctuate or "wax and wane" in their frequency and severity over time (8), usually peaking in adolescence and improving in late adolescence-early adult years. The majority of people (85.7%) with TS have a comorbid psychiatric condition (9): attention deficit hyperactivity disorder (ADHD) is the most common, affecting between 60 and 80% of patients with TS (10).

There is strong evidence demonstrating that adults with tic disorders experience a lower quality of life (QoL) with resultant impairments across many aspects of their lives. Increased tic severity in adults has been associated with greater functional impairments and more life dissatisfaction, compared to the general population (11). Higher rates of clinical depression and depressive symptoms have been found in individuals with TS, compared to individuals without TS (12). Data from the Swedish National Patient Register found tic disorder patients have an increased risk of attempting and dying by suicide compared to the general population (13). The visible nature of tics means people with tic disorders often receive unwanted, negative attention from other people: this can lead to people suppressing their tics in social situations to avoid and cope with negative attention (14). Social stigma surrounding tics has led to adults with TS to report fears of discrimination and leading to feelings of isolation (15).

Given the exertion of muscles involved in tics, pain may be considered an "invisible" or unseen aspect of living with tic disorder. Riley and Lang (16) described patients with various tics that caused them pain, including neck pain from neck jerking tics, self-injurious tics (e.g., touching a hot stove), and headaches from full-body tics. An online survey with TS patients found 97% of participants reporting experiencing tic-related pain (17), while Conelea et al. (11) found that 60% of adults with tic disorders reported at least one tic that caused them pain or physical damage. A recent study found 60% of children with TS reported pain arising from tics, with increased pain significantly associated with greater tic severity (18). Additionally, higher rates of generalized joint hypermobility have been reported in people with neurodevelopmental conditions (including TS), with a relationship found between self-reported musculoskeletal pain and increased joint hypermobility (19). Adults with tic disorders have also reported a worsening in their tics and increased self-injurious behaviors during the COVID-19 pandemic (20).

Despite the clear evidence of pain associated with tics, many have identified a lack of research within this area (16, 17, 21, 22). In April 2021, the National Institute for Health and Care Excellence published guidelines about the assessment and management of all chronic pain (23). It has been suggested that the persistent pain experienced from

Abbreviations: ADHD, Attention deficit hyperactivity disorder; CTD, Chronic motor or vocal tic disorder; QoL, Quality of Life; TD/TDs, Tic disorder/Tic disorders; TS, Tourette syndrome.

tics and tic disorders falls into the chronic secondary pain category. However, these guidelines do not specifically include the management of pain where an underlying condition accounts for the pain, such as arising from a tic disorder. There is a concern that patients who are diagnosed with secondary pain may not be properly recognized nor treated appropriately (23).

The pain associated with tics often has lasting effects; 87% described physical discomfort from tics impacted upon their everyday life (17). Adults with TS-related headaches have been found to have poorer QoL and higher tic severity compared to children with TS and headaches (21). As well as coping with tics, people with tics are often reliant on themselves to find ways of managing and coping with tic-related pain. Pain caused by tics has been reported as an influential factor in deciding to commence treatment, such as medication or behavioral therapy (24). A study with children and young people with TS found that to cope with tic-related pain, younger children reported seeking support from their parents, while adolescents preferred to isolate themselves to cope (18). Due to complex assessment and treatment pathways, extremely long waiting times, and insufficient funding, accessing specialist care is often difficult to access for many patients with TS (22, 25). Anderson et al. (17) found 65% of participants reported they felt their tic-related injuries had not been effectively treated.

The need to explore the methods individuals with TS use to manage pain has been emphasized by previous research (26). Those with more severe tics may be more likely to use tobacco, alcohol, or illegal drugs to manage tics (11). Patients may not take medication for tics due to side effects (17, 25, 27), and so may use other methods to manage tics and tic-related pain. A variety of behavioral and cognitive self-management techniques for individuals with chronic pain conditions have been reported (28), including methods to improve an individual's ability to manage and cope with pain (e.g., relaxation, distraction techniques) (29, 30). However, much like research regarding tic-related pain, there is a lack of in-depth investigation into pain management among people with tics. Exploring this area could help to improve the knowledge of healthcare professionals and identify further areas of clinical need to be incorporated into clinical care for TD patients. Subsequently, this may improve the support available for individuals with TDs and their family members. The aim of the present study was to investigate experiences of tic-related pain and use of pain management techniques in people with TDs. This was explored through a mixture of quantitative and qualitative approaches *via* an online survey to explore people's lived experiences of tic-related pain, the methods people have used to manage tic-related pain, and exploring whether they have sought and received any support and/or treatment from healthcare professionals for tic-related pain.

# Materials and methods

## Participants and recruitment

Participants were adults (≥16 years) with a suspected or confirmed TD diagnosis, who were experiencing tics and tic-related pain at the time of participation. Based on previous online surveys using similar methodologies (11, 17, 31), we aimed to recruit between 80 and 150 participants. Participation was open to anyone worldwide who could read and write English.

Several text-based and image advertisements were created to promote the online survey. The advertisements contained the link to the online survey (hosted on JISC Online Surveys): the first two webpages presented full information regarding the study. Eight national TS charities were contacted by the first author (ET), and four agreed to disseminate the advertisements on their websites and social media pages. The advert was also posted to one online TS support community, on the NIHR MindTech MedTech Co-operative Twitter account, and the second author (SA) circulated it to forty-seven TS patient support associations. The survey was open between 10th June and 13th July 2021.

## Online survey design

An online survey as developed, comprising of multiple-choice and open-ended questions, taking ∼30 min to complete. The first three webpages consisted of participant information (e.g., explaining study purpose, rights to withdraw, study ethical approval) and completion of an online consent form to indicate their willingness to participate. After consenting, the online survey consisted of six sections. The first section asked participants demographic questions about themselves. The second section asked participants about their tic disorder (e.g., whether they had a formal diagnosis, if they were currently prescribed medication for tics). An adapted version of the "interference" subsection of the self-report Brief Pain Inventory-Short Form (BPI-SF) (32) was used to assess perceived interference of tics. The interference subsection evaluates pain interference on seven aspects of daily life in the past week. This was adapted for the present study to ask participants about how much tics interfered on each of these seven aspects, with six additional aspects included based on tic disorder literature (11, 33). Each item was scored on a 1 ("No interference at all upon my daily life") to 5 ("Severe interference at all upon my daily life") scale, and included a "non-applicable" option. Average scores were calculated for each of the 13items.

The third section consisted of questions regarding participants' tic-related pain, including inviting participants

to qualitatively share their experiences of tic-related pain, and the adapted BPI-SF focussing on tic-related pain interference in the past week. The fourth section presented the Brief Resilience Scale (BRS) (34): this consists of six statements measuring psychological resilience and ability to cope, each measured on a 1 ("strongly disagree") to 5 ("strongly agree") scale. Scores range between 6 and 30, with an average score calculated to indicate low (scores <2.99), normal (scores 3–4.30) and high (scores >4.31) psychological resilience (34).

The fifth section presented a multiple-choice question asking participants whether they had sought out professional help for tic-related pain, and if so they were asked to select from a list of 13 healthcare professionals/services with the option to specify other healthcare professionals/services. A second multiple-choice question asked participants to select–from a list of 17 active and passive pain management techniques (30)–which techniques/methods they had used for managing tic-related pain, or to specify any additional techniques they employed. Participants were invited to qualitatively share what they found helpful and unhelpful in managing tic-related pain. The final section presented assessed current tic severity through the Adult Tic Questionnaire (ATQ) (35), a self-report questionnaire assessing the presence, intensity and severity of 27 specific vocal and motor tics. Scores are summed to produce a total tic severity score (range 0–216), with higher scores indicating greater severity. The final page consisted of debriefing information alongside signposting to worldwide TS/tic organizations and the research team's contact details.

## Public involvement

Four adults with TS reviewed the online survey and advertisements prior to going live, to ensure they were worded appropriately and sensitively. The advertisements and questions were deemed appropriately worded, with minor adjustments made to some survey questions based on feedback.

## Ethical considerations

The study was reviewed and approved by the University of Nottingham Division of Rehabilitation, Aging and Wellbeing ethics committee.

## Data analysis

Data were downloaded into a Microsoft Excel spreadsheet, and quantitative data were analyzed descriptively in SPSS V26 (IBM Corp., Armonk, N.Y., USA). Relationships between resilience and tic severity were explored *via* Spearman's rank order correlation, with statistical significance set at $p =< 0.05$. There was no missing data for the outcome measures. Responses to open-ended questions were analyzed using thematic analysis (36) by the first author (ET), using a data-driven inductive approach to analysis. The first stage involved familiarization through re-reading the responses and creating short codes summarizing the data. Secondly, similar codes were grouped together, leading into making connections between similar codes and collating these into potential themes. A thematic map was created to review the consistency and appropriateness of codes and themes, and discussed with BD for clarity and refinement. Theme names were generated, capturing the patterns in the data.

# Results

## Sample demographics

In total 181 participants (58.0% female, mean age 28.4 ± 12.2) years from 18 countries completed the survey (Table 1). The majority ($n$ = 153, 84.5%) had a formal tic disorder diagnosis, experienced premonitory urges prior to their tics ($n$ = 167, 92.3%, with over three-quarters ($n$ = 144, 79.5%) reporting at least one co-morbid condition. The total average tic severity score from the ATQ was 71.59 ($SD$ = 35.11, range = 9–193), with greater severity of motor tics (M = 45.49, SD = 18.62) reported compared to vocal tics (M = 26.09, SD = 19.16). Over half the sample reported their tics had become worse by "a lot" ($n$ = 58, 32.0%) or "a little" ($n$ = 47, 26.0%) since the start of the COVID-19 pandemic.

Spearman's rank order correlation found a significant negative relationship between total tic severity and resilience scores [$r_s(181) = -0.154, p = 0.03$], suggesting greater resilience was associated with less severe tics (Table 2). A Kruskal-Wallis test found a significant difference in total tic severity score by level of psychological resilience (low resilience, $n$ = 105, M = 75.26 ± 35.95; normal resilience, $n$ = 70, M = 63.36 ± 29.90; high resilience, $n$ = 6, M = 103.33 ± 52.22), $H(2) = 7.14$, $p = 0.028$. *Post-hoc* Mann-Whitney tests found this significant difference was only between the low (md$n$ = 72.0) and normal (md$n$ = 58.5) resilience groups ($U(n_{low} = 105, n_{normal} = 70) = 2982.00$, $z = -2.11$, $p = 0.035$), suggesting those in the lower resilience group had greater median total tic severity.

Looking at self-reported impact of tics on daily activities in the past week, the highest scores (out of 5) for interference were upon their academic studies (M = 3.63, SD = 1.16), self-esteem (M = 3.63, SD = 1.17), mood (M = 3.57, SD = 1.02), and sleep (M = 3.46, SD = 1.21) (Table 3).

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TABLE 1 Demographic characteristics of the sample ($N = 181$).

| | *N* (%) |
|---|---|
| **Gender** | |
| Male | 58 (32.0%) |
| Female | 105 (58.0%) |
| Non-binary | 18 (10.0%) |
| **Age (M, SD)** | 28.41 (12.19) |
| 16–18 yrs | 41 (22.7%) |
| 19–25 yrs | 58 (32.0%) |
| 26–35 yrs | 38 (21.0%) |
| 36–45 yrs | 24 (13.3%) |
| 46–55 yrs | 12 (6.6%) |
| 56–65 yrs | 6 (3.3%) |
| 66–71 yrs | 2 (1.1%) |
| **Country** | |
| United Kingdom | 64 (35.4%) |
| Norway | 41 (22.7%) |
| USA | 23 (12.7%) |
| Australia | 19 (10.5%) |
| Netherlands | 10 (5.5%) |
| Canada | 5 (2.8%) |
| New Zealand | 5 (2.8%) |
| Argentina | 2 (1.1%) |
| Belgium | 2 (1.1%) |
| France | 2 (1.1%) |
| Costa Rica | 1 (0.6%) |
| Finland | 1 (0.6%) |
| Germany | 1 (0.6%) |
| Guatemala | 1 (0.6%) |
| Ireland | 1 (0.6%) |
| Spain | 1 (0.6%) |
| Sweden | 1 (0.6%) |
| Uruguay | 1 (0.6%) |
| **Received TD diagnosis** | |
| Yes | 153 (84.5%) |
| No | 10 (5.5%) |
| Awaiting assessment | 17 (9.4%) |
| **Self-reported co-morbidities** | |
| Anxiety disorder | 94 (51.9%) |
| Depression | 74 (40.9%) |
| ADHD | 56 (30.9%) |
| OCD | 49 (27.1%) |
| ASD | 25 (13.8%) |
| Insomnia | 24 (13.3%) |
| Learning difficulties | 18 (9.9%) |
| SPD | 18 (9.9%) |
| Dyspraxia | 3 (1.7%) |
| Other | 27 (14.9%) |
| None | 37 (20.4%) |
| **Currently taking medication for TD** | |
| Yes | 47 (26.0%) |
| No | 134 (74.0%) |
| **Received behavioral therapy for TD** | |
| Yes | 63 (34.8%) |
| No | 111 (61.3%) |
| Unsure | 7 (3.9%) |
| **Experiences premonitory urges** | |
| Yes | 167 (92.3%) |
| No | 8 (4.4%) |
| Unsure | 6 (3.3%) |
| **ATQ total tic severity score (M, SD)** | 71.59 (35.11) |
| ATQ motor tics severity scale (M, SD) | 45.49 (18.62) |
| ATQ vocal tics severity scale (M, SD) | 26.09 (19.16) |
| **Self-perceived change in tics since COVID-19 pandemic** | |
| Much better | 4 (2.2%) |
| Little better | 9 (5.0%) |
| No change | 63 (34.8%) |
| Little worse | 47 (26.0%) |
| Much worse | 58 (32.0%) |
| **Self-reported condition causing pain (unrelated to tics)** | |
| Yes, diagnosed condition causing pain | 33 (18.2%) |
| Yes, not diagnosed but have condition causing pain | 11 (6.1%) |
| No | 111 (61.3%) |
| Unsure | 26 (14.4%) |

## Experiences of pain related to tics

The most common types of pain were caused by the physical effort of motor tics ($n = 177$, 97.8%); repetitive tics ($n = 141$, 77.9%); and the consequences of tics ($n = 131$, 72.4%).While the primary goal of tic medication is upon tic expression, patients may experience subsequent changes in pain following changes in tic expression due to taking medication: of the $n = 47$ currently taking medication for their tics, almost half ($n = 22$, 46.8%) reported it made no difference to their tic-related pain, with a third ($n = 17$, 36.2%) reporting it helped relieve or manage tic-related pain. Likewise, of the $n = 63$ who had received behavioral therapy for tics, the majority ($n = 35$, 55.6%) stated it had no difference to tic-related pain, with $n = 12$ (19.0%) reporting it helped relieve or manage tic-related pain and $n = 7$ (11.1%) reporting it increased or intensified pain (Table 4).

Looking at self-reported impact of tic-related pain in the past week, the highest scores (out of 5) for interference of tic-related pain were upon their mood (M = 3.31, SD = 1.24), sleep (M = 3.24, SD = 1.40), and upon enjoyment of life (M = 3.04, SD = 1.32) (Table 3).

TABLE 2 Total tic severity scores presented by resilience threshold.

| Brief resilience scale category | ATQ motor Tic severity subscale (M, SD) | ATQ vocal Tic severity subscale (M, SD) | ATQ total tic severity (M, SD) |
|---|---|---|---|
| Low resilience ($n = 105$) | 47.21 (19.27) | 28.05 (19.05) | 72.26 (35.95) |
| Normal resilience ($n = 70$) | 41.63 (16.43) | 21.73 (16.80) | 63.36 (29.90) |
| High resilience ($n = 6$) | 60.50 (22.23) | 42.83 (33.07) | 103.33 (52.22) |

TABLE 3 Self-reported interference of tics and tic-related pain across thirteen domains in the previous week.

| Domain | Impact of tics, M (SD) | Impact of tic-related pain, M (SD) |
|---|---|---|
| General activity | 3.24 (1.03) | 2.9 (1.21) |
| Mood | 3.57 (1.02) | 3.31 (1.24) |
| Walking ability | 2.41 (1.19) | 2.28 (1.41) |
| Typical daily work | 3.13 (1.20) | 2.73 (1.28) |
| Self-esteem | 3.63 (1.17) | 2.77 (1.41) |
| Family relationships | 2.52 (1.32) | 1.95 (1.23) |
| Relationships with friends | 2.56 (1.30) | 2.09 (1.23) |
| Relationship with partner | 2.24 (1.34) | 1.78 (1.15) |
| Social situations | 3.86 (1.07) | 2.74 (1.38) |
| School or education | 3.63 (1.16) | 2.78 (1.49) |
| Work/employment | 3.23 (1.32) | 2.72 (1.40) |
| Sleep | 3.46 (1.31) | 3.24 (1.40) |
| General enjoyment of life | 3.09 (1.21) | 3.04 (1.32) |

NB, Each domain is scored on 1-to-5 scale.

