

Cognitive tics in Gilles de la Tourette syndrome

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Abstract

BACKGROUND

Gilles de la Tourette syndrome (GTS) is characterized by motor and vocal tics. Cognitive tics (CTs) have been rarely recognized as part of GTS symptomatology and their prevalence and associates have not been systematically investigated.

OBJECTIVES

The aim of the study was to assess the incidence and clinical associations of CTs in a group of patients with GTS.

METHODS

We examined 227 consecutive GTS patients aged 5–50 years old (78.4% males). The median duration of GTS was 4 years (IQR: 3–7) in children and 18 years (IQR: 12–23) in adults. The patients were evaluated for GTS and comorbid mental disorders according to the DSM-IV-TR and DSM-5. CTs were defined as brief, sudden, recurring involuntary thoughts, analogous to typically recognized complex vocal tics and diagnosed during the interview. Correlations between CTs and clinical variables were evaluated in two analyses, lifetime and current. Children and adult groups were compared.

RESULTS

Lifetime CTs were reported by 48 patients (21.1%), in 33 of the cases at the time of evaluation. The median age at onset of CTs was 13.5 years (IQR 9.3–16). Five mental phenomena were evaluated: echolalia (n = 17), coprolalia (n = 16), palilalia (n = 13), counting (n = 11), repeating of words in mind (n = 7). In the multivariable analysis of lifetime CTs, tic severity (p = 0.025) and significant social skill problems (p = 0.050) demonstrated correlation, while for current CTs only tic severity (p = 0.028) and anxiety disorder (p = 0.028) remained significant. In logistic regression model for age groups, in children only age was a factor significantly associated with lifetime CTs (p = 0.033), whereas in adults there were no statistically significant associations with lifetime CTs. For current CTs, none of the variables reached statistical significance in children, while only anxiety disorder was a predictor of current CTs in adults (p = 0.018).

CONCLUSIONS

CTs are a part of tic spectrum with a substantial impact of comorbid psychiatric disorders. CTs are a late and age-related symptom of GTS.

Background

Gilles de la Tourette syndrome (GTS) is a neurodevelopmental disorder which most commonly affects children and adolescents, but in some cases persists into adulthood. According to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.) (DSM-5) in order to diagnose GTS, numerous motor tics and at least one vocal tic must be present for at least one year and appear before the age of 18 (1). Nevertheless, in approximately 85.7% of the patients with GTS, co-occurring psychiatric disorders are present (2). Individuals with GTS often report the presence of obsessions and compulsions. In fact, obsessive-compulsive disorder (OCD) could be found in approximately 30% of GTS patients and is, therefore, one of the most frequently encountered comorbidities (3). Moreover, many patients suffer only from obsessive-compulsive behaviour (OCB), subclinical form of OCD. Nevertheless, based on clinical practice, we observed that these patients additionally tend to experience other mental phenomena such as using foul language in thought, mentally repeating their own words (palilalia) and echoing in mind expressions heard during conversations or while watching television (echolalia). Repeated phrases of this nature can appear as either short wording or longer utterances, such as a sentence or part of a statement. Moreover, patients with GTS seem to evince a certain disposition to count objects in their surroundings, for instance, books on the shelf, corners of paintings, numbers of licence plates. According to O'Connor (4), this kind of mental phenomena can be defined as cognitive tics (CTs) and described as thoughts, phrases, urges, songs, words or scenes that intrude into the consciousness of the patient and are perceived as difficult to remove.

On the basis of current understanding, tics are sudden, rapid, recurrent, nonrhythmic motor movements or vocalisations (5). Even though this kind of description corresponds well with clonic tics, which are brief, fast, jerk-like movements (6), there are some tics which do not fulfil the above criteria and therefore should be distinguished. Longer and slower movement is typical for dystonic tics (7), whereas tonic tics are contractions of a muscle group and they are devoid of the movement effect or accompanied by only slight visible motion (8); and finally blocking tics are a presentation of a rapid cessation of muscle activity and voluntary action, e.g. walking or speech (9–11). According to current definition, tics are repetitive behaviours, not repetitive thoughts; hence CTs, which occur exclusively in the thoughts of the patient, do not fulfil the diagnostic criteria. Nevertheless, we decided to use the terminology suggested by O'Connor in order to avoid the confusion which could be caused by the introduction of additional terms.

It is crucial to differentiate CTs with the spectrum of obsessive-compulsive phenomena. OCD can be diagnosed when a patient reports obsessions/compulsions or both, the presence of which is time-consuming or debilitating in terms of daily functioning and cannot be attributed to physiological effects of a substance or another medical condition. Obsessions are defined as recurrent, persistent thoughts, urges or impulses that are perceived by the patient as intrusive and unwanted, therefore are usually associated with anxiety and distress. In contrast to obsessions, CTs are experienced as pleasant or neutral, do not lead to negative repercussions, are sequences in themselves (one type of CT does not connect to another phenomenon), while obsessions are often a coherent line of thoughts (4). The differentiation with mental compulsions, such as silent checking or praying every time a patient has a

bad thought, is even more challenging. Mental compulsions are performed by a patient as a response to obsessions or as an expression of the urge to apply self-imposed rigid rules, are driven to perform covert acts in thoughts that may be recognized by patients as senseless, excessive, difficult to resist and anxiety related until the act is completed. In contrast to compulsions, CTs are not performed to reduce mental distress or prevent some dreaded situations. They are rather of pleasant or stimulating nature.