TABLE 4 Self-reported causes of tic-related pain and impact of treatment upon tic-related pain.

| | *N* (%) |
|---|---|
| **Causes of tic-related pain** | |
| Physical effort of motor tics (e.g., muscular pain, joint pain, cramping) | 177 (97.8%) |
| Arising from repetitive tics (e.g., tendonitis, repetitive stress injury) | 141 (77.9%) |
| Consequences of tics (e.g., injury due to tics) | 131 (72.4%) |
| Physical effort of vocal tics (e.g., sore throat, sore nose) | 120 (66.3%) |
| Pain from self-injurious tics (e.g., striking another object) | 120 (66.3%) |
| Pain from suppressing tics | 108 (59.7%) |
| Pain from premonitory urge | 46 (25.4%) |
| Other | 3 (1.7%) |
| **Has medication for tics helped tic-related pain? ($n = 47$)** | |
| Yes - helped relieve or manage pain | 17 (36.2%) |
| Yes - increased or intensified pain | 1 (2.1%) |
| No, do not affect tic-related pain | 22 (46.8%) |
| Not sure | 7 (14.9%) |
| **Has behavioral therapy helped tic-related pain? ($n = 63$)** | |
| Yes - helped relieve or manage pain | 12 (19.0%) |
| Yes - increased or intensified pain | 7 (11.1%) |
| No, do not affect tic-related pain | 35 (55.6%) |
| Not sure | 9 (14.3%) |

## Help-seeking and self-management for tic-related pain

Almost two-thirds ($n = 118$, 64.6%) reported seeking out professional help for tic-related pain, with over half of these ($n = 71$, 60.1%) reporting having received help/treatment. Of these, commonly-reported sources of professional help for tic-related pain included non-specialist doctors ($n = 61$, 51.3%), physiotherapists ($n = 43$, 35.9%) and neurologists ($n = 40$, 34.2%) (Table 5).

The most commonly-reported pain management techniques for tic-related pain were distraction tactics ($n = 126$, 69.6%), using over-the-counter/non-prescription medication ($n = 125$, 69.1%), attempting to alter tic that causes pain ($n = 111$, 61.3%) and using relaxation techniques ($n = 107$, 59.1%) (Table 6).

## Qualitative analysis

Through analyzing the written responses, four themes were generated: "The tic-pain cycle," "The impacts of pain," "The importance of support," and "Successfulness of pain management techniques." These themes are multifaceted as they interlink and influence each other. For each cause (i.e., tic/pain/injury) there is an effect (i.e., pain/injury/action), which are dependent on an individual's experience of tics, pain, and support. For ease of clarification, the themes have been separated into subthemes and appropriate links are discussed in relevant sections. From the qualitative data, it was clear that participants had an informed insight regarding their tics and were highly aware on how it impacted on themselves and others around them.

### Theme 1: The tic-pain cycle

Although experiences differed, a reinforcement pattern between participants' tics and pain emerged; the repetitiveness of a tic was the main aggravator of pain, and this pain could

TABLE 5 Self-reported help-seeking from healthcare professionals for tic-related pain.

| | *N* (%) |
|---|---|
| **Help-seeking for tic-related pain** | |
| Sought help and received help/treatment | 71 (39.2%) |
| Sought help but did not receive help/treatment | 46 (25.4%) |
| No help sought | 61 (33.7%) |
| Not sure | 3 (1.7%) |
| **Who did you seek professional help from? ($n = 117$)** | |
| Non-specialist doctor (e.g., GP) | 60 (51.3%) |
| Physiotherapist | 42 (35.9%) |
| Neurologist | 40 (34.2%) |
| Psychologist | 29 (24.8%) |
| Psychiatrist | 24 (20.5%) |
| Osteopath | 14 (12.0%) |
| Behavioral therapist | 12 (10.2%) |
| Pain management service/clinic | 7 (6.0%) |
| Pediatrician | 6 (5.1%) |
| Psychotherapist | 6 (5.1%) |
| Other specialist doctor | 6 (5.1%) |
| Nurse | 4 (3.4%) |
| Occupational therapist | 3 (2.5%) |
| **Other*:** | |
| Child and adolescent mental health services | 2 (1.7%) |
| Chiropractor | 2 (1.7%) |
| Massage therapist | 2 (1.7%) |
| Bowen therapist | 1 (0.8%) |
| Endocrinologist | 1 (0.8%) |
| Medical cannabis clinic | 1 (0.8%) |
| Traumatologist | 1 (0.8%) |
| **Taking prescribed pain relief medication for tic-related pain** | |
| Yes, currently taking medication | 13 (7.2%) |
| Yes, in the past | 31 (17.1%) |
| No | 134 (74.0%) |

*Responses under "Other" were from an optional text-box where participants could share further healthcare professionals/services they had sought help from.

TABLE 6 Self-management techniques used to manage tic-related pain.

| Technique/method | *N* (%) |
|---|---|
| Used distraction tactics (e.g., watching videos, listening to music) | 126 (69.6%) |
| Taken over-the-counter/non-prescription pain relief medication (e.g., tablets, medicated gels) | 125 (69.1%) |
| Attempted to alter tic that causes pain (e.g., through suppression, redirection) | 111 (61.3%) |
| Used relaxation techniques (e.g., breathing techniques) | 107 (59.1%) |
| Used temperature-related treatment on site of muscle pain (e.g., heat or cold packs) | 105 (58.0%) |
| Hands-on treatment (e.g., massage, acupuncture) | 103 (56.9%) |
| Avoided certain activities which exacerbate tics and pain | 88 (48.6%) |
| Exercises (e.g., stretching exercises) | 86 (47.5%) |
| Used something to reduce tic impact (e.g., padded collar, gloves, brace) | 80 (44.2%) |
| Sought out support from other people with tics | 62 (33.7%) |
| Used psychological techniques (e.g., mindfulness, CBT) | 50 (27.6%) |
| Used cannabidiol-based products | 35 (19.3%) |
| Used cannabis | 27 (14.9%) |
| Used electronic pain relief (e.g., TENS) | 23 (12.7%) |
| Consumed alcohol | 21 (11.6%) |
| Used elastic therapeutic/kinesiology tape | 19 (10.5%) |
| Used drugs/substances | 9 (5.0%) |
| **Other*:** | |
| Physical activity | 10 (5.5%) |
| Sleeping well | 5 (2.7%) |
| Applying pressure to affected area | 3 (1.6%) |
| Botox injections for tics | 2 (1.1%) |
| Hot baths | 2 (1.1%) |
| Hot drinks to ease throat | 2 (1.1%) |
| Tobacco | 2 (1.1%) |
| Dietary changes | 1 (0.5%) |
| Herbal-based medicine | 1 (0.5%) |
| Humor to cope | 1 (0.5%) |
| Oxytocin nasal spray | 1 (0.5%) |
| Use of wheelchair | 1 (0.5%) |

*Responses under "Other" were from an optional text-box where participants could share further pain management techniques/methods.

then trigger more tics: *"I often go to bed with aches and pains and the more pain I'm in the more I tic"* (Participant 66, aged 25) (Figure 1). Consequently, tic-induced injuries could occur, and viewing or acknowledging these injuries could again cause tics: *"Seeing the bruises sets the hitting tics off"* (P134, aged 16). Aggravating these injuries caused further pain, prompting more tics: *"The pain was becoming constant … It was also making my tics worse and more painful themselves"* (P118, aged 17). This suggests reducing or improving the tics may be the most important thing to focus on in tic management.

However, it was unclear whether the steps within this cycle happened immediately after one another, or whether they occurred over a longer period of time. Some participants acknowledged a certain tic could be triggered within this cycle leading to its continuation: *"the pain of the bruises does not stop the tics, so I basically re-bruise it every day"* (P124, aged 17) – but others were vaguer in their description of any patterns. The emotional and mental state of participants also appeared to influence the tic-pain cycle, as many noted their tics and tic-related pain were exacerbated by heightened emotions: *"the pain*

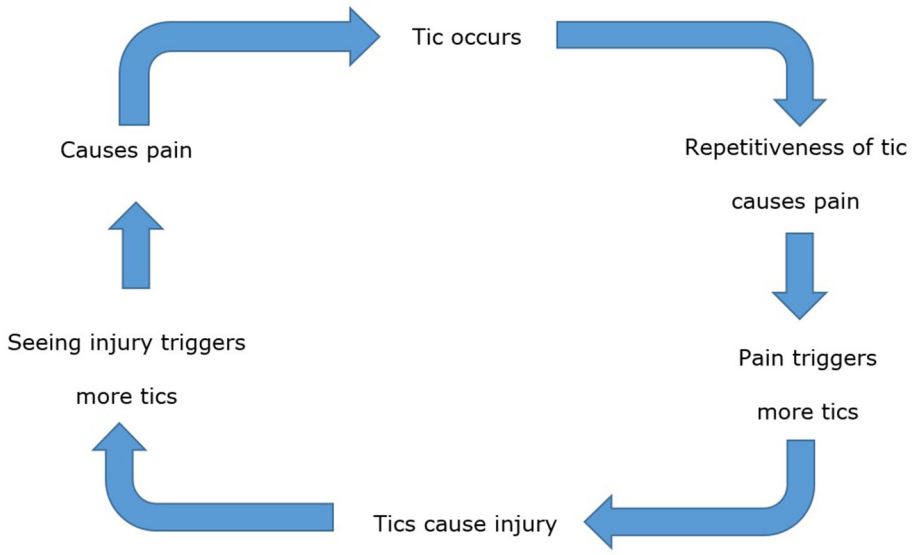


FIGURE 1
Theorized diagram of the "Tic-Pain Cycle."

*ntenses [sic] when i have more tics. and that mostly happens if i have a lot of stress, if i am nervus [sic], when i am tired*" (P32, aged 27). These emotions seemed to continue to impact and/or cause tics and subsequently cause further pain: *"Stress reduction also reduces tics, which in turn reduces tic related pain"* (P89, aged 18).

Some participants discussed effects on the pain by attempting to suppress their tics. Many noted that supressing tics made them worse (e.g., increased intensity or frequency), subsequently increasing pain: *"suppressing my tics .... makes them worse in the long run which makes the pain worse too"* (P116, aged 19).

One participant acknowledged the importance of treating tics: *"there is no real solution until tics can be treated/cured*" (P128, aged 22). However, many participants noted that the pain - not the tics - was the reason for seeking help, suggesting this relationship is complex.

## Theme 2: The impacts of pain

This theme describes how the tic-related pain affected participants psychosocially and physically. These two factors could be responsible in supporting decisions around help-seeking.

### Psychosocial impact of pain

Two main patterns of psychological impact were described by participants, reflecting *hopelessness* and *acceptance*. For many, their outlook on living with tic-related pain was bleak, as many were not able to "*cope with the constant pain related to [their] tics*" (P26, aged 49). Some participants noted feelings of anger: *"it hurts all over and it makes me angry and i cry"* (P81, aged 39). Many described the pain as unbearable, and some were led to suicidal thoughts, emphasizing the serious and adverse impacts of tic-related pain and highlighting the desperation this group of patients are experiencing.

The interference of pain and its impact on daily life in some cases led to some individuals reaching out for support. For example, one participant explained they sought help as: *"chronic pain had me suicidal"* (P173, aged 35). Feelings of desperation, anguish and low mood, caused by pain were commonly acknowledged among participants. However, the aspect of hopelessness in terms of finding relief from pain also discouraged others from seeking help: *"I have never sought help because I didn't believe there was anything anyone could do to help with my particular problems*" (P59, aged 66). These indicate participants' low expectations concerning successful support and treatment.

Inversely, some participants exhibited feelings of acceptance surrounding tic-related pain. This was dependent on participants' experiences of tics and pain, with this appearing more common in those who perceived their pain as less severe and/or more tolerable: *"The pain is fairly constant, just in the background*" (P118, aged 17). Some individuals expressed a need to be proactive in managing their tic-related pain: *"I wanted to be able to have more control and possibily [sic]*

*less tics, and so: less pain"* (P22, aged 30). Participants with this viewpoint appeared to have a more educated insight into the benefits of being self-sufficient in dealing with their pain: *"To find support and ways, to learn to prevent problems on the long term, and relieve on short term"* (P28, aged 46). However, other participants rejected seeking treatment for pain as their own methods of self-management were sufficient: *"At the end of the day its nothing a panadol or an Advil can't fix"* (P11, aged 17). This demonstrates a variety of experiences as, for some, tic-related pain can be less severe and more manageable.

### Physical impact of pain

This subtheme encompasses the physical side effects and injuries from tics and pain, and how these affected participants' ability to seek help. Within the open-ended questions, the most reported symptoms were headaches ($n = 55$), with general muscle and throat soreness also frequently described. Bruises and damage to teeth were the most frequent injuries. Other less common consequences, were arthritis, broken bones, and cauliflower ear. The length and severity of tic-related pain and injuries was dependent on the type of tic specific to the individual, and reflects the diversity of the lived experiences of people with tics and TDs.

Participants' decision to seek help appeared to be affected by their outlook regarding their injuries. For some, acquiring medical help seemed obvious*: "I'm in pain and I want help"* (P66, aged 25). Similar to the psychosocial impacts of tic-related pain, many participants called the pain unmanageable, suggesting their methods of self-management were unsuccessful. Some revealed the potential danger their tics could create: *"My self-injurious tics were very severe … I was scared I would seriously hrt [sic] myself"* (P172 aged 19). These feelings of distress and worry relating to injury were frequent, again emphasizing the emotional impact. Many also participants stated their tic-related pain *"was so intense and disabling in day-to-day life"* (P107, aged 23), highlighting the seriousness of its impact upon daily living.

The physical consequences from tics and pain again elicited feelings of hopelessness when potentially seeking out support. Many believed this was pointless: *"What are they gonna do? Prescribe me otc [over-the-counter] pain meds? I dont think it would be of much use and I don't want to annoy my doctors"* (P128, aged 22). Participants may have previously had their experiences belittled by healthcare professionals. This is important as it accentuates past negative encounters adversely affect individuals and discourage them from pursuing help. Furthermore, this signifies that many are silently suffering. However, on the other hand, the physical impacts of tics and tic-related pain prompted some participants to seek help. Many reported receiving help from healthcare professionals, such as receiving massages for sore muscles or Botox injections, to help reduce the frequency of their tics and resulting tic-related pain.

## Theme 3: The importance of support

This theme encompasses how various types of support effected participants' thoughts, feelings, and actions, with three generated subthemes: "failings of healthcare professionals," "inaccessibility of treatment," and "the balance of social support."

### Failings of healthcare professionals

Participants reported an unmistakable lack of understanding and empathy from healthcare professionals regarding their tics and related pain. Numerous participants described receiving inadequate care after seeking professional help: many reported their healthcare professionals were uneducated regarding TDs, dealing with tic-related pain, or dismissed their problems. One participant with spinal and rib tic-related injuries described their encounters with doctors: *"I've kind of just been told to deal with it, because I can't 'stay still', which was the recovery advice for the fractured ribs too … a fully qualified GP … asked me what tourettes was, and said 'is that a form of exercise?'"* (P8, aged 22).

Furthermore, many participants were aware of the societal stigma surrounding TDs, which led them to avoid seeking help due to potential embarrassment. One individual stated they had not sought treatment for tic-related pain as they were *"not sure how seriously I would be taken"* (P27, aged 49). Feelings of frustration and hopelessness were again extremely common relating to the failings of healthcare professionals: *"the health system where I live is not willing to help me because my issues are too complex. I have been refused or ignored at every turn"* (P145, aged 33). One participant noted they had *"lost faith in doctors"* (P155, aged 30) due to the difficulty in receiving a TD diagnosis and subsequent treatment. Experiences such as these provide further evidence to why participants may feel hopeless and reluctant to pursue help – healthcare professionals' insufficient TD knowledge appears to negatively impact on their ability to provide treatment.

### Inaccessibility of treatment

Another common issue highlighting the importance of healthcare support was difficulties in access. Many participants described how both tic and pain management treatments were costly and unaffordable, with long waiting times to see healthcare professionals. These contributed to feelings of disheartenment and lack of confidence in the healthcare system, leading some to feel discouraged in seeking further support. Due to not having knowledge about available support, others reported being unaware of where to search for help. The inaccessibility of support again led to feelings of hopelessness regarding participants' ability to deal with their tics and pain, further highlighting the importance of effective help on their wellbeing.

### The balance of social support

This subtheme refers to the physical and emotional assistance some participants received from family and friends. In general, they were sympathetic toward participants regarding their tic-related pain. Many participants described family members providing massaging or applying topical treatments to affected body parts: *"my legs would hurt … My mom would massage them for me"* (P33, aged 21). In some cases, this would replace the need to see healthcare professionals. Emotional support was also instrumental in encouraging participants to seek treatment: *"My wife forced me to seeking [sic] help. It was a time when the pain was insanely painful and I had thoughts of ending my life"* (P181, aged 41). However, some participants were negatively affected by perceived excessive social support: *"My family and friends wrap me in 'cotton wool' because of the fear associated with hurting me. They don't give me hugs for fear of crushing me … This causes a feeling of uselessness"* (P61, aged 23). This demonstrates the complexities and intricacies of social support, with an apparent fine line between providing an adequate amount and too much support.

Conversely, a small number of participants described a less supportive social network. Some participants described their friends and family having a lack of understanding regarding their tics and tic-related pain: *"friends and family never supported my tics, probably because they don't have them"* (P16, aged 34). Another participant felt deterred from seeking support from their parents concerning their tic-related pain as *"they seemed to be judgemental the first time I told them"* (P129, aged 21). Similarly, feelings of shame due to the stigma about tics prevented some participants for seeking out for support from family and friends: *"[a] doctor diagnosed me with tics but I was too ashamed and embarrassed to tell my parents about every tic I experienced"* (P128, aged 22). The apparent lack of understanding within social networks indicates issues around health beliefs and education regarding TDs and tic-related pain.