Obsessions and compulsions are also consistent and specific for a particular patient and do not tend to alter significantly in time, while CTs can be effectively substituted by a competing stimulation (4).

However, the differential diagnosis between tics and the symptoms of OCD phenomenology can cause problems in clinical practice. Ganos et al. (12) mention the term 'tic-like obsessions/compulsions' which they use synonymously with 'cognitive tics' and describe it as intermediate phenomena between tics and obsessions. Moreover, it is vital to bear in mind that OCD spectrum encountered in GTS is different from the one in pure OCD. While obsessions in pure OCD are mostly "egodystonic" and lead to execution of compulsions, obsessions in GTS are often "egosyntonic", usually not associated with anxiety and following compulsions but rather with urge and impulse (3, 12–15). Thereby, obsessions and mental compulsions in GTS can definitely mimic cognitive tics and vice versa. Moreover, comorbid disorders manifested by difficulties in thoughts control (i.e. depressive or anxiety disorder, attention-deficit/hyperactivity disorder, ADHD) or mental stereotypies, just as stereotyped behaviour in autism spectrum disorder (ASD) should be taken into consideration as possible clinical correlates of CTs. However, these associations are yet to be thoroughly studied and the assignment of CTs to tics, OCD or other psychopathology has not been settled.

We wanted to investigate both the lifetime and current, defined as at the time of evaluation, CTs, as only associations with current clinical characteristics reflect the actual relationship between the two variables. For example, the lifetime diagnosis of depression or OCD does not necessarily have to attribute to occurrence of CTs as both symptoms could have occurred at different moments in the lifetime. The exact relationship could be determined only when both symptoms are present at the same moment. The psychopathology related to GTS may be different in children and adults. Hirschritt reported that adults and adolescents were most likely to have OCD as well as mood, anxiety, eating, and substance use disorders, whereas children were more likely to have ADHD (2). This latter observation stays in line with the previous finding that up to 85% of the ADHD patients report symptom remission in adulthood (16). On the other hand, some patients, prospectively reporting the occurrence of CTs, may not have developed the symptoms of a given comorbid disorder yet. Previous research has demonstrated that ADHD symptoms began 1–3 years prior to tic onset (2, 17), OCD 1–6 years after the first tic onset (2, 18), and mood and substance use disorders even later (13 and 16 years, respectively) (2). These results suggest that psychiatric comorbidities may appear at any time during the course of GTS including early childhood, adolescence and adulthood. Based on these observations, we suspected that clinical characteristics of CTs may be different in children vs adults, as well as in lifetime vs current CTs. These differences could exist as symptoms of a particular comorbid disorder may be only temporarily present or may start later in the course of GTS.

To the best of our knowledge, there has not been studies which would investigate prevalence, age of onset and clinical correlates of CTs in clinical sample. Additionally, based on our and others' (4) observations, it is not clear if CTs may occur with the same frequency in children and adult patients with GTS and if they change over time similarly to tics. The aim of this study was i) to assess the prevalence, age at onset and clinical associations of CTs; ii) to assign this phenomenon to tics, OCD or another psychopathology; iii) to investigate and compare correlates of lifetime and current CTs; iv) to distinguish between the clinical correlates of CTs for children and adults. Based on available findings as well as our clinical experience, we hypothesized that i) cognitive tics are associated with tic severity, copro- and echophenomena, and psychiatric comorbidities; the prevalence of CTs may vary depending on the age of the patients; ii) CTs are part of tic phenomenology, neither OCD nor other psychopathology; iii) the factors that are associated with the lifetime prevalence of CTs differ from those that are related to current CTs; iv) clinical correlates of CTs in children differ from those in adults.

Methods

Study participants

The cohort of individuals with GTS comprised 241 consecutive patients, who were evaluated from 2013 to 2019. In 14 patients, data on the presence of CTs were not available, as these were young children unable to comprehend questions during the interview, resulting in a total sample size of 227 patients. In this group, the age of the patients ranged 5–50 years (median, IQR: 13, 10-22.5 years; 179 males, 78.9%). In total, 140 children (61.7%, median, IQR: 10, 8.75-12 years; 111 males, 79.3%), and 87 adults (median, IQR: 25, 21–32 years; 68 males, 78.2%) were enrolled. The median age of tic onset was 6.5-7 years (IQR). The median duration of GTS was 4 years (IQR: 3–7 years, range: 0–13) in children and 18 (IQR: 12–23 years, range: 6–39) in adults. 189 (83.3%) patients had at least one psychiatric comorbidity. Psychiatric comorbidities of GTS patients are presented in Table 1. One hundred and three patients have received therapy at the time of examination including behavioural therapy, tic reducing drugs and OCD symptom relieving medications.