## Theme 4: Successfulness of pain management techniques

Within participants' written responses, the pain management techniques that were the most notable in their varying success were medication, distraction and relaxation methods, and massaging of the affected muscles. Although medication was reported as most-used pain management technique, there was a diverse opinion of its usefulness. Specifically, it was clear participants felt it was both the most and least useful method of dealing tic-related pain. For some, the ease of access and successfulness of over-the-counter pain relief led them to acknowledge it positively: *"[Ibuprofen was] a godsend, you take 2 and 15 min later adios pain … for that brief moment, pure bliss"* (P11, aged 17). However, the obvious short-term impact of over-the-counter medication was unhelpful for others: *"painkillers … they take the edge off temporarily but it doesn't stop the pain"* (P163, aged 33).

Experiences also varied in the perceived usefulness of prescribed medication for tic and pain relief: *"medication that makes me tic less [relieves tic-related-pain]. Otherwise, idk, I take a lot advil"* (P137, aged 21). However, other participants felt the problematic side effects and ineffectiveness of taking long-term medication interfered with their ability to help manage pain: *"as soon as they wear off the bruises, burns, and other injuries hurt again. They can take weeks to fully heal, and its not safe to be on pain meds the whole time"* (P152, aged 30). While medication is an established treatment option for tics, it is not always the best for each individual.

Techniques that distracted or engaged participants' minds – including breathing techniques, mindfulness, meditation, watching videos, listening to music, and using stim toys - had varying degrees of successfulness in managing pain. These were often viewed as successful for two reasons. Firstly was whether this was used in combination with other pain relief methods: *"[breathing and stretching techniques] distracts myself and stop [sic] the tic, after the tic stops I try to stretch the area that is in pain to relieve the tensed muscles"* (P14, aged 34). Secondly, the distraction or relaxation methods were perceived as needing to sufficiently mentally engaging in order for participants to feel they are able to help them relieve tic-related pain: "*then I don't think about my tics and make them worse"* (P134, aged 16). On the other hand, for some participants relaxation techniques were noted to be very difficult for them to perform successfully: *"mindfulness, specifically mediation [sic]. I … struggle when I'm under stimulated … I end up thinking about my tics in lieu of anything else to focus on, which makes them worse"* (P134, aged 16).

Various forms of massages - including sports massage, physical/physiotherapy, and osteopathy - were noted to be the most helpful techniques to relieve pain: *"[they] address the muscle knots and build up of tension due to my tics"* (P15, aged 27). However, as evident within the theme *Inaccessibility of treatment,* these were often noted as expensive: *"financially difficult to do regularly and no NHS help"* (P45, aged 40).

# Discussion

The present study aimed to investigate the experiences of pain and use of pain management techniques in individuals with TDs and tics. To our knowledge, it is one of the first studies to focus on and explore the topic of pain in TDs, and adds to the limited literature investigating pain associated with tic disorders. The findings provide a valuable insight into the experiences of tic-related pain and methods used by this group to attempt to manage and alleviate such pain. Much like symptomology of tics,

the interrelated and multifaceted aspects of tic-related pain and pain management illustrate a wide range of experiences.

As anticipated, the physical effort of motor tics – such as muscular and joint pain, and soreness - was the most endorsed cause of tic-related pain, consistent with previous literature (16, 37, 38). Previous research has reported that painful tics are one major factor in decisions to seek out treatment for tics (24); of the participants currently taking tic medication, a third stated medication had helped manage tic-related pain, but almost half reported no impact or change. This same sentiment was echoed throughout the qualitative data. While the primary aim of tic medication is upon tic expression, it can be anticipated to impact on tic-related pain too through modifying tic expression. Many participants noted using medication as a method of pain relief, yet it was commonly described as ineffective. The evidence for the effect of medication upon decreasing tic severity varies by type of medication and are often accompanied by side effects (39), which may impact upon patients' QoL but also the adherence and decisions made about medication (25). Participants' reported using a variety of active and passive behavioral, cognitive, pharmaceutical and medical methods for managing tic-related pain, aligning with self-management strategies previously reported in an Australian sample experiencing chronic pain (30). Something of note here is participants' use of strategies to alter tics causing pain - such as through suppression or re-direction – and these strategies may themselves be painful, as over half mentioned they experienced pain through suppressing their tics. Again, this notion was reinforced within the written answers from participants. Compared to matched controls, people with tic disorders have an increased risk of attempting and dying by suicide compared to a general population sample (13). It could be suggested that tic-related pain could play an important part in further impacting upon the mental health and QoL in individuals with tic disorders. This would seem to be an important aspect to think about in clinical care.

Similar to research conducted by Anderson et al. (17), while over a third reported seeking out and receiving professional help, a quarter had sought out help but not received it – possibly for various reasons. From the qualitative data, participants reported a lack of empathy and knowledge about tics from healthcare professionals, which appeared to impact their decisions and willingness to seek treatment. Healthcare professionals' lack of understanding about tic disorders and inadequate treatment and management pathways for tics have been highlighted by people with tics and their families (15, 25, 31, 40, 41). While educating healthcare professionals about tic disorders and management pathways may help them provide treatment and improve the QoL of TD patients, at the same time the limited treatment options for tic disorder patients and difficulties accessing specialist help - as well as participants' reports of the complex relationship between tics and tic-related pain - may make it difficult to provide sufficient treatment. The NICE pain guidelines (23) advise that when assessing all types of chronic pain, clinicians should take a person-centered approach to identify factors contributing to the pain and how the pain affects the person's life. A positive development is that the recommendations suggest individualized assessment of patients in pain and for shared decision-making with the patient. There is the potential to include pain assessment and treatment for people with painful tics and encourage healthcare professionals to be aware of and use the NICE chronic pain guidelines for patients with tic disorders and painful tics.

The inaccessibility of treatment may have also influenced participants' abilities and preferences for seeking and receiving professional help. As noted in previous research (22, 25), many participants reported that the long waiting times and high cost of seeing healthcare professionals prevented them from accessing regular support for their tic-related pain. A recent international survey found a lack of specialized tic disorder clinics within the UK, USA, Canada, and Europe (42). This has important implications: if individuals cannot receive help for their tics, they will be unable to obtain support for the consequential pain. Therefore, access to evidence-based treatment and support is vital for the mental, emotional, and physical impacts of tics and other impactful aspects of living with tics – such as pain – that further impact on patients' QoL.

The repetitive nature of tics caused pain for many, leading to a theorized repetitive "tic-pain" cycle. Similar cyclical patterns have been reported among individuals with TS. One example are tic attacks (sudden bouts of tics and tic-like behaviors, lasting several minutes or hours): these have been described as a "vicious cycle" created by disproportionate attention toward a combination of physical sensations, cognitive elements, and anxiety-related beliefs (43), resulting in increased tic frequency and anxiety symptoms, which trigger further tic attacks. Similarly, tics and premonitory urges are known to increase due to stressful contextual triggers (44). Although the specific cognitive processes were not explored in the present study, the "tic-pain" cycle appears to contain similar features. As highlighted by the written responses in the present study, physical sensations experienced from tics, and emotional reactions from pain such as anger, frustration, and anxiety, can prompt further tics (45). The combination of these psychological and environmental factors may initiate and reinforce the "tic-pain cycle" - and it is evident that this relationship is complex. While responses on the adapted interference scale suggested that tics had a greater interference on participants' lives, qualitative responses suggested the pain from tics was more problematic than tics for some participants. Further investigation is required to understand this potential "tic-pain cycle."

Overall, participants' free-text responses indicated how much tic-related pain impacted on their emotional wellbeing: feelings of hopelessness, desperation, and suicidal thoughts due to tic-related pain were reported. Participants with greater tic

severity were more likely to have low psychological resilience scores, compared to those who screened within the "normal" range. Emotional functioning and resilience have been identified as important aspects of QoL in patient populations (33, 46, 47), and understandably tic severity can have greater impact upon individuals and their ability to cope with stressful events. Heightened levels of depression have been commonly reported among individuals with tic disorders and chronic pain (33, 48, 49). Additionally, decreased resilience is associated with greater depression (50) and greater disability among patients with chronic pain (46)-specifically among middle-aged and younger individuals (51). Treatment and management of tics should go beyond addressing tic frequency and severity, and expand onto other aspects contributing to QoL – such as ability to cope and resiliency (52), as well as the chronic secondary pain experienced from tics.

The present study also adds to the limited research investigating the physical impacts of tics, and highlights the enduring effects of tic-related pain. Through the free-text comments, headaches were commonly self-reported among participants, similar to recent international research (21, 53). Other more serious injuries due to tics were also reported, such as broken and fractured bones, slipped spinal disk, and arthritis. Self-injurious tics have been linked to an increased risk of TS patients developing a traumatic brain injury (54). These acute consequences indicate a need for treatment to be available to help those affected by tic-related pain and injuries.

From both the quantitative and open-ended data, the most reported pain management techniques were distraction, over the counter medication, and various hands-on treatment, such as massages. Many participants noted a difficulty in using mentally-stimulating distraction methods, such as breathing techniques, mindfulness, or meditation. As these methods require significant concentration and attention, it may be that tics themselves interrupt ability to practice these pain-management methods, and symptoms of co-occurring conditions (e.g., ADHD) may also hinder implementation – meaning that other pain-management techniques may need to be used. Distraction methods involving listening to music and playing games have been used with varying effectiveness in helping individuals with chronic pain cope and improve their QoL (55–58). A small pilot study found dancing along to music videos can be successful in helping reduce tic severity (59). Additionally, music has been found to help increase individuals with ADHD abilities to focus and sustain attention (60). Given the high comorbidity between TD and ADHD (10), this could be of use. Furthermore, as indicated by the "tic-pain" cycle, improvement of tics may help individuals to reduce pain, or assist those with pain to cope better. Therefore, future research could investigate the effectiveness of distraction methods that incorporate both music and exercise. In terms of clinical guidance for patients with tics who are experiencing pain, what is needed are clear pathways for patients to access pharmacological, psychological, physical therapy, exercise, acupuncture, electrical physical modalities, self-management and pain management programmes for their painful tics.

## Limitations

The present study did not aim to identify the prevalence of tic-related pain in individuals with TDs, and only captured participants' experiences at one point in time. Given that the study was conducted online, individuals without internet access, or those who did not visit the social media pages and websites where the study was advertised, would not have seen the advertisement and therefore not accessed the online survey. Participant attrition may arise from the longer length of online surveys (such as in the present study), potentially meaning individuals with TS and comorbid ADHD may be under-represented (11), and so the results may not be fully generalisable to all people with TDs. Furthermore, although recruitment was through TS organizations across several different countries, the perspectives of those who could not respond in English was not collected. We also did not measure participants' satisfaction or appraisal of professional help they had sought out for their tic-related pain. Finally, the gender skew – in that more females with TDs participated in the present study - is noticeable and does not typically align with trends in TD literature reporting greater prevalence in males (61). There are well-known sex and gender disparities in the biopsychosocial experience of pain, and treatment and management of pain (62): findings from 13 European countries report greater prevalence of pain in women than men (63), and our sample could potentially reflect this. Previous research has found that compared to females, males with TDs were 1.78 times more likely to report tics resulting in pain (64). In finding a similar gender skew in their online survey with adults with TDs, Conelea and colleagues (11) speculate that this could be for several reasons including response bias in females being more likely to participate in research, and that it could reflect greater prevalence of TDs in adulthood in women compared to men.

# Conclusions

The present study is one of the first to conduct an in-depth exploration of pain and pain management techniques in individuals with tics and TDs. These results suggest tic-related pain is a complex and widespread issue, emphasizing a need for research into the impacts of pain on the QoL within this population. Significant work is still required to better equip both medical providers and the healthcare system to help patients with tics and pain. Evaluation regarding the effectiveness of pain relief methods is another area to be explored. By further investigating these matters, we can help to create and promote

improved patient care for this population. The current lack of any NICE guidelines for tics and TDs continues to add to the difficulties to access not just treatment and management of TDs, but also in turn any recommended treatment or management of the pain associated with this condition.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving human participants were reviewed and approved by University of Nottingham Division of Rehabilitation, Aging and Wellbeing Ethics Committee. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

## Author contributions

ET, SA, and ED contributed to the conception and design of the study and wrote sections of the manuscript. ET and SA led on participant recruitment. ED performed quantitative analysis. ET led on qualitative analysis with support from ED. ET wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Urge intolerance predicts tic severity and impairment among adults with Tourette syndrome and chronic tic disorders

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**Background:** Individuals with Tourette Syndrome and Persistent Tic Disorders (collectively TS) often experience premonitory urges—aversive physical sensations that precede tics and are temporarily relieved by tic expression. The relationship between tics and premonitory urges plays a key role in the neurobehavioral treatment model of TS, which underlies first-line treatments such as the Comprehensive Behavioral Intervention for Tics (CBIT). Despite the efficacy of CBIT and related behavioral therapies, less than 40% of adults with TS respond to these treatments. Further examination of the relationship between premonitory urges, tic severity, and tic impairment can provide new insights into therapeutic targets to optimize behavioral treatment outcomes. This study examined whether urge intolerance—difficulty tolerating premonitory urges—predicted tic severity and tic-related impairment among adults with TS.

**Methods:** Participants were 80 adults with TS. Assessments characterized premonitory urge, distress tolerance, tic severity, and tic impairment. We used structural equation modeling (SEM) to examine the construct of urge intolerance—comprised of premonitory urge ratings and distress tolerance ratings. We first evaluated a measurement model of urge intolerance through bifactor modeling, including tests of the incremental value of subfactors that reflect premonitory urge severity and distress tolerance within the model. We then evaluated a structural model where we predicted clinician-rated tic severity and tic impairment by the latent variable of urge intolerance established in our measurement model.

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**Results:** Analyses supported a bifactor measurement model of urge intolerance among adults with TS. Consistent with theoretical models, higher levels of urge intolerance predicted greater levels of clinician-rated tic severity and tic impairment.

**Conclusion:** This investigation supports the construct of urge intolerance among adults with TS and distinguishes it from subcomponents of urge severity and distress tolerance. Given its predictive relationship with tic severity and tic impairment, urge intolerance represents a promising treatment target to improve therapeutic outcomes in adults with TS.

KEYWORDS

**Tourette Syndrome, premonitory urge, distress tolerance, adults, impairment**

## Introduction

Tourette Syndrome and other persistent tic disorders (collectively referred to as TS) are neuropsychiatric conditions characterized by the recurrence of sudden, involuntary motor and vocal tics. Prevalence estimates suggest that TS affects ≈ 1% of youth, and symptoms often persist into adulthood for many patients (1–3). In addition to tics, individuals with TS often experience a variety of comorbid psychiatric conditions [e.g., attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), anxiety disorders, depressive disorders] and co-occurring challenges with affect and behavioral regulation (e.g., suicidality, affect lability) (4–8). Tics, accompanying premonitory urges, and co-occurring psychiatric conditions contribute to significant impairment for individuals with TS across the lifespan (9–15). Behavioral therapies—such as habit reversal training (HRT), the Comprehensive Behavioral Intervention for Tics (CBIT), and Exposure with Response Prevention (ERP)—have emerged as first-line interventions for individuals with TS (16–18). For individuals who exhibit a positive response to behavioral treatments, therapeutic gains are maintained for over 6 months (19, 20) and can have lasting benefits for up to 11 years (21). Despite the benefit of behavioral treatments for some adults with TS, less than 40% respond to this treatment approach (22). Thus, there is a critical need to understand factors that influence treatment response to evidence-based behavioral therapies in this age group, which can ultimately lead to the identification of novel therapeutic targets that optimize treatment outcomes (23, 24).

Behavior therapy for TS is grounded within a neurobehavioral model of tics. While this model acknowledges neurobiological contributors (e.g., neurotransmitters, brain circuitry, genetics), it suggests that tic expression is influenced by external (e.g., environmental context) and internal factors (e.g., premonitory urge, affective states) (25, 26). These internal and external factors serve as primary targets of intervention in behavior therapy (25). For instance, premonitory urges serve as antecedents to tics and are alleviated by tic expression, which in turn create a negative reinforcement cycle thought to maintain tic expression (27). In behavior therapy, individuals with TS learn to build awareness to tics and associated antecedents (e.g., urges) and implement competing responses to inhibit tics contingent upon antecedents (25, 26). Consequently, greater distress tolerance of premonitory urges would likely allow individuals to effectively implement competing responses even during intense premonitory urges, and therefore be associated with better behavioral therapy outcomes (e.g., reductions in tic severity and tic impairment). To date, the inability to tolerate premonitory urges (i.e., urge intolerance) has received limited investigation (28). Although the precise mechanisms underlying behavioral therapies are not fully explicated (26), urge intolerance represents an important construct that warrants further investigation.

The construct of urge intolerance is comprised of two central features: premonitory urge severity and distress tolerance. At present, no rating scales have been designed to specifically measure individuals' intolerance of urge sensations. In the absence of specific rating scales, existing validated rating scales (i.e., Premonitory Urge for Tics Scale [PUTS], Distress Tolerance Scale [DTS]) can be combined to understand this clinically-relevant construct. Indeed, prior work has started to explore urge intolerance (a latent variable derived from combined PUTS and DTS ratings) among youth with TS, and found that greater levels of urge intolerance predicted greater levels of parent- and child-reported functional impairment (28). However, further research is essential to understand the construct of urge intolerance across the lifespan, which may potentially explain the different rates of treatment response to behavior therapy between youth and adults.

Accordingly, this study investigated urge intolerance in adults with TS. First, structural equation modeling was used to build and test models of urge intolerance using validated

rating scales. We hypothesized that a bifactor model of the latent construct of urge intolerance, comprised of urge severity and distress tolerance, would demonstrate good model fit. Second, the relationship between the latent construct urge intolerance and clinician-rated tic severity and tic impairment on the Yale Global Tic Severity Scale (YGTSS) was examined. We anticipated that greater levels of urge intolerance would predict greater levels of clinician-rated tic severity and tic impairment among adults with TS.

# Method

## Participants

The present sample included 80 adults with TS who participated in a 11.17-year (SD = 1.25) long-term follow-up assessment for a randomized clinical trial of behavior therapy for tics in youth with TS (21, 29). Participants needed to be enrolled in the original clinical trial of behavior therapy to participate in this long-term follow-up assessment. There were no significant differences on demographic and clinical characteristics between participants who completed the long-term follow-up assessment, those who declined to participate in the long-term follow-up assessment, and those who were lost to follow-up [see Espil et al. (21) for further details].

Participants were 23 years of age on average ($M$ = 22.87, $SD$ = 2.70), predominantly male ($n$ = 60, 75%), and mostly Caucasian ($n$ = 69, 86%). Most participants met criteria for a diagnosis of Tourette's disorder ($n$ = 74, 92%), while other participants met criteria for a current diagnosis of chronic motor tic disorder ($n$ = 6, 8%). Common co-occurring conditions among participants included: anxiety disorders ($n$ = 18, 23%), ADHD ($n$ = 11, 14%), and OCD ($n$ = 7, 9%). Less than one-third of participants ($n$ = 8, 29%) were taking medication for tic management (e.g., antipsychotic or alpha-2 adrenergic agonist medication).

## Measures

Yale global tic severity scale (YGTSS) (30). The YGTSS is a clinician-administered assessment that measures tic severity in the past week across five domains: number, frequency, intensity, complexity, and interference domains (30). Item ratings are summed for motor and vocal tics to produce a Total Tic Severity score (range: 0–50). Clinicians also record a global rating for tic-related impairment in the past week (range: 0–50). The YGTSS has shown good reliability and validity across studies (30–32).

Premonitory urge for tics scale (PUTS) (33). The PUTS is a 9-item self-report questionnaire that measures premonitory urge phenomena (33). Items inquire about the frequency and discomfort associated with premonitory urges, and are rated on a 4-point scale. Items are summed to produce a total score (range: 0–36), with higher scores indicative of greater levels of premonitory urge severity. The PUTS has good internal consistency and external validity across individuals with TS (34, 35).

Distress tolerance scale (DTS) (36). The DTS is a 15-item self-report questionnaire that assesses an individual's ability to tolerate distress (36). Items are rated on a 5-point scale, and are summed to yield a total score (range: 15–75). Higher total score values indicate less distress tolerance. The DTS has demonstrated good convergent and divergent validity (36).

## Procedures

All procedures followed ethical standards for human subject research and were approved by local institutional review boards (IRBs). Participants from the original clinical trial were contacted to participate in a long-term follow-up assessment (21, 29). Eighty participants (i.e., 63.4% of the original sample) were interviewed in-person or via Skype by trained raters to ascertain clinical history and psychiatric diagnoses on the Mini-International Neuropsychiatric Interview (37). Next, clinician-administered assessments were completed to characterize current tic severity (YGTSS). Finally, participants completed self-report measures of premonitory urges (PUTS) and distress tolerance (DTS). Please see Espil et al. (21) for further details.

## Analytic plan

Descriptive statistics and correlations characterized the sample and associations between relevant clinical constructs. Structural equation modeling (SEM) in Mplus examined the construct of urge intolerance using items from the PUTS and DTS (38). SEM is ideal for investigating latent theoretical constructs that cannot yet be directly measured or observed (39). Additionally, SEM allows for the further exploration of relationships between a latent construct and other observed characteristics.

A bifactor structural model was selected to measure the latent construct of urge intolerance. A bifactor approach specifies that the covariance among a set of items can be accounted for by a single, general factor that captures the common variance among all items in the set, while also allowing for subfactors to explain item subgroups (40). A bifactor model approach is recommended when there is a strong justification for capturing a superordinate construct along with distinct subordinate constructs. The bifactor model confers several statistical advantages. In addition to better specifying the model (i.e., delineating general and specific subfactors within a single model), this approach allows for simultaneous

evaluation of item loading on both the general factor (i.e., urge intolerance) and unique subfactors (PUTS, DTS) (41). In order to evaluate the fit of the hypothesized bifactor model of urge intolerance with its corresponding urge and distress tolerance subfactors, the incremental value of including distinct subfactors of premonitory urge severity and distress tolerance within the model was examined. To evaluate the incremental value of each component of the model, nested models were compared through adjusted likelihood ratio tests (42). In the first step, we evaluated model fit for a full bifactor model, comprised of the PUTS and DTS items loading onto the general urge intolerance factor, as well as their respective urge severity and distress tolerance subfactors. In the second step, a constrained version of the bifactor model was evaluated, with the general latent factor urge intolerance fixed at 0, and the PUTS and DTS items freely loading onto their respective subfactors of urge severity and distress tolerance. In the third step, the bifactor model with urge severity subfactor was examined, with the distress tolerance subfactor fixed at 0. Finally, in the fourth step, the bifactor model with the distress tolerance subfactor was examined, with the urge severity subfactor fixed at 0.

Finally, after establishing a bifactor measurement model of urge intolerance, we examined a structural model where we predicted clinician-rated tic severity and tic impairment by the latent variable urge intolerance among adults with TS.

Models were estimated using weighted least squares mean and variance adjusted (WLSMV) estimation. Model fit was examined using the Comparative Fit Index (CFI), the Standardized Root Mean Square Residual (SRMR), and the Root Mean Square Error of Approximation (RMSEA). Following the precedent established by Hu and Bentler (43), acceptable model fit was defined by CFI values $\geq$0.95, SRMR values $\leq$0.08, and RMSEA values $\leq$0.06. Standardized path coefficients ($\beta$) for paths are reported for all models.

# Results

## Characteristics and clinical correlates

Adult participants exhibited a moderate level of tic severity ($M = 16.22$, $SD = 9.54$) and impairment ($M = 10.00$, $SD = 10.77$) (44). Participants reported experiencing premonitory urge severity ($M = 21.01$, $SD = 7.25$) that is comparable with other samples of adults with TS (34). Finally, adults reported moderate levels of distress tolerance ($M = 37.46$, $SD = 11.41$).

There was a moderate relationship between premonitory urge severity and distress tolerance ($r = 0.39$, $p = 0.001$), such that participants who endorsed greater levels of premonitory urges reported lower levels of distress tolerance. Premonitory urges exhibited moderate correlations with clinician-rated tic severity ($r = 0.37$, $p = 0.002$) and tic impairment ($r = 0.43$, $p < 0.001$), such that greater levels of premonitory urges were associated with greater levels of tic severity and impairment. Similarly, distress tolerance was moderately correlated with clinician-rated tic severity ($r = 0.39$, $p = 0.001$) and tic impairment ($r = 0.39$, $p = 0.001$), such that greater levels of tic severity and impairment were associated with lower levels of distress tolerance. Participants' age and sex were not significantly correlated with premonitory urge and distress tolerance ratings. However, participant age exhibited a small association with clinician-rated tic severity ($r = 0.26$, $p = 0.020$) and impairment ($r = 0.29$, $p = 0.009$), such that greater tic severity and impairment was associated with older participant age. Collectively, these findings highlight the modest positive relationships between premonitory urge severity, distress tolerance, tic severity, and tic impairment among adults with TS.

## Evaluating bifactor model of urge intolerance

### Step 1: General urge intolerance factor, urge severity and distress tolerance subfactors

First, we evaluated the least constrained model (Figure 1)—with all PUTS and DTS items loading onto the general latent factor, urge intolerance, and each items' respective subfactor, urge severity and distress tolerance. Model fit indices were acceptable (CFI = 0.95, RMSEA = 0.08 [90% CI = 0.06–0.09], SRMR = 0.08). Table 1 provides item loadings for the model. As shown in Table 1, the majority of PUTS and DTS scale items loaded onto the general factor of urge intolerance.

### Step 2: Urge severity and distress tolerance subfactors, general urge intolerance factor fixed at 0

Next, we evaluated whether the exclusion of the general factor of urge intolerance improved the overall model fit. Here, the general factor of urge intolerance was constrained to 0. All items of the PUTS and DTS were exclusively allowed to load onto their respective subfactors of urge severity and distress tolerance. Relative to the full model, model fit statistics deteriorated (CFI = 0.86, RMSEA = 0.12 [90% CI = 0.10–0.13], SRMR = 0.17). Chi-square results indicated that the constrained model (model 2) fit significantly worse than the full model (model 1), $\chi^2(24) = 111.94$, $p < 0.001$. Stated differently, the full, unconstrained model (with the general urge intolerance factor and the premonitory urge and distress tolerance subfactors) demonstrated significantly better model fit than the partially constrained model with the general urge intolerance factor constrained to 0.

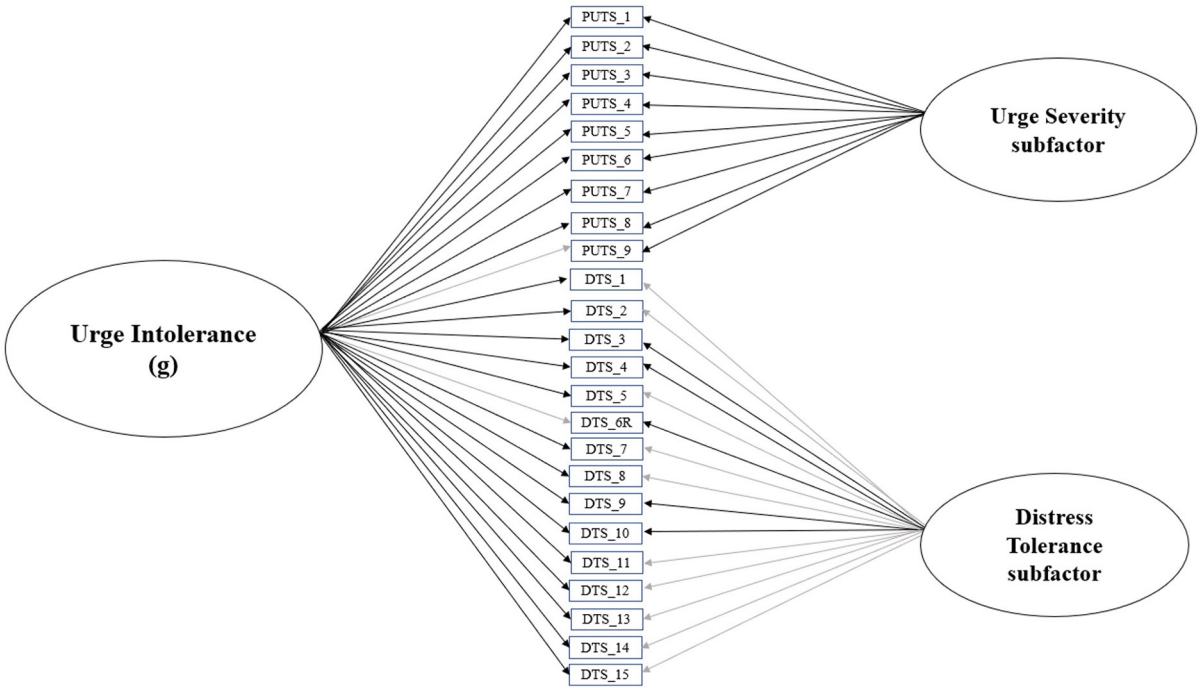


FIGURE 1
Final bifactor model of urge intolerance, with urge severity and distress tolerance subfactors. Black lines indicate significant standardized item loadings, while gray lines indicate non-significant standardized item loadings.

### Step 3: General urge intolerance factor, urge severity subfactor (distress tolerance fixed at 0)

Next, we evaluated whether the exclusion of the subfactor of distress tolerance improved the overall model fit. Here, the subconstruct of distress tolerance was constrained to 0. Essentially, items on the DTS were only allowed to load onto the general subfactor urge intolerance. Relative to the unconstrained model (model 1), model fit indices deteriorated (CFI = 0.93, RMSEA = 0.09 [90% CI = 0.07–0.10], SRMR = 0.09). Chi-square results indicated that the partially constrained model (model 3) fit significantly worse than the full saturated model (model 1), $\chi^2(15) = 54.05$, $p < 0.001$. Stated differently, the saturated model (with the general urge intolerance factor and both distress tolerance and premonitory urge subfactors) demonstrated significantly better model fit than the partially constrained model with the distress tolerance subfactor constrained to 0.

### Step 4: General urge intolerance factor, distress tolerance subfactor (urge severity fixed at 0)

Following this, we evaluated whether the exclusion of the subfactor of urge severity improved the overall model fit. Here, the subconstruct of urge severity was constrained to 0. Essentially, items on the PUTS were only allowed to load onto the general subfactor urge intolerance. Relative to the unconstrained model (model 1), model fit indices deteriorated (CFI = 0.92, RMSEA = 0.09 [90% CI = 0.07–0.11], SRMR = 0.09). Chi-square results indicated that the partially constrained model (model 4) fit significantly worse than the full saturated model (model 1), $\chi^2(9) = 25.60$, $p < 0.01$. Stated differently, the saturated model (with the general urge intolerance factor and both distress tolerance and premonitory urge subfactors) demonstrated significantly better model fit than the partially constrained model with the urge severity subfactor constrained to 0.

### Final model

Collectively, these findings suggest that the full bifactor model of urge intolerance (Figure 1), which includes the general urge intolerance factor as well as its premonitory urge and distress tolerance subfactors, is the optimal fit. Consequently, the full bifactor model was used for subsequent analyses.

## Urge intolerance, urge severity, and distress tolerance as predictors of TS severity and impairment

Figure 2 illustrates the relationship between the latent construct of urge intolerance, its subfactors premonitory urge

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TABLE 1 Final retained bifactor model of urge intolerance with premonitory urge and distress tolerance subfactors.

| Item | G-factor urge intolerance | S-factor premonitory urge | S-factor distress tolerance | Residual (1-$R^2$) |
|---|---|---|---|---|
| PUTS_1 | 0.43 (0.10)* | 0.50 (0.09)* | | 0.56 |
| PUTS_2 | 0.24 (0.11)* | 0.77 (0.07)* | | 0.35 |
| PUTS_3 | 0.41 (0.10)* | 0.79 (0.06)* | | 0.22 |
| PUTS_4 | 0.45 (0.10)* | 0.74 (0.06)* | | 0.24 |
| PUTS_5 | 0.49 (0.09)* | 0.67 (0.07)* | | 0.31 |
| PUTS_6 | 0.46 (0.10)* | 0.42 (0.09)* | | 0.61 |
| PUTS_7 | 0.38 (0.10)* | 0.88 (0.05)* | | 0.09 |
| PUTS_8 | 0.28 (0.11)* | 0.78 (0.06)* | | 0.32 |
| PUTS_9 | 0.07 (0.12) | 0.48 (0.11)* | | 0.76 |
| DTS_1 | 0.77 (0.07)* | | 0.19 (0.18) | 0.37 |
| DTS_2 | 0.70 (0.09)* | | 0.32 (0.17) | 0.41 |
| DTS_3 | 0.69 (0.11)* | | 0.47 (0.17)* | 0.30 |
| DTS_4 | 0.75 (0.10)* | | 0.39 (0.16)* | 0.29 |
| DTS_5 | 0.70 (0.09)* | | 0.27 (0.18) | 0.44 |
| DTS_6R | 0.10 (0.22) | | 0.86 (0.11)* | 0.26 |
| DTS_7 | 0.45 (0.08)* | | 0.01 (0.14) | 0.80 |
| DTS_8 | 0.57 (0.08)* | | 0.01 (0.17) | 0.67 |
| DTS_9 | 0.58 (0.15)* | | 0.61 (0.14)* | 0.29 |
| DTS_10 | 0.66 (0.12)* | | 0.45 (0.16)* | 0.37 |
| DTS_11 | 0.71 (0.08)* | | 0.26 (0.17) | 0.43 |
| DTS_12 | 0.70 (0.08)* | | 0.15 (0.17) | 0.49 |
| DTS_13 | 0.80 (0.06)* | | −0.02 (0.21) | 0.36 |
| DTS_14 | 0.56 (0.11)* | | −0.23 (0.16) | 0.63 |
| DTS_15 | 0.83 (0.06)* | | 0.19 (0.18) | 0.28 |

Standard estimates and (s.e.) for all item loadings in the bifactor model reported. *Denotes significant loadings in the model ($p < 0.05$).

severity and distress tolerance, and clinician-rated tic severity and impairment. Table 2 presents standardized path coefficients in the model. Model fit indices were acceptable (CFI = 0.95, RMSEA = 0.07 [90% CI = 0.05–0.08], SRMR = 0.08). Urge intolerance predicted tic severity (β = 0.35, $p$ = 0.001) and impairment (β = 0.32, $p$ = 0.005). Specifically, greater levels of urge intolerance predicted higher levels of tic severity and impairment.