Procedures

All the patients were personally reviewed and evaluated by the neurologist experienced in tic and movement disorders (PJ). The patients were recruited from one Outpatient Clinic. Some of them were referred to the Clinic by general neurologists and psychiatrists, due to problematic diagnosis or tics refractory to treatment, and some patients or their parents sought medical advise on their own because of troublesome tics. The study was designed as a one-time registration study, as patients were evaluated only once, and no additional clinical data obtained in follow-up visits were included in the analysis.

The patients were evaluated for the clinical diagnosis of GTS and comorbid psychiatric disorders according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR and DSM-5) as some patients were included in the study before the release of DSM-5. The diagnoses of mental disorders that had been made in psychiatric clinics, before our evaluation, were confirmed. We checked whether these

psychiatric symptoms were present or absent at the time of our examination. The patients were assessed systematically with the aid of self-constructed questionnaire consisted of a list of demographic and clinical data which we went through each time the patient was evaluated. Nine most prevalent comorbid disorders in GTS were assessed: ADHD, OCD, OCB, ASD, Learning Disorder, Mood Disorder, Anxiety Disorder, Oppositional Defiant Disorder, Conduct Disorder. All patients and their parents were questioned actively regarding the symptoms of above mentioned disorders. In contrast to children and adolescents in whom most clinical informations were provided by their parents, adults reported them themselves. If obsessions and compulsions did not cause marked distress and did not significantly interfere with the person's normal functioning, we diagnosed OCB. We used the list of obsessions and compulsions included in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to establish clinical spectrum of OCD/OCB. Significant social skill problems served as a principal feature of autistic traits, as only a few patients in the cohort had the diagnosis of ASD based on earlier psychiatric evaluations. Significant social skill problems were defined as difficulties in establishing and maintaining contacts with other people, lack of colleagues and friends, misreading the intentions of peers and adults, excessive suspiciousness toward other people, tendency to blame other people for failures, difficulties in functioning in the peer group. These patients were referred to specialized centers to confirm the diagnosis of ASD, but because of one-registration design of the study, these individuals were classified as having only significant social skill problems regardless of later confirmation of ASD diagnosis. In case of other severe psychiatric comorbidities the patients were referred to psychiatrist to confirm the diagnosis.

In order to assess the current tic severity, the Yale Global Tic Severity Scale (YGTSS) was used (19). CTs were not counted in YGTSS. We applied the same method in order to evaluate tic severity in the lifetime analysis, as there are no more applicable alternatives available for this purpose. All questions asked during the interview were part of routine practice and therefore no refusal rate is reported in this study.

Definition and differential diagnosis of cognitive tics

CTs were identified during the dialogue-based interview through an active inquiry, as none of the patients reported them spontaneously. Due to lack of instruments validated for the assessment of CTs, we used the clinical definition established by previous investigators (4) modified by the author of the study (PJ) with regard to tic disorder. The characteristics of CTs including the type, age of onset, and persistence during evaluation were included in questionnaire which we used to obtain demographic and clinical data.

Patients received questions on whether they had ever experienced short-lasting thoughts which appeared spontaneously in the mind. CTs were defined as brief, sudden, recurring mental acts, which had the equivalent among typically recognised complex vocal tics such as coprolalia, echolalia, palilalia and repeating of words or phrases. We also included counting in the group of evaluated phenomena, although we were aware of the limitation arising from the fact that in many patients, differentiation between compulsive counting and a tic-like behaviour can be problematic. Complex and long-lasting thoughts, e.g. mentally jumping over telegraph poles along the roadside, drawing three-dimensional constructions in mind or having in mind the same tune for hours, were not classified as CTs. This type of diagnostic attitude precluded confusing CTs with delusional disorder, ruminations in depression and obsessions,

hyperquantivalent ideas or other psychiatric disorders. Nevertheless, none of the patients included in the study group was diagnosed with a psychotic disorder or bipolar disorder (Table 1).

CTs were differentiated with obsessions and mental compulsions according to differential diagnosis described in the introduction. For this purpose, interviews with patients covered questions about their emotional attitude towards appearing thoughts, the consequences of the thoughts, the natural form of the thoughts' sequence, the possible aim of the thoughts, the resistance the patient made against these thoughts, and if they were acceptable or not for the subject.

Lifetime CTs vs current CTs

Two, lifetime and current, comparative analyses were conducted in our study. For the purpose of the analysis concerning the prevalence of CTs during lifetime, patients were divided into two groups: the first group incorporated patients without any history of CTs (lifetime CTs- group), while the second group comprised individuals who had experienced CTs in the past or at the time of evaluation (lifetime CTs + group). In the second comparative analysis concerning the current presence of CTs, patients were divided into two groups: the current CTs + group consisted of patients with CTs present within one week preceding the evaluation, while the current CTs- group included patients who did not report CTs during this time. By extension, patients without CTs in their medical history, as well as those who reported experiencing CTs in the past but not at the time of evaluation, were included under the current CTs- group. Moreover, in the analysis relating to the current presence of CTs, all the variables were examined in reference solely to their state at the time of the examination, which created the conditions to determine the existence of any possible correlation between the demographic and clinical parameters and the CTs. Finally, the abovementioned analyses were compared, as our aim was to collate the factors which influence the lifetime prevalence of CTs with those which have an impact on the current presence of these symptoms. We cross-referenced results from these two analyses, as we assumed that certain factors might make no contribution to the occurrence of CTs even though they were positive for a specific patient but not simultaneously present with evaluated phenomena. Additionally, as we expected significant distinctions, separated analyses for children and adult groups were conducted as a part of lifetime and current comparison.

Statistical analysis

The statistical analyses were performed using STATISTICA version 13.1 and SPSS version 25 software. The Shapiro-Wilk test was used to assess the normality of distribution. In the case of the parametric variables, data was presented as arithmetic means and standard deviations (mean \pm SD). For the non-parametric variables, we chose median and quartiles (25:75) to present data. The categorical variables were presented as frequencies (percentages). Parametric data was compared using an independent t-test. For the nonparametric data, we used the Mann-Whitney U-test. Chi square test was performed for comparison of categorical data.

In both analyses, p-value had to reach < 0.05 for the comparisons between the groups to be considered significantly different. In the course of the primary analyses, we isolated variables which emerged as

significant and entered them into a logistic regression analysis. The multivariate model provided final results regarding correlates for the lifetime or current CTs in GTS patients. Additionally, sex and age served as control variables in the multivariate model.

The same statistical methods as mentioned above were used to assess the correlations of variables with lifetime and current CTs in child and adult groups. All the variables that were found to be significant in univariate analysis were included in the multivariate analysis.

Results

General characteristics

Five types of mental phenomena were evaluated: cognitive echolalia (n = 17), cognitive coprolalia (n = 16), cognitive palilalia (n = 13), cognitive counting (n = 11) and repeating words or phrases in the mind (n = 7). Cognitive tics were reported in both patients who experienced their vocal equivalent as well as in those who did not present analogous vocalisation. A vocal manifestation of echophenomena (pali- and echolalia), coprolalia and counting were more frequent than the mental presentation of the corresponding symptoms. The presence of CTs was associated with more frequent appearance of their corresponding vocalisation (Table 2).

Lifetime vs current CTs

Lifetime CTs were reported by 48 of 227 patients (21.1%), while in 33 of the cases CTs were continuing at the time of evaluation. In 15 patients, CTs disappeared entirely before the clinical evaluation. The patients with CTs were older at evaluation. Gender did not differ between CTs+ and CTs- groups (Table 3).

In the comparative analysis of the lifetime CTs+ and CTs- groups, there was no difference in sex distribution. However, patients who reported CTs were significantly older than patients in the CTs- group. Moreover, patients with CTs had more severe tics, more frequently experienced premonitory urges and suffered more often from psychiatric comorbidities (Table 3). Tic severity and significant social skill problems were values which remained significant in the multivariate logistic regression analysis (Table 4).

In the comparative analysis of the current CTs+ and CTs- groups, there was also no difference in sex distribution. However, patients who reported the current presence of CTs were significantly older than those from the current CTs- group. The univariate analysis provided evidence that factors which are significantly correlated with currently present CTs are as follows: higher severity of tics, more common diagnosis of OCD and higher prevalence of anxiety disorder (Table 5). Finally, the above mentioned variables were entered in logistic regression models and the multivariate logistic regression analysis demonstrated that for the current CTs+ group, YGTSS and anxiety disorder remained significant (Table 6).

Children vs adults with CTs

The prevalence of CTs differed between adults and children: 31.0% (27/87) and 15.0% (21/140), respectively ($p = 0.016$). The age of the onset of CTs was known in 34 of cases with the median value 13.5 years (IQR 9.3–16). In 11 of the cases, CTs had started during childhood (before 11 years of age), in 15 of the cases during adolescence (12–18 years of age) and in 8 of the cases in adulthood.

In the children group, variables which, in univariate analysis, were significantly associated with lifetime CTs and were later included in the logistic regression model were: age, YGTSS, premonitory urges and OCD. In the adult group significant associations, according to univariate analysis, were demonstrated between lifetime CTs and the following variables: anxiety disorder and significant social skill problems (Table 3). In the multivariate analysis, only age was determined as a factor significantly associated with lifetime CTs in children ($p = 0.033$), whereas in the adult group there were no statistically significant associations with lifetime CTs (Table 4).

In the children group, the univariate analysis also demonstrated that tic severity and prevalence of significant social skill problems were significantly associated with current CTs and therefore these variables were later entered into the logistic regression model. In the adult group, the univariate analyses presented significant associations between current CTs and the following: YGTSS and anxiety disorder (Table 5). According to multivariate analysis of predictors of current CTs, none of the variables reached statistical significance in the children group, while only anxiety disorder was a predictor of current CTs in the adult group ($p = 0.018$, Table 6).

Discussion

In this study we precisely defined CTs as short lasting mental acts which had the equivalent among complex vocal tics such as coprolalia, echolalia, palilalia, counting and repeating of words or phrases. In such diagnosed group, we found that cognitive tics occurred in more than 1/5 of the patients, they correlated significantly with tic severity and also with some psychiatric comorbidities, especially anxiety disorder and significant social skill problems.