## Discussion

This study examined urge intolerance in adults with TS—a latent construct that encapsulates the ability to tolerate aversive premonitory urges. The bifactor model of the latent construct of urge intolerance was found to be the optimal fit and consisted of a general urge intolerance factor, as well as both premonitory urge and distress tolerance subfactors. In this model, greater levels of urge severity (higher scores on the PUTS) and lower levels of distress tolerance (higher scores on the DTS) contributed to greater levels of urge intolerance (greater difficulty tolerating premonitory urge sensations). Consistent with theorized models, urge intolerance predicted clinician-rated tic severity and tic impairment. Although mixed evidence has been found for the relationship between premonitory urges and tic severity, these findings suggest that the influence of distress tolerance may partly explain the variable relationships premonitory urges and tic severity.

Based on these findings, there are at least two key implications for the field of TS. In regard to the assessment of TS, it is important for clinicians to consider and characterize urge intolerance when conducting evaluations of patients with TS. While this study leveraged existing validated rating scales and used SEM models, there is a need for the development of a standardized rating scale of urge intolerance for individuals with TS. This rating scale could blend items from both the PUTS and DTS, and potentially incorporate other related somatosensory sensations that may be interpreted as urges (e.g., "not just right" sensations). In addition to convergent validity with the PUTS, DTS, and tic severity scales, convergence with objective measures such as tic suppression tasks could also be informative. While empirical testing and validation of such a rating scale

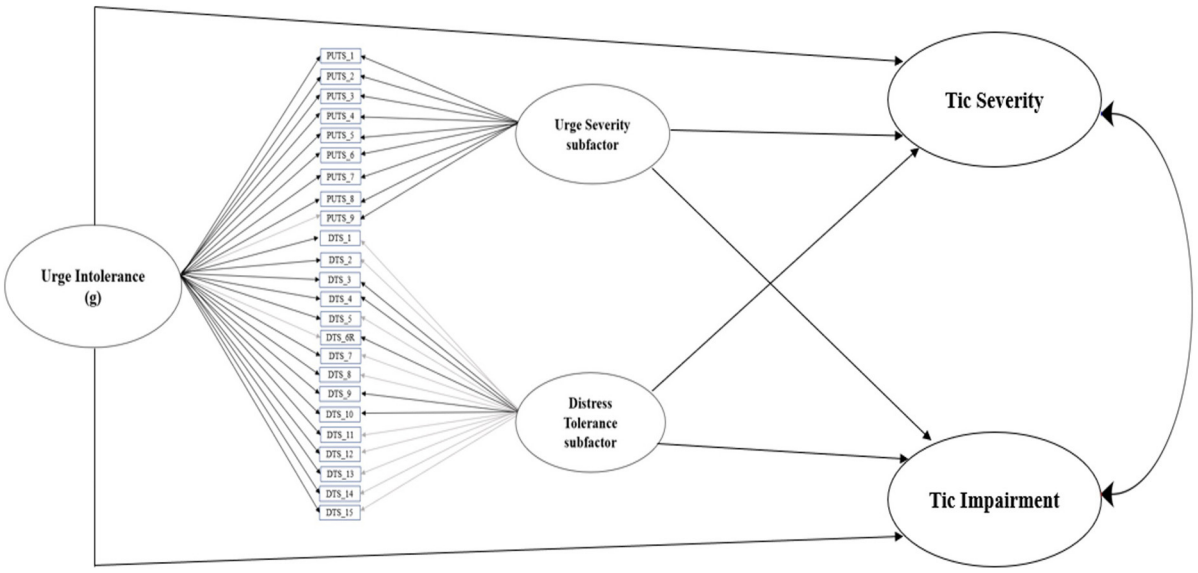


FIGURE 2
Final bifactor model of urge intolerance, with urge severity and distress tolerance subfactors, predicts YGTSS tic severity and tic impairment. Black lines indicate significant standardized item loadings, while gray lines indicate non-significant standardized item loadings.

TABLE 2 Standardized path coefficients for bifactor model of urge intolerance, with premonitory urge and distress tolerance subfactors, predicting YGTSS tic severity and tic impairment.

| | Dependent variable 1: Tic severity | Dependent variable 2: Tic impairment |
|---|---|---|
| Urge intolerance | 0.35 (0.10)* | 0.32 (0.12)* |
| Premonitory urge | 0.23 (0.10)* | 0.34 (0.09)* |
| Distress tolerance | 0.21 (0.09)* | 0.28 (0.08)* |

Standard estimates and (s.e.) for all factor loadings in the bifactor model on dependent variables reported.
*Denotes significant loadings in the model ($p < 0.05$).

would take time, such a standardized scale would allow for a reliable and efficient approach to assess this potentially clinically meaningful construct.

In regard to the behavioral treatment of TS, it is important to consider that urge intolerance was found to predict both tic severity and tic impairment. This suggests that urge intolerance may serve as a novel treatment target to further tic severity reductions among adults with TS. Specifically, CBIT and related behavioral interventions build attention to premonitory urges (i.e., awareness training) and implement behavioral strategies to inhibit tics until premonitory urges are manageable (i.e., competing response training) (16–18). Thus, individuals who have greater difficulty tolerating distressing premonitory urges may have difficulty effectively implementing competing responses in the context of intense premonitory urges. While this possibility requires further empirical investigation, two potential therapeutic strategies exist that could be used to target and improve urge tolerance (i.e., reduce urge intolerance) among individuals with TS to help optimally implement behavioral treatment strategies. One set of skills focuses on mindfulness-based interventions. Gev et al. (45) found that youth with TS experienced reduced levels of tic frequency, distress, and premonitory urges when implementing acceptance-based strategies to address urge phenomena relative to tic suppression strategies. Similarly, Reese and colleagues found that adolescents and adults with TS exhibited improvements in tic severity and functional impairment following a mindfulness-based stress reduction (MBSR) intervention for tics (46, 47). The second set of potential therapeutic strategies focuses on providing distress tolerance skills, which are commonly taught in Dialectical Behavioral Therapy (DBT). This includes training individuals to bring mindful awareness to distressing emotions, physical sensations, and situations and equips them with coping strategies to manage these challenges (48). DBT skills training has been shown to increase distress tolerance capabilities across clinical and non-clinical populations (49, 50). Although future research is essential to determine whether these therapeutic strategies would enhance distress tolerance to premonitory urges (i.e., urge tolerance), such enhancements would have clear implications for reducing tic severity and tic impairment. As urge intolerance

is related to TS outcomes for both youth and adults (e.g., tic severity, tic-related impairment) (28), it represents a novel and important therapeutic target. Further research is needed to explore the associations among distress tolerance, urge intolerance, and health-related quality of life among individuals with TS (51). Future work should test treatment strategies that target and improve urge intolerance—particularly during childhood—which may improve patients' clinical trajectories across the lifespan.

Despite the strengths of the present investigation, some limitations exist. First, our bifactor model of the latent construct of urge intolerance was based on subjective, self-report measures (i.e., PUTS, DTS). While these measures are commonly used and facilitate generalizability to other TS studies, they are both self-report ratings. Future research should include a multi-modal assessment of urge intolerance. Alongside self-report ratings, this examination could include clinician-administered measures of premonitory urges (I-PUTS), and standardized tic suppression tasks. This could provide further insights into the relationship between premonitory urges, urge intolerance, and tic severity. It is also important to acknowledge that while many of the instruments utilized in this investigation (i.e., YGTSS, PUTS) have been extensively validated within this clinical population, the DTS has received limited psychometric evaluation in work with adults with TS. Future research is needed to establish the reliability and validity of the DTS within this clinical population. Second, the sample size in the present study was relatively modest for SEM analyses. Despite this, we were able to validate the bifactor model of urge intolerance and identify significant pathways between urge intolerance and TS clinical scales. Finally, the present sample was drawn from a long-term follow-up assessment of a clinical trial for youth with TS. While the sample clinical characteristics are comparable to other samples of adults with TS, future studies should seek to replicate and expand upon findings in both treatment-seeking and non-treatment seeking samples of adults with TS.

In summary, this study provides further evidence for the construct of urge intolerance among patients with TS. Findings highlight the importance of urge intolerance in relation to tic severity and impairment. While behavioral therapies like CBIT remain the front-line treatment for youth and adults with TS (16, 22, 29, 52), patients who do not fully respond to behavioral therapies for tics may benefit from additional therapeutic strategies that target urge intolerance. This could include mindfulness-based interventions and/or distress tolerance skills to enable patients to tolerate distressing premonitory urge sensations. For youngsters with TS, developmentally tailored strategies could be taught alongside CBIT to help youth better tolerate distressing premonitory urges. In turn, youth would be able to optimally implement behavioral strategies (i.e., competing responses) to inhibit tic expression and response to behavioral therapy. This is important because youth who exhibit a treatment response to CBIT in childhood continue to experience therapeutic improvement 11 years later (21) which may be accompanied by other therapeutic benefits as well. Meanwhile for adults with TS, the utilization of strategies targeting urge intolerance could help improve the implementation of behavioral strategies (i.e., competing responses) in the context of treatment. This could lead to greater treatment response rates among those receiving behavior therapy for TS. Ultimately, this line of research holds the potential to provide new insights into the mechanisms underlying tic severity reductions and improve therapeutic outcomes for patients with TS. However, future research is needed to replicate and extend these findings and explore them within the context of treatment.

## Data availability statement

Generated datasets are not available at this time due to forthcoming manuscripts. However, we intend to make the datasets available to qualified investigators upon request once all articles are finalized. Requests to access the datasets should be directed to JM, jfmcguire@jhmi.edu.

## Ethics statement

The studies involving human participants were reviewed and approved by respective institutions, including UCLA Semel Institute for Neuroscience and Human Behavior, Marquette University, and Weill-Cornell Medicine. The patients/participants provided their written informed consent to participate in this study.

## Author contributions

KR contributed to the conceptualization, methodology, formal analysis, validation, and writing–original draft. AD, ER, DW, and JP all contributed to the conceptualization, methodology, formal analysis, and writing–review and editing. JM contributed to the conceptualization, methodology, validation, supervision, and writing–review and editing. All other study authors contributed to the data curation, and/or writing–review and editing. All authors contributed to the article and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note



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# An exploration of eating behaviours and caregiver mealtime actions of children with Tourette syndrome

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Food avoidant behaviours are common concerns amongst individuals with Tourette syndrome, with high levels of food selectivity reported in children and food neophobia and avoidant restrictive eating behaviours in adults. However, less is known about food approach behaviours. The current study aimed to explore differences in food approach and food avoidant eating behaviours in children with Tourette syndrome (TS) and their relationship to caregiver mealtime actions. Thirty-seven caregivers of children with Tourette syndrome were compared with children with Autism Spectrum Disorders, children with Attention-Deficit/Hyperactivity Disorder and a control group. Caregivers completed the Child Eating Behaviour Questionnaire and Parent Mealtime Action Scale-Revised. Caregiver-reported findings revealed that children with Tourette syndrome exhibited more food approach behaviours, specifically greater food responsiveness, emotional overeating and desire to drink, compared to controls. Children from the three neurodiverse groups had similar levels of emotional overeating and food selectivity, which were all significantly higher than the control group. Positive persuasion was uniquely identified as a mealtime strategy adopted by caregivers of children with Tourette syndrome. The results suggest that children with Tourette syndrome are at more risk of showing a broader array of food difficulties than previously reported, including food avoidant and approach behaviours. It is encouraged that clinicians monitor eating behaviour in appointments with children with Tourette syndrome.

KEYWORDS

**food avoidant, food approach, Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), food selectivity, Tourette syndrome (TS), emotional eating, neurodiversity**

## Introduction

Eating behaviour research has developed two concepts which broadly describe movements towards or away from food consumption, named food approach and food avoidant behaviours, respectively. Food avoidant behaviours include food selectivity (also known as food fussiness), the rejection of familiar and novel food, slowness in eating, emotional undereating and regulating eating through internal cues, namely satiety responsiveness (as characterised by the Child Eating Behaviour Questionnaire)

(1). In contrast, food approach behaviours encompass movements and desires towards food, which can be characterised by emotional overeating, desire to drink and responses to external stimuli, including enjoyment of food and food responsiveness. Within the literature, emotional over- and undereating have been defined as the consumption of more or less food than is considered to be within typical eating patterns and is largely considered as a stress response an individual experiencing unwanted feelings. Moreover, food responsiveness is related to overeating as individuals are heavily influenced to eat in response to external cues, such as sight and smell. This eating behaviour is in contrast to satiety responsiveness, whereby the individual responds to internal cues of fullness to cease consumption. Collectively, increased food responsiveness and emotional overeating mean that children eat when they are not necessarily hungry. A reduced ability to regulate mechanisms related to hunger decreases with age (2) and has been found to have adverse consequences in terms of weight, nutritional intake and subsequent health complications. Since children with Tourette syndrome (TS) have been shown to differ in their response to food [e.g., (3)], the present study investigates food approach and food avoidant behaviours in children with and without TS, in comparison to children with Autism Spectrum Disorders (ASD) and Attention-Deficit/Hyperactive Disorder (ADHD), to understand the eating profiles, but also to address children's eating in relation to caregiver mealtime actions.

Recently, research has explored food avoidant behaviours in individuals with TS, a neurodevelopmental disorder characterised by involuntary, repetitive and non-rhythmic motor and phonic tics (4). Food avoidant behaviours were found to be common concerns amongst individuals with TS (3), with higher levels of food selectivity reported in children outside of the normative period of 6 years of age (5). Moreover, there was evidence to suggest that anomalous eating behaviours are present in adulthood, with higher levels of food selectivity, food neophobia and avoidant/restrictive eating behaviours reported in adults with TS compared to individuals without (3, 6). Research has also shown similar levels of heightened food selectivity in children with TS and two other neurodevelopmental disorders, namely ASD and ADHD, even when accounting for comorbidity in comparison to children showing typical development (7). This finding weakens the argument that additional comorbid diagnoses may underlie increased food selectivity found in TS.

To date, the literature has focused solely on food avoidant behaviours in TS. However, to provide context to the breadth of eating challenges and wider eating profile of children with TS, food approach behaviours must also be considered. Food selectivity appears to be a transdiagnostic characteristic of neurodivergent children with disordered eating found to be widespread in children with a diagnosis of ASD or ADHD (8). Despite these similarities, research has also suggested that children with ASD and ADHD seem to differ in their overall eating profiles. For example, children with ASD show greater food avoidant behaviours compared to controls, including heightened food selectivity and emotional undereating (9). Children with ASD have also been shown to have obsessive eating routines (10) whereas, binge, hedonic and emotional overeating have been found to influence the positive association between symptoms of ADHD and BMI (11).

Some similarities in levels of food selectivity may be partially accounted for by the heightened sensory sensitivity, a commonly reported symptom in neurodevelopmental disorders (5). For example, sensory-focused eating is frequently reported in neurodiverse children leading to a limited diet (10). In contrast, some differences indicated within the literature may be better explained by impulsivity, a core symptom of ADHD, which has been related to uncontrolled eating behaviour, weight gain and bulimia nervosa symptoms (12). Symptoms specific to TS include tics, which have not been previously evidenced to influence eating behaviours, instead have been thought to be influenced by nutritional intake. Many individuals with TS also describe an aversive and unpleasant internal urge that precipitates the release of a tic, known as a premonitory urge (13). Whilst up to 93% of patients report experiencing a premonitory urge, this characteristic is not currently included in the DSM-5 diagnostic criteria. Given that premonitory urges are sensory phenomena and previous research has correlated sensory processing with eating behaviours, such urges may be associated with eating behaviours in individuals with TS. Overall, considering the adverse consequences in terms of weight and diet quality for some eating behaviours and their prevalence in children within neurodiversity research, exploring the wider eating profiles of children with TS and how they compare to comorbid disorders, is needed.

In addition to the health consequences of maladaptive eating behaviours, the literature consistently reports that these behaviours can be disruptive to mealtimes leading to increased parental stress, issues maintaining routines and inappropriate mealtime interactions (14). For example, caregivers' mealtime behaviours have been widely associated with eating behaviours, particularly of young children showing typical patterns of development. During the early years, caregivers have greater control over mealtimes in terms of when food is presented, what foods are offered, and their quantities. Furthermore, research has suggested strategies that the caregiver can use to provide an effective environment and deal with challenging eating patterns to encourage the development of healthy eating behaviours. Modelling, for example, can be a positive strategy to improve acceptance of fruit and vegetables (15). In contrast, parental strategies, including pressure to eat and high levels of control are counterproductive by encouraging maladaptive eating patterns. For example, an authoritarian and restrictive parenting style has been associated with increased emotional eating in children (16). These strategies have also been associated with a reduced ability of the child to regulate their energy intake, and a paradoxical

interest in forbidden foods which are more commonly used in children who are considered overweight (17).

While a large volume of literature emphasises the role of the caregiver in influencing their child's eating behaviour, it is increasingly being evidenced in both qualitative and quantitative research that there is a bidirectional relationship between caregiver mealtime behaviours and child eating behaviours (18, 19). A complex interplay of variables influences a child's eating behaviour with both the child and caregiver having agency to contribute to the mealtime experience. In the ASD literature, research has shown caregivers are more likely to encourage and prompt eating compared to controls which aligns with typical caregiver responses to their children exhibiting food avoidant behaviours (9). Furthermore, caregivers have been found to prepare more special meals for children with ASD compared to children without (20).

In comparison to other neurodiverse populations, there is currently an absence of research focusing on the role of the caregiver at mealtimes for children with TS. However, this is particularly important to address for children with TS given food avoidance previously demonstrated differences in caregiver responses to food refusal. More specifically to TS, anecdotal evidence has suggested that children with TS show a predisposition to higher weight status, with a national survey in Iran indicating the greatest prevalence of tic disorders was in males who were either overweight or obese (21). Additional research has suggested that a diagnosis of TS increases the risk of having obesity and is associated with a significant risk of cardiometabolic disorders (22, 23). Furthermore, the medication used to treat TS, such as neuroleptic drugs, make individuals particularly vulnerable to weight gain (24). Moreover, longitudinal work has shown that a child with a heavier weight status predicts later use of controlling feeding practises, suggesting a possible cyclic relationship with weight status as a mediating factor.

The current study was exploratory in nature and its purpose was 3-fold: (1) to explore any differences in food approach, and food avoidant behaviours in TS compared to a control group, (2) to explore further any of these differences in eating behaviours compared to other commonly occurring neurodiverse children, namely those with ASD or ADHD and (3) to explore relationships between child eating behaviours and caregiver mealtime behaviours. It was hypothesised that similar to previous findings differences in avoidant eating behaviours, namely food selectivity, would be found between children with TS and controls, but no significant differences between the ADHD and ASD groups. Similar to the findings that ASD and ADHD show more differences from each other in their food approach behaviours, the TS group was expected to show more differences across this domain when comparing the neurodiverse conditions (3). Given the relationship established between food selectivity and caregiver mealtime behaviours, it was expected to be a relationship between caregivers' actions and children with TS eating behaviours.

# Materials and methods

## Participants

One hundred and twenty-four caregivers [22–67 y; $M$ ($SD$) = 41(8) y], 118 mothers and four fathers and two legal guardians (grandmother), completed the online survey. One hundred and five caregivers described their nationality as British, one as French, six as Canadian, one as Maltese, one as Italian and eight as American. Caregivers were asked to confirm whether their child had a clinical diagnosis of a neurodevelopmental disorder. Authors are aware of the comorbidity between neurodevelopmental disorders and therefore, only children with a sole clinical diagnosis of one of the three disorders focused on in this study were included. Of the responses, 37 children had a diagnosis of TS (6 females, 31 males) and were between the ages of 6 years 7 months and 15 years 0 months. The Premonitory Urge for Tics Scale (PUTS) (25) was completed by caregivers alongside their children, only in the TS group. A score above 31 indicates extremely high intensity with probable severe impairments. In the current sample scores ranged from 9 to 36 ($M = 22.54$, $SD = 5.97$). Of the children with TS diagnosis taking medication ($n = 15$), the most commonly reported was melatonin ($n = 8$). Other prescription drugs recorded were sertraline ($n = 4$) and clonidine ($n = 3$).

The comparison groups included a control group, children with ASD and children with ADHD. The control group comprised 36 children without a clinical diagnosis of a neurodevelopmental disorder between the ages of 6 and 16 years (13 females, 23 males). Caregivers of children with ASD completed the Autism Spectrum Screening Questionnaire (26); all children reached the cut-off scores ($M = 25.87$, $SD = 10.12$). Thirty-six children between the ages of 6 and 17 years with a clinical diagnosis of ASD were included in the current study. Finally, twenty children with a clinical diagnosis of ADHD (8 females, 12 males) between the ages of 6 and 16 years were included in the current study. All children in this group met the required T-score of 65 or above on the Connors' Parent Rating Scale-Revised (27). The groups did not differ in age, $F_{(3,114)} = 1.88$, $p = 0.138$.

## Measures

Participants provided background information about their age, ethnicity, height, and weight, as well as their child's sex, date of birth, height and weight and any clinical diagnosis including comorbid disorders. Participants were able to enter their child's weight anthropometric measurements

in the format most convenient and the researchers later converted the measurements according to the metric system. All caregivers were then asked to complete the following two standardised questionnaires:

### The children's eating behaviour questionnaire (CEBQ: 5)

The CEBQ is a 35-item measure designed to identify the frequency of a child's eating behaviour on eight independent scales, which can be grouped into two subsets of eating behaviour. Firstly, the food approach eating profile which is the average of four subscales encompasses a desire to carry drinks on their person (desire to drink), eating as a response to external stimuli (food responsiveness & enjoyment of food) and over-eating as an emotional response to negative feelings (emotional overeating). Secondly, the food avoidant eating profile which is the average of four subscales measuring the ability to regulate eating through internal cues (satiety responsiveness), slowness in eating, reducing food consumption as an emotional reaction to negative feelings (emotional undereating) and rejecting a large amount of novel and familiar foods (food fussiness). 'Food selectivity' was the chosen term for the current study to highlight the behaviours exist outside of the normative developmental period as well as reflecting severity of consequences of such behaviours. As the eight subscales are independent and can be additionally grouped to categorise eating behaviours, they were treated as separate when running the statistical analysis, meaning no adjustments were used. Caregivers rated the frequency with which their child exhibits the behaviour on a 5-point Likert scale ranging from 1 (never) to 5 (always). Development of the questionnaire revealed good internal reliability coefficients (Cronbach's alpha) for all the subscales, ranging from 0.74 to 0.91 (4). The Cronbach alpha for the present study ranges between 0.63 and 0.96.

### Parent mealtime action scale-revised (PMAS-R; 35)

The PMAS-R is a 31-item questionnaire with the following nine subscales: setting snack limits, using positive persuasion, insistence on eating, fat reduction techniques and use of rewards during mealtimes, providing daily fruit and vegetable availability, showing snack modelling, making children special meals different from the family meal, and allowing too many food choices. Caregivers rated how often they exhibited these mealtime behaviours on a 5-point Likert scale ranging from 1 (never) to 5 (always). The mean internal reliability of Cronbach alpha is 0.66 and the mean test-retest reliability score of 0.71 (22). The scale was developed with a non-clinical sample, however, has been consistently used within and validated in a clinical sample (22) and there is a mean internal reliability Cronbach alpha of 0.68 in the current study.

## Procedure

The research was granted ethical approval from the University of Hertfordshire Ethical Advisory Committee, Protocol Number: aLMS/PGT/UH/02784(4), and the research was performed in accordance with the Declaration of Helsinki. Participants were recruited through Tourettes Action charity, online forums and local organisations that agreed to advertise the study. A survey link was provided for participants to learn about the study *via* an online participant information sheet which provided further details. If after reading the information sheet, participants wished to take part in this research, participants were first required to give informed consent by signing an online consent form before progressing to the survey. The questionnaires were presented in the same order to each participant and took ∼25 min to complete. The questionnaire remained active for 2 months. Families were provided with no financial incentive to take part. At the end of the study, participants were provided information with sources of support for any concerns around their child's eating behaviours.

## Data analysis

Firstly, BMI z-scores (BMIz) for children were calculated using the Child Growth Foundation's (28) growth references which adjust for age and sex. Standard definitions for thinness, overweight and obesity corrected for age and sex were used to categorise children's BMI (kg/m$^2$; 22). Standard definitions for thinness, overweight and obesity corrected for age and gender were used to categorise children's BMI (29, 30). Data analysis was conducted in IBM SPSS Statistics (RRID: SCR_016479). A One-way ANOVA was conducted to compare differences in BMIz between the four groups. Secondly, two-tailed Pearson's correlations were used to establish whether child age and sex were related to food approach and food avoidant eating behaviours. Thirdly, to examine whether there were differences in food approach, food avoidant and caregiver feeding behaviours between children with TS and the control group a series of independent *t*-tests were conducted on all subscales of the CEBQ. Fourthly, One-way ANOVAs were conducted to explore differences in all subscales of the CEBQ and PMAS-R between the four groups. Finally, two-tailed Pearson's correlations were conducted to analyse the relationship between food avoidant and approach behaviours, BMIz, and caregiver mealtime behaviours.

# Results

## Participant characteristics

Outside of the main questionnaires, there was a small subset from each of the four groups who chose to complete the current weight and height of their child. Nineteen caregivers of children

with TS, 18 caregivers of children without a clinical disorder (control group) and 16 caregivers in ADHD and ASD groups provided this information. There was no significant difference in BMIz scores between the four groups, $F_{(3,66)} = 1.667$, $p = 0.183$. Of the TS sample who provided child BMI data ($n = 27$), 29.6% were categorised as underweight. More specifically, 7.4% were categorised as grade 2 (a BMI below 17) and 22.2% were categorised as grade 3 (a BMI below 16). Moreover, 22.2% of children in the TS group were categorised as overweight, and 14.8% were classified as obese. Of the controls who provided child BMI data ($n = 27$), 25.9% were categorised as underweight [grade 1 (a BMI below 18.5) = 3.7%, grade 2 = 11.1%, grade 3 = 11.1%], 11.1% ($n = 3$) were overweight and 3.7% were classified as obese. Although a Pearson chi-square test revealed no significant difference in the number of children categorised as a healthy compared to unhealthy weight status between each of the groups, $X^2(1, N = 54) = 3.650$, $p = 0.056$, significantly more children with TS were categorised as being overweight and obese compared to the control group, $X^2$ $(1, N = 73) = 4.51$, $p = 0.034$.

The data was then analysed to establish whether the children's age or sex were related to their food approach and food avoidant behaviours. An independent samples $t$-test revealed no significant difference in food approach, $t_{(122)} = 0.435$, $p = 0.664$, and food avoidant behaviours, $t_{(122)} = -0.1.009$, $p = 0.315$, between males and females when comparing the total sample of children. Therefore, sex was not controlled for in further analyses.

Two-tailed Pearson's correlations revealed a positive relationship between food approach behaviours and age, $r_{(37)} = 0.67$, $p < 0.001$, and a negative relationship between food avoidant behaviours and age, $r_{(37)} = -0.74$, $p = 0.001$, in children with TS. These findings suggest younger children showed a different pattern than older children. No significant correlations between age, food approach and food avoidant behaviours were identified for the control group, children with ASD or children with ADHD ($p > 0.05$). Child demographic information and descriptive statistics for all standardised measures are shown in Table 1.

## What were the eating behaviours of children with TS compared to controls?

Independent $t$-tests were conducted to examine whether there were group differences in food avoidant and approach behaviours between children with TS and the controls. As shown in Table 2, children with TS show greater food approach behaviours than the control group, more specifically greater food responsiveness, emotional overeating and desire to drink. There was no significant difference in the overall food avoidant eating profile between the two groups. However, of the food avoidant subscales children with TS scored significantly higher on food selectivity and emotional undereating than the controls.

## How did the eating behaviours of children with TS compare to children with ASD or ADHD?

One-way ANOVAs were conducted to identify differences between food approach and food avoidant eating behaviours between the four groups. As shown in Table 1, significant differences were found in food selectivity, food responsiveness and emotional over- and under-eating. *Post hoc* Tukey's HSD tests revealed that children with TS had similar levels of food selectivity and emotional overeating compared to children with ASD and children with ADHD. All three clinical groups had a significantly higher tendency of emotional overeating and food selectivity compared to children showing typical development. Higher levels of food responsiveness were found in children with TS compared to the controls, whereas children with ASD had higher levels of emotional undereating compared to the controls. No other significant differences in eating behaviours were found between the groups.

## What were the relationships between eating behaviours, caregiver mealtime actions and BMIz?

One-way ANOVAs were run to examine differences in caregiver mealtime behaviours, as measured across eight subscales of the PMAS-R between children with TS, children with ASD, children with ADHD and the control group (see Table 3). Caregivers of children with TS reported using insistence and positive persuasion less compared to the caregivers of the control group. Some differences were also observed in caregiver mealtime actions for children with ASD, including reduced availability of fruit and vegetables compared to controls and more special meals compared to caregivers of children with ADHD.

A series of Two-tailed Pearson's correlations were conducted to examine associations between the eating behaviours found to be significantly different among the four groups and caregiver mealtime actions (results are shown in Table 4). When subsequent partial correlations were conducted to control for age, no significant correlations between any of the subscales were found. Caregiver and child behaviours were subsequently explored in relation to child BMIz scores. Two-tailed Pearson's correlations revealed that emotional overeating was positively associated with BMIz in the TS group, $r_{(20)} = 0.55$, $p = 0.012$. There were no other significant correlations between BMIz and eating behaviours in any of the four

TABLE 1 Results of One-way ANOVAs, and Tukey's HSD *post hoc* tests, for eating behaviours between the children with Tourette syndrome, Autism Spectrum Disorder, Attention Deficit Hyperactive Disorder or controls.

| | Mean (SD) | | | | | | |
|---|---|---|---|---|---|---|---|
| | TS ($n = 37$) | CG ($n = 36$) | ASD ($n = 31$) | ADHD ($n = 20$) | $F_{(3,120)}$ | $p$ | Tukey's HSD |
| **Demographics** | | | | | | | |
| Age (y) | 10.15 (2.64) | 9.09 (2.44) | 10.43 (3.32) | 10.41 (3.59) | | | |
| Height (cm) | 146.22 (18.01) | 140.44 (14.57) | 145.43 (26.92) | 142.24 (22.05) | | | |
| Weight (kg) | 38.23 (17.22) | 36.27 (17.02) | 42.72 (19.66) | 52.60 (15.64) | | | |
| BMIz | 0.57 (4.12) | −0.89 (1.78) | 0.87 (1.36) | 0.82 (2.14) | | | |
| **CEBQ** | | | | | | | |
| *Food approach* | 3.12 (0.97) | 2.59 (0.48) | 3.10 (0.74) | 3.01 (0.99) | 2.54 | 0.060 | – |
| Desire to drink | 2.81 (1.28) | 2.17 (0.72) | 2.69 (1.14) | 2.43 (1.12) | 2.41 | 0.071 | – |
| Enjoyment | 3.52 (1.29) | 3.74 (0.66) | 2.47 (1.15) | 3.60 (0.94) | 0.45 | 0.719 | – |
| Food responsiveness | 3.32 (1.32) | 2.48 (0.76) | 2.84 (1.20) | 3.18 (1.42) | 3.54 | 0.017 | TS > CG |
| Emotional overeating | 2.71 (1.07) | 1.92 (0.68) | 2.61 (1.00) | 2.83 (1.11) | 5.83 | 0.001 | TS > CG, ASD > CG, ADHD > CG |
| *Food avoidant* | 2.87 (0.79) | 2.66 (0.59) | 2.90 (0.89) | 2.86 (0.74) | 2.07 | 0.108 | – |
| Emotional undereating | 2.91 (0.78) | 2.48 (0.76) | 3.26 (0.86) | 3.00 (0.83) | 5.11 | 0.002 | ASD > CG |
| Food selectivity | 3.42 (1.27) | 2.76 (0.87) | 3.74 (1.03) | 3.37 (1.01) | 4.95 | 0.003 | TS > CG, ASD > CG, ADHD > CG |
| Satiety responsiveness | 2.68 (1.08) | 2.75 (0.75) | 2.80 (0.90) | 2.59 (0.76) | 0.27 | 0.849 | – |
| Slowness in eating | 2.39 (1.26) | 2.63 (0.82) | 2.59 (0.97) | 2.50 (1.07) | 0.39 | 0.763 | – |

TS, Tourette syndrome; CG, Control Group; ASD, Autism Spectrum Disorders; ADHD, Attention-Deficit/Hyperactive Disorder; BMIz, Body Mass Index z-score; CEBQ, Child Eating Behaviour Questionnaire.

TABLE 2 Independent t-tests exploring differences in eating behaviours between children with TS and the control group.

| | *df* | *t* | *p* |
|---|---|---|---|
| *Food approach* | 53 | −2.92 | 0.005 |
| Desire to drink | 57 | −2.62 | 0.01 |
| Enjoyment | 54 | 0.92 | 0.36 |
| Emotional overeating | 61 | −3.72 | < 0.001 |
| Food responsiveness | 58 | −3.34 | < 0.001 |
| *Food avoidant* | 71 | −1.26 | 0.21 |
| Emotional undereating | 71 | −2.29 | 0.03 |
| Food selectivity | 64 | −2.56 | 0.01 |
| Satiety responsiveness | 64 | 0.31 | 0.77 |
| Slowness in eating | 62 | 0.99 | 0.32 |

groups. Regarding BMIz and caregiver mealtime actions, a negative correlation was identified with positive persuasion in the control group; a positive correlation with many special meals in the ASD group and a positive correlation with fat reduction techniques in the ADHD group. It is important to note that all significant correlations with caregiver mealtime actions were no longer significant when controlling for age ($p > 0.05$).

## Are there relationships between premintory urges and eating behaviours?

Two-tailed Pearson's correlations revealed that the PUTS was not correlated with any subscale of the CEBQ or the PMAS-R ($p < 0.05$). There was a significant correlation between BMIz and premonitory urges, $r_{(19)} = 0.57$, $p = 0.01$ suggesting those with more premonitory urges had higher BMIz, this relationship remained significant even when controlling for age, $r_{(18)} = 0.37$, $p = 0.012$. The child's age was not significantly associated with tic severity, $r_{(31)} = 0.22$, $p = 0.230$. In children with TS, both emotional overeating and tic severity was positively related to BMIz. Therefore, a multiple linear regression was carried out with both as predictors of BMIz. This revealed a significant model, $R^2 = 0.49$, $F_{(2,18)} = 7.59$, $MSE = 78.63$, $p = 0.005$, with both being found to be independent predictors (emotion overeating, $\beta = 0.42$, $t = 2.28$, $p = 0.036$; PUTS, $\beta = 0.46$, $t = 2.50$, $p = 0.024$). Children with TS who were reported as having more premonitory urges and/or were more emotional eaters had higher levels of BMIz.