We formulated a hypothesis that particular mental phenomena reported by certain GTS patients may be a form of tic manifestation and we juxtaposed it with the theory that these symptoms are a representation of another psychopathology. Inferring from the positive correlation between CTs and YGTSS (Tables 4, 6), we consider that higher tic severity may increase the risk of CTs' appearance. The opposite situation, when CTs add significantly to the impairment caused by tics, is less likely because CTs themselves are perceived by patients as egosyntonic and never reported as particularly troublesome and hence they do not require additional or more intensive treatment. Additionally, correlation between premonitory urges and CTs, which emerged statistically significant in univariate analysis, provides further evidence validating the hypothesis of CTs' affiliation to tic spectrum. Premonitory urges, which exclusively occur in tic disorders, rendered to be associated with CTs especially in children group, nevertheless, also in adult group values reached borderline significance (Table 3). Based on the association of CTs with tic severity and premonitory urges preceding tics, we prone to classify the examined phenomena as the tic spectrum

symptoms rather than recognize them as a manifestation of OCD or another psychopathology. There is a possibility of CTs' occurrence in both patients suffering from the vocal equivalent as well as in those who do not present symptoms of this kind. Echophenomena (pali- and echolalia), coprolalia and counting were most commonly presented in a form of vocalisation, nevertheless, this subgroup did not considerably outnumber the subgroup of patients who experienced analogous symptoms mentally. Moreover, both variants, vocal and cognitive, of a given tic do not necessarily appear in one particular individual, and CT accompanies its vocal equivalent in less than half of cases (Table 2). These observations indicate only a certain degree of relationship between the mental and vocal forms of the tic. As vocal echophenomena, coprolalia and counting are more frequently reported by patients with CTs, we can only speculate that the presence of these vocal tics can increase the risk of its mental equivalent's occurrence or the situation is exactly the opposite.

Nevertheless, the affiliation of CTs to the tic spectrum should be made with caution because of the correlation between the CTs and psychiatric disorders (Tables 3, 5). With regard to OCD, it should be mentioned that the difference in the number of patients in both groups: with OCD and with YGTSS score evaluated, could have certain impact on the results of these analyses. Moreover, the same type of statistical analysis pointed that CTs tend to co-occur with depression and anxiety (Tables 3, 5), which are closely related to OCD. The concomitance of CTs with depression, which is one of the most common consequences of OCD, and anxiety, which is a typical consecution of obsession and often a causative factor of compulsion, necessitate consideration of whether they represent a collective spectrum of symptoms. The fact that the age of CT onset falls in most patients in early adolescence, a period when tics begin to subside and after the peak tic severity seen usually between 10–12 years (20), also suggests that tic severity does not have to be the crucial factor regarding CTs' appearance. Furthermore, the logistic regression analysis pointed to a correlation between CTs and significant social skill problems ($p = 0.050$, Table 4), which are the principal feature of ASD. Due to the lack of sufficient number of patients with the ASD diagnosis, we presumed significant social skill problems to be the principal feature of autistic traits in our group of patients. Significant social skill problems are one of the criteria which have to be met during the ASD diagnosis, thus their presence may enforce the cooccurrence of ASD in GTS patients in our study. On the other hand, they should be considered as an ASD equivalent with caution, as they can also appear independently, and further diagnostic tests could not confirm the suspicion of ASD. Notableness of the association between CTs and significant social skill problems arises from the fact that on its basis it can be hypothesized that CTs may be a form of stereotypic mental act resembling motor stereotypy observed in patients with ASD. As there was no systematic assessment of autistic traits in our cohort, this finding should be considered as a promising hypothesis, which should be confirmed in a study with a larger group of high-functioning autistic patients with preserved communication skills. Another evidence which enforces the theory about the complexity of CTs' pathogenesis is the correlation of current CTs with current anxiety disorder, established in logistic regression analysis ($p = 0.028$, Table 6). This information, in addition to association of CTs with lifetime significant social skill problems in multivariate analysis (Table 4) and supported by univariate analyses correlations of these mental

phenomena with current OCD (Table 5) and lifetime depression (Table 3), prompt us to suspect that psychiatric comorbidities are a crucial factor in CTs' prevalence.

We also hypothesized that patients' age could be a variable associated with the rate of CTs. Age of CTs onset falls during adolescence in most patients although it may occur at any time during the course of the disease. There is an evident association between the prevalence of this mental phenomenon and the age of the patient established in one-way analysis of variance (Tables 3, 5). Even though the multivariate analysis did not demonstrate the same statistical correlation, the borderline values of the significance were reached (in lifetime CTs $p = 0.089$, in current CTs $p = 0.056$, Tables 4, 6). The fact that CTs appear several years after the development of the first tic suggests that most individuals do not present with CTs. We also found that CTs occurred in adult patients twice as often as in children. It is possible that younger patients actually report CTs to a lesser extent than older individuals, much like premonitory urges (21, 22), or that CTs may have natural tendency to manifest over time. However, it may also indicate difficulty in obtaining information from younger children and that the diagnostic material collected from children is less reliable because of the children's incomprehension of the questions during the interview and the lack of parents' insight into child's mental state. Taking into consideration the fact, that CTs were never reported spontaneously by patients and were realized only due to active inquiry, the proper cooperation and communication appear essential in diagnosing these phenomena. The acknowledgment of this may contribute to the understanding why the issue of CTs is still not sufficiently examined as the majority of studies in GTS involve child population.

We found significant differences in correlates of CT's in children and adults group. In logistic regression model in children, age at evaluation was a factor significantly associated with lifetime CTs ($p = 0.033$), whereas in adults there were no statistically significant predictors of lifetime CTs. For current CTs, none of the variables reached statistical significance in children, while anxiety disorder was a predictor of current CTs in adults ($p = 0.018$). These differences between children and adult patients with GTS can provide with noteworthy conclusions regarding the pathogenesis of these symptoms. Taking into consideration the fact that certain co-occurring disorders have the tendency to be present in the specific age groups (Table 1), we can speculate that whole group of symptoms, depending on the age of the patient, can be a factor which could be related to CTs' appearance. In this case CTs would have various causes, distinct for age groups and specific for particular patients. Thereby, the differences in clinical picture of children and adults groups provide further evidence that pathogenesis of CTs' is complex, depends on multiple factors and is related to phenotypic variability of GTS.

Another possible consideration of CTs character arises from the careful understanding of its definition: CTs are pleasant or neutral, stimulating in their nature rather than regulating negative emotional states. Current research emphasizes two main basic human needs that should be taken into general consideration in describing and understanding psychiatric phenomena: regulation of negative emotional states and reward seeking (stimulation) (23, 24). Importantly, these needs may be addressed with different strategies (mature or immature, short or long-term, conscious or unconscious, constructive or destructive). A commonly used regulative/reward-seeking strategy is the use of psychoactive substances

like for instance alcohol or stimulants. Although GTS is associated with a decreased risk of substance use disorders with the prevalence of 6.2%, it seems to be related to overrepresentation of children in research sample groups. Substance abuse is significantly higher among adults compared to adolescents and children: 18.5% vs 2.6% vs 0.0%, respectively, with the median age of onset of 16 years (2). In the cohort of 141 adult patients with GTS reported by Haddad, more than ¼ of them developed alcohol or drug abuse (25). However, substance use disorders were more prevalent among individuals with comorbid OCD and ADHD (2, 25) in comparison to GTS without these comorbid disorders. Plausibly, in GTS, while comorbidity with OCD or ADHD is present, alcohol or other substances may be more likely used to reduce tics, serve as self-medication and provide stimulation. It can be very carefully speculated that CTs may in some cases act like an internal stimulatory, immature mechanism, while obsessions may act as an internal, immature regulatory (short-term) strategy. CTs may be stimulating (4), so in those patients they may encourage autostimulation. The certain evidence which encourages this hypothesis is similar age of onset of substance use disorders reported by Hirschtritt et al. (2) and CTs found in our study (median: 16 and 13.5, respectively). The prevalence of alcohol or substance use disorder was not assessed in our study, yet it would be important and interesting to address this issue in future studies and to investigate whether presence of CTs may serve as protector or rather as a risk factor of substance use in GTS and other clinical and non-clinical samples.

The value of performed study arises from both extending of scientific knowledge in the topic of mental phenomena in patients with GTS and prospective clinical application of acquired data. In opposition to OCD, CTs do not require treatment as are perceived by patients as neutral and egosyntonic. It also seems important to pay attention to the presence of mental phenomena resembling tics which do not fulfill current diagnostic criteria of this hyperkinetic movements and, although unobservable, may belong to the spectrum of tic phenomenology. Our results suggest that GTS-affected patients who also have CTs at the time of examination should be carefully evaluated for the existing anxiety disorders and more severe tics. This could certainly influence the choice of appropriate treatment.

There are several limitations to our study which include: lack of control group; lack of any validated instrument in CTs' assessment; the established CT definition limited to tic phenomenology with exclusion of overlapping, long-lasting mental phenomena from OCD spectrum; recall bias that could potentially influence the reported prevalence rate and age at onset of CTs; the one-time registration study design that could influence the rate of CTs and psychiatric comorbidities; referral bias as the patients were evaluated by neurologist and the cases with more severe psychopathology were referred to psychiatric clinics, which explains low numbers of OCD and depression in children group, as well ASD in all GTS group.

Conclusions

We conclude that tics can be defined not only as repetitive behaviour, but also as repetitive thoughts. Some complex tics may appear in two forms, vocal and mental. CTs should presumably be considered as a part of the tic phenomenology with a crucial impact of comorbid psychiatric disorders, especially anxiety disorder and social skill problems. CTs are a late symptom of GTS, tend to appear over the course

of the disease, hence are an age-dependent symptom. Whereas in all GTS groups the main risk factor for CTs is tic severity, the age at evaluation in children and anxiety disorder in adults are significantly correlated with CTs.

Declarations

Ethics approval and consent to participate

Collecting of clinical data from patients with GTS has been approved by the Ethics Committee of Medical University of Warsaw (KB/2/2007). All subjects gave written informed consent in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the individuals and/or minors' legal guardian/next of kin for the participation in this study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

None to declare.