# Discussion

The current study explored the eating behaviours of children with TS in comparison to a control group and how their

TABLE 3 Results of one-way ANOVAs, and Tukey's HSD *post hoc* tests, for caregiver mealtime actions between the children with Tourette syndrome, Autism Spectrum Disorder, Attention Deficit Hyperactive Disorder or controls.

| | Mean (SD) | | | | | | |
|---|---|---|---|---|---|---|---|
| | TS ($n = 37$) | CG ($n = 36$) | ASD ($n = 31$) | ADHD ($n = 20$) | $F_{(3,120)}$ | $p$ | Tukey's HSD |
| **PMAS-R** | | | | | | | |
| Snack limits | 4.00 (1.28) | 4.01 (0.95) | 3.69 (1.06) | 4.02 (1.00) | 0.66 | 0.581 | – |
| Daily fruit & –vegetables | 4.25 (0.76) | 4.57 (0.69) | 3.84 (1.21) | 4.05 (1.36) | 3.22 | 0.025 | ASD < CG |
| Positive persuasion | 3.74 (0.71) | 3.79 (0.69) | 2.88 (1.34) | 3.03 (1.10) | 7.45 | <0.001 | TS <ASD, TS < ADHD, ASD < CG, ADHD < CG |
| Use of rewards | 2.56 (0.80) | 2.75 (0.76) | 2.54 (0.86) | 2.50 (0.91) | 0.61 | 0.607 | – |
| Insistence | 1.88 (0.97) | 2.61 (0.92) | 1.71 (0.61) | 2.35 (1.04) | 7.17 | <0.001 | TS < CG, ASD < CG, ASD > ADHD |
| Snack modelling | 2.34 (0.81) | 2.09 (0.65) | 2.04 (0.82) | 2.33 (0.89) | 1.25 | 0.297 | – |
| Special meals | 2.29 (0.67) | 2.66 (0.70) | 2.71 (0.70) | 2.08 (0.85) | 4.80 | 0.003 | ADHD < CG, ADHD < ASD |
| Fat reduction techniques | 3.16 (0.95) | 2.66 (0.87) | 2.68 (0.99) | 2.95 (0.99) | 2.27 | 0.084 | – |
| Many food choices | 3.02 (0.66) | 2.63 (0.51) | 2.73 (1.00) | 2.75 (0.91) | 1.77 | 0.157 | – |

TS, Tourette syndrome; CG, Control Group; ASD, Autism Spectrum Disorders; ADHD, Attention-Deficit/Hyperactive Disorder; PMAS-R, Parent Mealtime Action Scale-Revised.

profile compares to children with a diagnosis of ASD or ADHD. Caregiver-reported findings revealed that children with TS exhibited more food approach behaviours, specifically greater food responsiveness, emotional overeating and desire to drink, compared to controls. While the overall profile of food avoidance was not found to be significantly different between groups, children with TS did display significantly higher levels of food selectivity and emotional undereating compared to the controls. When comparing eating behaviours with other neurodiverse populations, similarities in food selectivity and emotional overeating were identified in all three neurodiverse groups. Importantly, children with TS who exhibited higher emotional overeating appeared more at risk of having a BMIz. The current study also identified differences in caregiver mealtime actions and some associations between child and caregiver behaviours in all four groups; however, this was no longer significant when controlling for age.

Differences in eating behaviours between children with TS and the control group were identified. Firstly, consistent with previous research, children with TS showed heightened food fussiness (3). Secondly, similar to research on children with ADHD (31, 32), greater desire to drink, emotional overeating and food responsiveness were identified in children with TS. Increased food responsiveness and emotional under- and overeating are related to eating based on external cues, meaning children could eat when they are not necessarily hungry. Infants' innate ability to regulate food intake (2) decreases with age (33), resulting in greater influence from external stimuli in the development of eating behaviours. A reduced ability to regulate mechanisms related to hunger has been found to have adverse consequences in terms of weight.

Similar to previous research [e.g., (34)], it was found that increased BMIz was associated with greater food approach behaviours, specifically increased emotional overeating was associated with higher BMIz in children with TS only. Emotional overeating refers to the consumption of food as a response to feeling negative emotions; therefore, the individual may eat when they are not hungry which can lead to greater consumption of food and therefore weight gain. Eating in response to emotions may reflect a reduced ability to self-regulate their appetite (35) and deficits in the emotional regulation (36). Therefore, research has suggested that interventions for emotional eating should focus on stress reduction techniques and the promotion of positive mood (37). These findings are particularly pertinent as research has indicated that there is a greater prevalence of anxiety disorders in children with tic disorders (38).

While there was no significant difference between the BMIz scores between the groups, the weight classification of children with TS was noteworthy. Regarding weight classification, children with TS fell at the two polar ends of the weight categories with 66% of children classified as having an unhealthy weight status, and more children were categorised as overweight or obese compared to the control group. This finding is aligned with the prevalence of psychiatric disorders being higher among children and adolescents who are overweight, specifically research found the most prevalence of tic disorders in males with overweight or obesity (21). While exploring the role of medication on BMI was outside the scope of the current study, it is important that future research explores this factor as some medications can be appetite-suppressing (e.g., ADHD treatment) whereas others can lead to weight gain

TABLE 4 Two-tailed Pearson's correlations between parent mealtime action subscales and child eating behaviours.

| | Snack limits | Daily fruit & vegetables availability | Positive persuasion | Use of rewards | Insistence | Snack modelling | Special meals | Fat reduction techniques | Many food choices |
|---|---|---|---|---|---|---|---|---|---|
| **CG** | 0.27 | −0.15 | −0.14 | 0.31 | 0.21 | 0.07 | 0.35* | 0.35* | 0.27 |
| *Food approach* | | | | | | | | | |
| Emotional overeating | 0.17 | −0.33* | −0.17 | 0.29 | 0.01 | −0.13 | 0.32 | −0.06 | 0.59*** |
| Food responsiveness | 0.27 | −0.09 | −0.13 | 0.25 | 0.30 | 0.03 | 0.39* | 0.43** | 0.28 |
| *Food avoidant* | −0.023 | −0.23 | −0.13 | 0.11 | 0.04 | 0.02 | 0.20 | −0.16 | 0.50** |
| Food selectivity | −0.03 | −0.33* | −0.17 | 0.07 | −0.08 | 0.02 | 0.34* | −0.14 | 0.53*** |
| Emotional undereating | 0.04 | 0.003 | −0.07 | 0.32 | 0.06 | −0.06 | 0.35* | −0.07 | 0.48** |
| BMIz | 0.08 | −0.10 | −0.61** | −0.34 | −0.19 | 0.24 | −0.19 | −0.17 | −0.05 |
| **TS** | 0.18 | 0.03 | −0.11 | −0.25 | −0.40* | −0.21 | −0.49** | 0.57*** | −0.31 |
| *Food approach* | | | | | | | | | |
| Emotional overeating | 0.11 | 0.18 | −0.07 | −0.18 | −0.24 | −0.07 | −0.53*** | 0.51*** | −0.32* |
| Food responsiveness | 0.20 | −0.04 | −0.06 | −0.09 | −0.33* | −0.13 | −0.47** | 0.56*** | −0.28 |
| *Food avoidant* | −0.42** | −0.10 | 0.40* | 0.22 | 0.31 | 0.006 | 0.45** | −0.41** | 0.41* |
| Food selectivity | −0.47** | −0.11 | 0.38* | 0.12 | 0.23 | −0.08 | 0.55*** | −0.22 | 0.34* |
| Emotional undereating | −0.19 | 0.01 | 0.31 | 0.34* | 0.26 | −0.14 | 0.31 | −0.09 | 0.28 |
| BMIz | −0.14 | 0.07 | 0.35 | 0.32 | 0.13 | −0.08 | −0.38 | 0.27 | −0.13 |
| **ASD** | −0.03 | 0.13 | 0.08 | −0.05 | −0.10 | 0.20 | −0.08 | 0.10 | −0.03 |
| *Food approach* | | | | | | | | | |
| Emotional overeating | 0.17 | 0.23 | 0.00 | 0.05 | −0.28 | 0.18 | −0.08 | 0.27 | 0.17 |
| Food responsiveness | 0.00 | 0.02 | 0.07 | −0.01 | −0.11 | 0.12 | −0.02 | 0.07 | 0.00 |
| *Food avoidant* | 0.19 | −0.07 | 0.11 | 0.09 | 0.02 | −0.14 | 0.06 | 0.16 | 0.19 |
| Food selectivity | 0.12 | 0.00 | 0.29 | 0.36* | 0.02 | 0.08 | 0.17 | 0.27 | 0.12 |
| Emotional undereating | 0.29 | −0.04 | 0.15 | 0.01 | −0.24 | −0.17 | −0.01 | 0.19 | 0.29 |
| BMIz | −0.08 | −0.31 | 0.44 | 0.03 | 0.23 | 0.29 | 0.58* | 0.35 | −0.06 |
| **ADHD** | 0.09 | 0.38 | 0.33 | 0.24 | 0.13 | 0.57** | 0.04 | 0.43 | 0.09 |
| *Food approach* | | | | | | | | | |
| Emotional overeating | 0.09 | 0.38 | 0.39 | 0.16 | 0.06 | 0.51* | 0.01 | 0.33 | 0.09 |
| Food responsiveness | 0.08 | 0.29 | 0.29 | 0.29 | 0.14 | 0.55* | 0.00 | 0.32 | 0.08 |
| *Food avoidant* | 0.13 | −0.13 | −0.08 | −0.02 | 0.10 | −0.35 | 0.07 | −0.11 | 0.13 |
| Food selectivity | −0.14 | −0.24 | −0.06 | −0.08 | −0.03 | −0.38 | −0.06 | −0.08 | −0.14 |
| Emotional undereating | 0.24 | 0.03 | −0.01 | 0.00 | −0.11 | −0.21 | 0.12 | 0.01 | 0.24 |
| BMIz | −0.14 | −0.07 | −0.18 | 0.25 | 0.40 | 0.09 | −0.14 | 0.59* | 0.32 |

BMIz in children with TS, Tourette syndrome; ASD, Autism Spectrum Disorder; ADHD, Attention-Deficit Hyperactive Disorder; or the CG, control group. ***$p \leq 0.001$; **$p < 0.01$; *$p < 0.05$. All correlations were no longer significant when controlling for age.

(e.g., neuroleptics) (22). Overall, it is clinically important for clinicians to monitor weight and address any eating concerns, particularly for children displaying emotional overeating.

Premonitory urges are uncomfortable physical sensations preceding tics and are considered an important predictor of tic severity, even when controlling for age (39). The current study failed to establish a relationship between PUTS and any of the subscales of CEBQ or PMAS-R, potentially suggesting that severity of tics not to be a predictor of eating behaviours. Importantly, this measure has been identified as one of five recommended instruments for severity of tics. However, it is more reflective of the sensory phenomena associated with tics and may be more suitable for those of 10 years and older. Therefore, one of the major limitations of the current study is the lack of inclusion of a tic severity and frequency measure, such as the YGTSS a self-report measure that indicates clinically relevant exacerbations of tics, or The Proxy Report Questionnaire for Parents and Teachers, which has also been identified as a highly promising tool [for a full review of tic measure see (40)]. A tic frequency and severity questionnaire is important to include in future research to be able to establish whether those with more intense and

severe motor and/or vocal tics show more disturbance in eating behaviours.

It was important to compare the eating behaviours of children with TS with other neurodiverse populations with no overlapping comorbidities to explore the argument of whether eating behaviours in TS can simply be explained by the underlying effects of ASD or ADHD. Given that similar levels of emotional overeating and food selectivity were identified across the three clinical groups, this shows that comorbidity does not explain these maladaptive patterns. Nevertheless, the authors do acknowledge that due to the comorbidities between the three clinical disorders and despite no comorbid diagnoses at the time of the study, there may be some overlap and later diagnoses to follow meaning the groups may not have been completely distinct. However, some differences in eating behaviours were identified. While the ASD and ADHD groups showed no significant differences in comparison to the controls, the TS group was unique in showing significantly higher food responsivity. These findings demonstrate that whilst neurodiverse populations do share symptomology, diagnoses and some eating behaviours, there are some distinctive eating behaviours related specifically to TS. Ultimately, clinicians need to monitor and ask about any eating concerns even when the child is presenting with a sole diagnosis of TS. Further to this, it is widely acknowledged that TS is comorbid with anxiety disorders, such as Obsessive-Compulsive Disorders (41), so it would be important for future research to establish how these disorders contribute to the eating profile of individuals with TS.

The role of the caregiver in children's eating behaviours was also investigated in the current study. There were differences in caregiver mealtime techniques between the four groups. Caregivers of children with TS reported the use of more insistence and positive persuasion compared to the three clinical groups. Caregiver mealtime behaviours were not associated with BMI, which is agreeable with research on children with ASD (42) and typically developing children (43). Food approach behaviours were negatively associated with special meals and fat reduction techniques, and the inverse was found for overall food avoidance in children with TS. Fat reduction techniques are used by caregivers of children with healthy diets, but also by caregivers of children who are overweight (44). These findings highlight the complex and multi-directional nature of caregiver and child mealtime behaviours.

In terms of special meals, it is common that caregivers to stop reoffering a given food after only three to five failed attempts and begin to make special meals (45). Meals separate from the family often include palatable high-calorie foods which are more likely to be accepted. This technique can be useful to increase weight if the child is underweight, however for children with food fussiness this technique can maintain and perpetuate the child's restricted diet (44). As food selectivity is especially common in children with TS, guidance to promote effective strategies for caregivers is needed. One caveat is that when controlling for the age of the child, the relationships were no longer significant between caregiver and child mealtime behaviours in the current study. This suggests that children are less influenced by their caregivers as they begin to make their own choices, and other factors may become more influential. Taken together, it is important to educate caregivers on effective strategies, such as repeated exposure, especially in their child's younger years. Early interventions are particularly relevant as eating behaviours established in childhood can continue into adolescents and adulthood (46).

One limitation of the current study is its cross-sectional design, which inhibits conclusions of causal relationships between caregiver mealtime behaviours and child eating behaviours. Longitudinal research is needed to draw conclusions about the bidirectional child-caregiver association in relation to eating behaviours taking into consideration any parental neurodevelopmental and co-morbidities (47). In addition, there was also missing data for the BMIz, and caregiver-reported anthropometrics may have led to a miscalculation of BMI. While objective measures are ideal, research has demonstrated a high level of accuracy in caregiver-reported height and weight measurements when compared with objective measurements (48). The data was collected *via* caregiver-report meaning there may be some social desirability on completion of the caregiver mealtime action measure. Perhaps the use of observations may prove useful in future research to explore the caregiver-child interaction during mealtimes to provide an insight which may be missed when through self-report (49). Understanding the eating behaviours of children with TS and factors which can influence these behaviours is clinically relevant for the development of effective interventions (50). The current study has demonstrated the adverse effect of increased emotional overeating on BMI, but research has also shown that eating behaviours can have an adverse impact on nutrient intake, which needs requires further investigation.

While the current study focused specifically on comparing TS with ADHD and ASD. It is important to note that TS has many underlying comorbidities. For example, a large proportion of TS patients meet a concurrent diagnosis for OCD (30–50%) (51). Furthermore, elevated rates of tics symptomology (10–30%) have also been reported in OCD patients (52, 53). To address eating difficulties associated with tics and/or TS, future studies will need to screen for co-morbidities such as anxiety disorders to understanding their role on eating behaviours in children with TS. Similarly, assessing for sensory processing disorders and their severity would help understand their role in eating behaviours.

Overall, this research identified that children with TS have a different eating profile to children with typical development, specifically heightened food approach behaviours, with implications of heightened emotional overeating increasing BMI status. Caregiver mealtime behaviours, specifically fat reduction and special meal techniques were associated with food

approach and food avoidant eating behaviours. However, this relationship was more prominent in younger children. It is encouraged that clinicians monitor eating behaviour and BMI status in appointments with children with TS.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving human participants were reviewed and approved by University of Hertfordshire University Ethical Advisory Committee, Protocol Number: aLMS/PGT/UH/02784(4). The participants provided their written informed consent to participate in this study.

## Author contributions

AL and BS contributed to the conception and design of the study. BS performed the statistical analysis and wrote the first draught of the manuscript. AL wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Case report: Advice for schools on managing functional tic-like behaviours

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There has been an increase in the occurrence of sudden onset functional tic-like behaviours in adolescents during the COVID-19 pandemic, which has had a significant impact on the affected individual's ability to engage with education. The aim of this article is to generate discussion and inform practice within schools with regard to the management of functional tic-like behaviours. An advice sheet for schools has been produced based on clinical expertise and experience of consulting with schools around the management within education settings. Case examples are presented highlighting the importance and impact of these strategies. We also highlight the need for further evaluation of the effectiveness of the advice sheet in collaboration with schools and families.

KEYWORDS

**schools, functional tic-like behaviours, advice, education, support, case study**

## Introduction

Tics have been defined as sudden, rapid, recurrent movements or sounds which are not rhythmic and are commonly seen in conditions such as Tourette syndrome (1). Tics, and tic-like movements or sounds, can also occur as part of a functional neurological disorder (FND) and these are currently being referred to as functional tic-like behaviours (FTLBs) (2, 3). While there are many similarities between tics and FTLBs, there is emerging evidence of some key differences. These include a sudden onset, more complex movements, less likelihood of experiencing a pre-monitory urge and less reported suppressibility than Tourette-related tics. There are often associations with higher rates of anxiety, self-harm, and copro-phenomena, a higher female predominance and a later age of onset (2). FTLBs are likely to worsen if inadvertently rewarded, for example, by being given too much attention, or if they result in being removed from an activity that is

not usually enjoyed (4). Anecdotally, we hear that these symptoms often provoke strong responses from others, which can be reinforcing for the symptoms.