Authors' contributions

PJ conceived and designed the study and acquired data. PJ and AD set up the electronic database. AJ and NS analysed the data. AJ, PJ, NS and AD interpreted the data and reviewed and edited the manuscript. AD and PJ wrote the original draft of the manuscript.

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Tables

Table 1. Psychiatric comorbidities in children, adolescents and adults with GTS.

Comorbid mental disorder	Children (n=95)	Adolescents (n=44)	Adults (n=88)
ADHD	30.5%, n=29	20.5%, n=9	20.5%, n=18
OCD	6.3%, n=6	18.2%, n=8	37.5%, n=33
OCS	40%, n=38	36.4%, n=16	47.7%, n=42
Depression	0%, n=0	6.8%, n=3	33.0%, n=29
Anxiety disorder	44.2%, n=42	61.4%, n=27	51.1%, n=45
Significant social skill problems	12.6%, n=12	13.6%, n=6	13.6%, n=12
ODD	25.3%, n=24	11.4%, n=5	3.4%, n=3
ASD	3.2%, n=3	6.8%, n=3	2.27%, n=2

GTS - Gilles de la Tourette syndrome, ADHD - attention deficit hyperactivity disorder, OCD - obsessive-compulsive disorder, OCS - obsessive-compulsive symptoms, ODD - oppositional defiant disorder, ASD - autism spectrum disorder. Groups are defined as children (aged 5-11), adolescents (aged 12-18), adults (aged >18).

Table 2. Prevalence of CTs and vocal tics in CTs+ and CTs- groups.

	Patients with cognitive tics (CTs+ group) (n=48)	Patients without cognitive tics (CTs- group) (n=179)	p* (CTs+ vs. CTs-)
Coprolalia			0.002
Vocal only	20 (41.7%)	36 (20.1%)	
Cognitive only	16	0	
Both (Vocal + Cognitive)	8	0	
Echolalia			0.0003
Vocal only	20 (41.7%)	31 (17.3%)	
Cognitive only	17	0	
Both (Vocal + Cognitive)	7	0	
Palilalia			0.053
Vocal only	14 (29.2%)	30 (16.8%)	
Cognitive only	13	0	
Both (Vocal + Cognitive)	6	0	
Counting			0.031
Vocal only	19 (39.6%)	22 (12.3%)	
Cognitive only	11	0	
Vocal + Cognitive	7	0	

*p given only for vocal phenomena, p<0.05 is shown in bold

Table 3. Comparison of lifetime CTs- and CTs+ groups.

	All GTS patients (n=227)			Children and adolescents with GTS (n=140)			Adults with GTS (n=87)		
	CTs+ (n=48)	CTs- (n=179)	p	CTs+ (n=21)	CTs- (n=119)	p	CTs+ (n=27)	CTs- (n=60)	p
Age at evaluation [years] [median] (IQR)	18 (12-25)	12 (9-22)	0.01	11.0 (10-15)	10 (8-12)	0.005	24 (19-32)	25 (22-32)	0.32
Sex (male/female)	40/8	139/40	0.69	20/1	91/28	0.15	20/7	48/12	0.83
YGSS [median] (IQR)	61 (36-74)	42 (26-59)	<0.001	59 (38-66)	37 (22-55)	0.01	62 (34-79)	50 (37-62)	0.07
Premonitory urges	n=39 (81.3%)	n=94 (52.5%)	<0.001	n=15 (71.4%)	n=51 (42.9%)	<0.001	n=24 (88.9%)	n=43 (71.7%)	0.097
ADHD	n=13 (27.1%)	n=43 (24.0%)	0.66	n= 9 (42.9 %)	n= 29 (24.4%)	0.079	n=4 (14.8%)	n=14 (23.3%)	0.36
OCD	n= 17 (35.4%)	n=30 (16.8%)	0.005	n=5 (23.8 %)	n=9 (7.6%)	0.022	n=12 (44.4%)	n=21 (35%)	0.40
OCS	n=23 (47.9%)	n=73 (40.8%)	0.37	n= 10 (47.6%)	n=44 (37.0%)	0.36	n=13 (48.1%)	n=29 (48.3%)	0.36
Depression	n=11 (22.9%)	n=21 (11.7%)	0.048	1 (4.8%)	2 (1.7%)	0.37	n=10 (37.0%)	n=19 (31.7%)	0.62
Anxiety Disorder	n=32 (66.6%)	n=82 (45.8%)	0.01	n=13 (61.9%)	n=56 (47.1%)	0.21	n=19 (70.4 %)	n=26 (43.3%)	0.02
Significant social skill problems	n=12 (25%)	n=36 (20.1%)	0.007	n= 5 (23.8 %)	n=13 (10.9%)	0.1	n=7 (25.9%)	n=5 (8.3%)	0.03

CTs- cognitive tics, GTS - Gilles de la Tourette Syndrome, YGTSS - Yale Global Tic Severity Scale, ADHD - Attention-Deficit Hyperactivity Disorder, OCD - Obsessive Compulsive Disorder, OCS - Obsessive Compulsive Symptoms, IQR-interquartile range. Lifetime prevalence of psychiatric symptoms and disorders is shown. For non-parametric variables, data are presented as median and interquartile range. Categorical variables are presented as frequencies (percentages). $p < 0.05$ is shown in bold.