Since the onset of the COVID-19 pandemic, clinicians globally have noticed an increase in tic-like symptoms in young people already diagnosed with tic disorders (5). A significant increase in the sudden onset of FTLBs, has also been observed (3, 6–9). It is hypothesised that the pandemic could have impacted negatively on the mental health of young people through biopsychosocial factors, with pre-existing or otherwise undiagnosed mental health and/or neurodevelopmental difficulties (3, 6). Anecdotally, within our clinic, we have been informed by our patients of the wide ranging impact of these FLTBS on daily life, in particular, higher reported school absence and difficulties engaging in the curriculum.

As FND, including FTLBs, is thought to be triggered by a range of predisposing and precipitating biopsychosocial factors, in our clinic we advise a holistic approach to management, with careful assessment and formulation guiding an individual plan for each young person. Using a five Ps formulation approach is a helpful way to determine any underlying predisposing and precipitating factors for the presenting difficulty, factors which may be perpetuating the difficulty and any protective factors which may support management (10).

With regard to management, studies have highlighted the importance of psychoeducation about FND and a focus on externalised attention training techniques to reduce an exacerbation of symptoms that are caused by suggestibility (11, 12). There is also an emerging evidence base for FND and FTLBs management plans which are built upon Cognitive Behavioural Treatment (CBT) principles to address underlying anxiety, depression, and trauma (13). This approach can also address maladaptive behaviours and challenge unhelpful beliefs related to the movements (14). It is of note that many of the usual recommended interventions for the management of typical tics, such as medication, are not effective for FTLBs (2). Due to the similarity in presentation between FND and FTLBs, we may be able to draw on interventions shown have efficacy in FND populations, such as psychoeducation, externalised attention and CBT, and trial these with those experiencing FTLBs. Anecdotal reports from patients within clinic and one study investigating psychoeducation, CBT and externalised attention in FTLBs (11) lend support to this idea.

Schools may be able to play a vital role in supporting holistic management plans to aid symptom reduction in FTLBs and to minimise the interference of these episodes, therefore promoting participation. Qualitative research has highlighted that teachers feel they lack the professional training needed to understand and support individuals with Tourette syndrome within schools (15) and anecdotal feedback from schools our clinic has consulted with indicates the same with regard to FND and FTLB's.

Generally, there is a paucity of rigorous evidence supporting school intervention for the management of non-academic conditions, however, some studies do highlight certain interventions, such as extra time in exams, being beneficial for academic attainment in those with ADHD (16). With regard to managing FTLBs in schools, there is no known research investigating available support, however, research investigating therapeutic support for young people with FND highlights the importance of including school management plans as part of the overall treatment package (17). The importance of learning interventions, where necessary, and social reintegration is also highlighted as part of the overall management of FND (14).

The aim of this paper is to share some of our clinical expertise and experience when helping to manage FTLBs within schools. This is presented *via* case studies and an advice sheet (see **Supplementary appendix**). Our aim is to promote a wider understanding and to generate multiagency models for optimal ways of supporting young people with FTLBS within schools so that the affected children can increase their access to education. These strategies should be viewed as part of a wider, holistic support package for those presenting with FTLBs episodes, rather than as an isolated intervention.

## Case descriptions

All young people presented were reviewed in the Tics and Neurodevelopmental Movements Service (TANDeM) at Evelina London Hospital, UK between January 2019 and January 2022 and diagnosed by a multi-disciplinary team as having FTLBs. A total of 10 children have been described here and their clinical characteristics, school intervention and outcomes are presented in **Table 1**. Six of the young people received additional therapy or medication from their local services as part of their overall care package and three remained on waiting lists to receive therapy. Two young people are presented in further detail for clarity.

### Clinical case report: Patient 1

#### History

LA is a 12 year old girl. She was born to term, there were no concerns regarding development and there is no significant medical history. She lives at home with her mother and father, who has some physical disabilities.

#### Movements

LA experienced a sudden onset of tics in the first year of secondary school and following the first COVID-19 lockdown. The movements began with leg twitches and, over the course of 3 days, they progressed to florid facial

TABLE 1 Clinical characteristics, school intervention, and outcome of young people presenting with FTLBs.

| Patient ID and sex | Age of symptom onset | Functional symptoms | Co-occurring conditions | School intervention | Other intervention | Outcome |
|---|---|---|---|---|---|---|
| 1 F | 12 | FTLBs | Anxiety, self-harm | Teachers to redirect attention away from functional tics, not to ask questions about the tics in school.<br>Make modifications and provide extra support in maths to lessen anxiety | None | Reduction in school-based FTLBs and increased access to curriculum. |
| 2 F | 13 | FTLBs, vacant episodes, drops, freezing moments, breath holding | Tourette's syndrome | Teachers redirect attention away from functional tics and allow use of coping strategies.<br>Access to a mentor and student services.<br>Allow use of stairs and machinery, which was previously stopped for safety. | None (on CAMHS waiting list) | FTLBs significantly reduced, only drop attacks present. Able to use preventative strategies to prevent onset and has decreased time away from class. |
| 3 F | 9 | FTLBs, functional loss of movement in legs and hands and double incontinence. | Anxiety, trauma | Access to a computer for writing.<br>Teachers to support pupil with externalised attention strategies.<br>Time out card and safe space.<br>Extenuating circumstances for school exams and additional time.<br>Advising school not to send child home during an episode. | Trauma-focussed CBT | Complete resolution of functional symptoms and fully engaged in all lessons. |
| 4 F | 14 | FTLBs, non-epileptic seizures | Tourette syndrome<br>Anxiety<br>Depression | Redirect attention away from functional tics and support externalised attention strategies.<br>Access to student services and inclusion for gradual reintegration back into school.<br>Regular mentor sessions. | Behaviour therapy for tics | FTLBs and non-epileptic seizures still present.<br>Reduction in anxiety<br>Full reintegration back into school. |
| 5 F | 14 | FTLBs, non-epileptic seizures | Anxiety<br>Attention deficit Hyperactivity disorder | Redirect attention away from functional tics.<br>Access to student support.<br>Not sending young person home following an episode. | None (on CAMHS waiting list) | Functional symptoms remain but fully accessing curriculum. |
| 6 F | 11 | FTLBs, drop attacks, freezing episodes | Anxiety | To leave classroom earlier to avoid busy corridors.<br>Access to sensory room at school.<br>Time out card.<br>Advised teachers to not comment on tics.<br>Extra time and separate room for exams. | CBT anxiety | FTLBs still present but fully accessing curriculum. On-going challenges with substitute teachers and communication. |
| 7 F | 14 | FTLBs, non-epileptic seizures, loss of movement in legs, locking of limbs | Tourette's syndrome, autism spectrum disorder, anxiety | Redirect attention away from functional tics.<br>Time out card.<br>Access to student support. | CBT anxiety | Functional symptoms remain the same but fully accessing curriculum. |
| 8 F | 10 | FTLBs | Compulsions, visual migraines | Redirect attention away from functional tics.<br>Mentor with school.<br>Regular liaison between home and school. | None (on CAMHS waiting list) | FTLBs remain at school. Awaiting ASD assessment to inform additional school support. |
| 9 F | 13 | FTLBs, locking of legs, loss of movement in legs | Anxiety | 1:1 support to reintegrate back into the classroom. Extra time and a separate room for exams. | Counselling | Significant reduction in FTLBs. Daily tics occurring but not impairing and fully reintegrated back into classroom. |
| 10 F | 13 | FTLBs, non-epileptic seizures, faint-like episodes | Obsessive compulsive disorder, self-harm, attention deficit hyperactivity disorder | Redirect attention away from functional tics and support with externalised attention strategies.<br>Advised school not to call ambulance for non-epileptic seizures.<br>Access to student support.<br>Time out card | Guanfacine for ADHD | FTLBs still present.<br>Non-epileptic seizures have reduced.<br>Increased access to classroom. |



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tics and a squeaking tic. The tics could occur continuously, without a break, and would last the length of a lesson. There was no ability to suppress the movements. There is no history of tics as a younger child. Functional analysis of LA's movements revealed that, while the movements occurred both at home and at school, there was a much greater likelihood of these movements occurring prior to, or during, maths.

### Mood

In addition, to school-based anxiety in relation to maths, LA had experienced a period of low mood and self-harm around the time her movements began.

### Education

LA is academically motivated and generally does well at school but experiences difficulty in maths and had recently been moved down several ability groups.

### Social functioning

Once the bullying episode had been resolved with the support of school, there were no further friendship issues.

### Diagnosis

LA was diagnosed with FTLBs.

### Formulation

The onset of these movements was likely to have been triggered by low mood and anxiety in relation to the bullying episode, starting a new school in the context of the pandemic and wider family stresses. Each episode of FTLBs was triggered by an episode of perceived threat, such as a maths lesson. Such episodes caused an increase in anxiety which manifested physically as FTLBs.

### Treatment

A holistic intervention plan was recommended which included support for the family stressors. In relation to school liaison, our formulation was shared with the Special Educational Needs Co-ordinator and advice was given on how best to support LA. A cognitive assessment (WISC V and WIAT III) was carried out highlighting a specific difficulty with maths and a processing speed in the "extremely low" range. Advice was given to the school regarding management of these difficulties, including extra time in exams, a regular check in with the maths teacher to ensure understanding and a sensitive approach to how questions were asked of LA within maths lessons.

### Outcome

LA experienced a significant reduction in her FTLBs, experiencing only minimal tics, following the school intervention alone. These minimal tics did not impact on her ability to engage in her lessons.

## Clinical case report: Patient 2

### History

PL is a 13 year old female who was born to term. She met her developmental milestones age appropriately. She has hay fever and eczema but is otherwise well. She lives at home with her parents and is the middle of three children.

### Movements

PL experienced mild motor and vocal tics from the age of 5 years and was diagnosed with Tourette syndrome at age eight. She began to develop FTLBs and FND during the COVID-19 pandemic. PL's FTLBs involved a florid and complex pattern of motor and vocal tics which prevented her from engaging in any activity. Her functional neurological symptoms included non-epileptic seizures (eye rolling and appearing non-responsive), drop attacks, breath holding, and freezing episodes. All these symptoms would occur only in school and on a daily basis, they could last over an hour and were reportedly linked to anxiety and stress. The functional symptoms affected PL's ability to engage in school and she missed lessons on a daily basis. School had concerns about safety and had stopped PL using stairs and machinery. A functional analysis of the FTLBs highlighted these episodes were more likely to occur in response to sensory overload, exam stress and friendship worries.

### Mood and other presentations

PL had a history of anxiety, however, had not received treatment for this. PL also has a history of experiencing sensory sensitivities, which became more challenging in secondary school due to noise levels.

### Education

PL was described as hard working and high achieving with no academic concerns.

### Social function

There were no concerns regarding social functioning and PL has a stable friendship group. She regularly supports friends with some of their challenges, which creates some stress for her.

### Diagnosis

In addition to her diagnosis of Tourette syndrome, PL was diagnosed with FND, including FTLBs.

### Formulation

Our formulation hypothesised that PL has a genetic vulnerability to experiencing functional symptoms due to her underlying neurodevelopmental differences. The sensory sensitivities and friendship stresses she experiences led to increased anxiety and this triggered an onset of her functional symptoms. It is likely that these episodes were being maintained by removing access to certain activities which caused PL

to feel singled out, adding additional stress, and thus reinforcing the pattern.

### Treatment

PL previously took Clonidine for the management of her tics, however, this was stopped in early adolescence due to a natural reduction in motor and vocal tics. Other than this, there had been no previous interventions. The recommended holistic intervention package included a counselling referral for the management of anxiety and a psychoeducation session on managing FTLBs. PL's school were informed about the nature of FTLBs and FND. School were reassured about risk and PL was able to access the things that had been removed, such as the use of machinery in Technology lessons. In collaboration with PL and her family, a plan was put in place to support her in school. The strategies included weekly access to a mentor, the ability to use her own stress management techniques within lesson (drawing and music) and a time out pass.

### Outcome

At the time of review, PL's functional symptoms have reduced to occurring approximately once per week as opposed to daily. Her access to her education has increased in that she is now attending all her lessons. There is a need for on-going liaison and consultation between the family and school to refine and improve strategies. PL remains on the waiting list to receive counselling.

An advice sheet on managing FTLBs in school was generated based on clinical expertise, case discussion, experience of consulting with and gaining feedback from schools and young people on what had been effective, as highlighted in the case reports. This advice sheet is displayed in **Supplementary appendix**.

## Discussion

There has been a significant increase globally in the presentation of FTLBs over the course of the pandemic, with considerable repercussions on quality of life and access to education. Research has demonstrated the longer-term impact of pandemic-related disruption to education specifically when neurodiversity, anxiety, and unmet needs are present, leading to an increase in school refusal (18). This highlights the pressing need for health and education services to work together and share information regarding how to support young people with these unmet needs. The advice sheet developed by the TANDeM service aims to consolidate the most effective management strategies trialled by schools and to give advice on how to determine which strategies might be most impactful for an individual.

Initial clinical experience of school consultation and particular management strategies suggests a potential positive impact of school input on symptom reduction and access to education. The most common strategies implemented by schools in our case studies were reducing attention around FTLBs, supporting the young person with their own management strategies, access to student support or equivalent and exam modifications. With regard to outcomes, six out of the ten children showed a reduction in symptoms and all of them reported an improvement in the time and quality of access to education. This is an important point as it highlights that, if young people are well-supported, they can manage within school despite FTLBs. These changes in school support often have a positive impact on symptom reduction even in the absence of formal therapy.

The advice sheet has limitations as it has not yet been through a rigorous evaluation process and, therefore, these preliminary, anecdotal findings regarding symptom improvement must be treated with caution. Additionally, we are not able to claim correlation between the use of the advice sheet and any symptom improvement as many of the young people have undergone other interventions as part of their recommended holistic care package. A more rigorous evaluation process is planned as the next step in our process and the publication of this leaflet will enable this process. There is a clear need to gain school and patient feedback to ensure the accessibility, feasibility, and effectiveness of the advice given. There have been no reports of a negative impact from the advice used.

In conclusion, there is an urgent need to provide management advice to schools to support those with FTLBs. There is a need for further investigation into the current proposed advice sheet to determine its usefulness and its wider impact. It is timely, however, to release this advice now to generate awareness of the importance of school management, to further stimulate multi-agency collaborations and to promote the discussions on optimal pathways for care in health, social settings, and in education.

## Patient perspective

### Case 1

It was useful to have the assessment as it helped me and the school realise my anxiety with numbers was a real thing and wasn't just in my head. My school talked to me and my mum about how they and my teachers could support me and it has made a big difference. I rarely get my tics now.

### Case 2

On the positive side my school are now beginning to listen to my advice and understand that as hard as it is to do nothing

when I am non-responsive and in a FND attack, the best thing is to give me my music and let me listen to that and bring myself out of it. They still can over worry but seeing my mum deal with me a couple of times now I think has helped them realise I know what is best for me and it is fine to leave me. I think my mum and I creating a written plan for them to follow in these circumstances will help give them confidence in knowing they aren't doing anything wrong by leaving me. Negatively, unfortunately not everyone in the school knows how to deal with my attacks. The support staff know me well but teaching staff often panic if they see me have an attack. So we are hoping that the plan we have created will be distributed to anyone teaching me to reduce initial worry.

## Data availability statement

The original contributions presented in this study are included in this article/**Supplementary material**, further inquiries can be directed to the corresponding author.

## Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individuals and their legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

## Author contributions

TO and TH contributed to the design and conception of the manuscript. TO wrote the first draft of the manuscript. TO, TH, SR, SA, AL, and JS contributed to the written manuscript. TO, TH, CG, AB, and JS designed the advice sheet for schools and were involved in gaining feedback from patients. SS, LT, TO, and TH contributed to the schools survey design and analysis. All authors contributed to manuscript revision and read and approved the submitted version.

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## Conflict of interest

SS was self-employed by Tic Tock Therapy.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.1001459/full#supplementary-material

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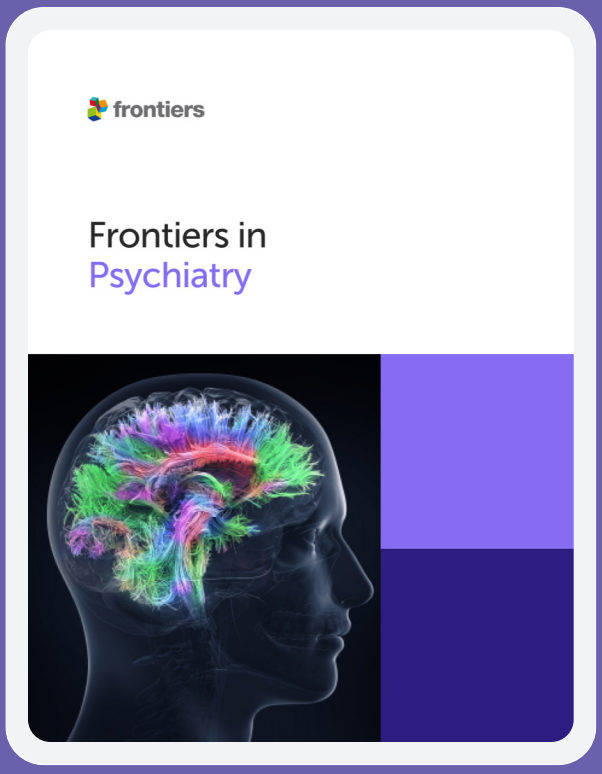


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