Table 4. Logistic regression analysis for the predictors of lifetime CTs in GTS.

	All GTS patients		Children with GTS		Adults with GTS	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	1.036 (0.994-1.080)	0.089	1.216 (1.015-1.451)	0.033	0.981 (0.912-1.055)	0.600
Sex	0.786 (0.315-1.960)	0.605	0.187 (0.022-1.614)	0.127	1.328 (0.202-4.025)	0.623
YGTSS	1.021 (1.003-1.039)	0.025	1.020 (0.995-1.046)	0.119	-	-
Premonitory urges	1.388 (0.915-2.104)	0.123	1.216 (0.745-1.983)	0.435	-	-
OCD	1.396 (0.597-3.265)	0.442	1.930 (0.486-7.662)	0.350	-	-
Depression	0.666 (0.228-1.945)	0.457	-	-	-	-
Anxiety disorder	1.720 (0.814-3.636)	0.156	-	-	2.492 (0.893-6.954)	0.081
Significant social skill problems	2.434 (0.999-5.930)	0.050	-	-	2.387 (0.620-9.195)	0.206

CTs- cognitive tics, GTS - Gilles de la Tourette Syndrome, YGTSS - the Yale Global Tic Severity Scale, OCD - obsessive-compulsive disorder.
 $p < 0.05$ is shown in bold.

Table 5. Comparison of CTs+ and CTs- current groups.

	All GTS patients (n=227)			Children with GTS (n=140)			Adults with GTS (n=87)		
	CTs current+ (n=33)	CTs current- (n=194)	p	CTs current+ (n=13)	CTs current- (n=127)	p	CTs current+ (n=20)	CTs current- (n=67)	p
Age at evaluation [years] [median] (IQR)	18 (12-25)	13 (9-20)	0.014	11 (10-12)	10 (8-12)	0.35	23.5 (19-32.5)	25 (21-32)	0.80
Sex (male/female)	28/5	151/43	0.66	13/0	98/29	0.15	15/5	53/14	0.93
YGTSS [median] (IQR)	62 (40-76)	43 (26-60)	0.0003	60 (38-70)	37 (22-58)	0.036	62.5 (49.5-80.0)	51 (35-65)	0.037
Premonitory urges	n=26 (78.8%)	n=61 (31.4%)	0.21	n=8 (61.5%)	n=22 (17.3%)	0.62	n=18 (90%)	39 (58.2%)	0.16
ADHD	n=7 (21.2%)	n=42 (21.6%)	0.955	n=6 (46.2%)	n=30 (23.6%)	0.077	n=1 (5%)	n=12 (17.9%)	0.155
OCD	n=9 (27.3%)	n=26 (13.4%)	0.041	n=2 (15.4%)	n=9 (7.1%)	0.290	n=7 (35%)	n=17 (25.4%)	0.398
OCS	n=14 (42.2%)	n=70 (36.1%)	0.485	n=6 (46.2%)	n=42 (33.1%)	0.344	n=8 (40%)	n=28 (41.8%)	0.887
Depression	n=3 (9.1%)	n=7 (3.6%)	0.156	n=0	n=2 (1.6%)	0.649	n=3 (15%)	n=5 (7.5%)	0.306
Anxiety Disorder	n=21 (63.6%)	n=78 (40.2%)	0.012	n=8 (61.5%)	n=58 (45.7%)	0.275	n=13 (65%)	n=20 (29.9%)	0.004
Significant social skill problems	n=6 (18.2%)	n=17 (8.8%)	0.097	n=4 (30.8%)	n=12 (9.4%)	0.021	n=2 (10%)	n=5 (7.5%)	0.714

CTs- cognitive tics , GTS - Gilles de la Tourette Syndrome, YGTSS - Yale Global Tic Severity Scale, ADHD - Attention-Deficit Hyperactivity Disorder, OCD - Obsessive Compulsive Disorder, OCS - Obsessive Compulsive Symptoms, IQR-interquartile range. Current prevalence of psychiatric symptoms and disorders is shown. p<0.05 is shown in bold

Table 6. Logistic regression analysis for the predictors of current CTs in GTS.

	All GTS patients		Children with GTS		Adults with GTS	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	1.042 (0.999-1.087)	0.056	1.070 (0.853-1.342)	0.556	1.006 (0.928-1.090)	0.889
Sex	0.623 (0.216-1.797)	0.382	0.000	0.998	1.311 (0.374-4.600)	0.672
YGTSS	1.023 (1.002-1.043)	0.028	1.015 (1.020-1.085)	0.352	1.021 (0.994-1.050)	0.125
OCD	1.238 (0.478-3.205)	0.660	-	-	-	-
Anxiety disorder	2.560 (1.106-5.928)	0.028	-	-	3.893 (1.261-12.018)	0.018
Important social skill problems	-	-	2.306 (0.506-10.512)	0.280	-	-

CTs - cognitive tics, GTS - Gilles de la Tourette syndrome, YGTSS - the Yale Global Tic Severity Scale, OCD - obsessive-compulsive disorder. p<0.05 is shown in bold.