JOURNAL OF PSYCHOPATHOLOGY
2019;25:190-194

Headache in paediatric and adult patients with Gilles de la Tourette syndrome

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Abstract

Objective

Gilles de la Tourette syndrome (GTS) is a neuropsychiatric disorder characterized by multiple motor and vocal tics and commonly associated with co-morbid conditions. Despite early reports of increased prevalence of headache in both children and adults with GTS, little is known about the nature of this co-morbidity. We conducted a collaborative study based in specialist clinics to compare the prevalence and characteristics of headache in paediatric and adult patients with GTS.

Methods

We assessed a total of 140 patients with GTS for the presence and characteristics of headache: 109 children and adolescents (age range 6-17 years) and 31 adults (age range 18-55, randomly selected from a clinical sample of 200 patients) seen at specialist clinics. A further comparison was performed between the group of adults with headache (n =15) and a subgroup of gender-matched children with headache (n =16).

Results

In our study, the prevalence of headache was 48.4% in adults with GTS and 22.9% in children with GTS (p = 0.01). Adults with GTS presented with higher tic severity and poorer quality of life compared to younger patients (p = 0.01). There was a significant difference in the headache types: tension type headache was significantly more commonly reported by adults with GTS, whereas migraine was significantly more commonly reported by children with GTS (p = 0.02). Adults with GTS and co-morbid headache consistently presented with higher tic severity and poorer quality of life compared to children with GTS and co-morbid headache (p = 0.01).

Conclusions

Headache is confirmed as a relatively common co-morbidity of GTS, particularly in adult patients seen at specialist clinics. The higher prevalence of headache in adults with GTS (especially tension-type headache) compared to younger patients could be related to higher tic severity and poorer quality of life in our adult clinical sample. If replicated, these findings can inform clinical practice in guiding targeted screening and management interventions for headache in patients with GTS across the lifespan.

Key words
Gilles de la Tourette syndrome • Tics • Headache • Children • Adults

Received: April 29, 2019
Accepted: May 2, 2019

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Introduction

Gilles de la Tourette syndrome (GTS) is a complex neurodevelopmental disorder characterized by the chronic presence of multiple motor tics plus at least one vocal tic [1 2]. The majority of patients with GTS present with co-morbid behavioural problems, especially obsessive-compulsive disorder (OCD) and attention-deficit and hyperactivity disorder (ADHD), as well as frequent affective symptoms and impulsivity [3]. Relatively little is known about the neurological co-morbidities of GTS, despite previous reports of neurological soft signs [4] and increased risk for common neurological conditions such as epilepsy [5]. The results of preliminary studies exploring the occurrence of headache in both children [6-8] and adults [7] with GTS

have raised the possibility of an increased risk across the lifespan. In order to better understand the relationship between GTS and headache, we conducted a collaborative study across specialist clinics to compare the prevalence and characteristics of headache in paediatric and adult patients with GTS.

Methods

A total of 140 patients with GTS were recruited for the present study. One hundred and nine children and adolescents with GTS (age range 6-17 years) were recruited from the specialist movement disorders clinics of the Child Neuropsychiatry Unit, University of Insubria (Varese, Italy), the 'C. Besta' Neurological Institute (Milan, Italy), and the University of Pavia (Pavia, Italy). Moreover, 31 adult patients with GTS (age range 18-55) were randomly selected from a larger clinical sample of 200 patients seen at the specialist Tourette syndrome clinic, Department of Neuropsychiatry, National Centre for Mental Health (Birmingham, United Kingdom).

All patients provided informed consent to participate in the study and were clinically evaluated by a neuropsychiatrist with experience in GTS, who collected a comprehensive medical and family history and reviewed comorbid diagnoses, including OCD and ADHD. The patients were assessed using the Diagnostic Confidence Index (DCI)[9], a clinician-rated measure of lifetime likelihood of GTS diagnosis in patients presenting with tic symptoms, based on the presence of specific clinical characteristics (including waxing and waning course, presence of premonitory urges, tic suppressibility) and selected complex tics (including coprolalia, echolalia, echopraxia, and palilalia). In total, the DCI covers 27 clinical features associated with GTS, all of which have a corresponding weighted score. The total DCI score is expressed as a percentage, with higher scores indicating higher confidence that the patient has GTS. In addition, the severity of tic symptoms was assessed using the Yale Global Tic Severity Scale (YGTSS) [10], a clinician-rated scale assessing the severity of both motor and vocal tics across five different domains: number, frequency, intensity, complexity, and interference. Each of these is scored from 0 to 5, and combined to produce a global tic severity score. An additional measure of overall impairment, which addresses functioning in social, academic and occupational environments, is scored from 0 to 50. These two scores are combined to produce the total YGTSS score, ranging from 0 to 100, with higher scores indicating increased tic severity. The Visual Analogue Scale (VAS) of the age-specific versions of the Gilles de la Tourette Syndrome-Quality of Life scale (GTS-QOL) was used to evaluate patient perception of health-related quality of life (HR-QOL) in both children and adults with GTS [11 12]. Self-rated VAS scores range from 0 to 100, with 100 indicating the highest possible satisfaction with life. Finally, all patients underwent a comprehensive neurological examination and were screened for the diagnosis of headache according to the clinical criteria detailed in the third edition of the International Classification of Headache Disorders (ICHD-3) [13].

Both clinician-rated and self-rated scores obtained from all young and adult patients were described and compared. Statistical analyses were performed using the PASW (SPSS) Statistics version 17.0.3 (IBM, New York, USA): Chi-Square analysis was used for categorical data, whereas continuous variables were assessed with parametric (Student t) and nonparametric (Mann-Whitney U and Wilcoxon) tests. P values inferior to 0.05 were considered statistically significant.

Results

Our clinical samples consisted of 31 adults with GTS (mean age 31.6 years, sd 10.0) and 109 children and adolescents with GTS (mean age 12.0 years, sd 2.7). The proportion of female patients was higher in the adult group compared to the children group (29.0% and 17.4%, respectively), although the difference was not statistically significant ($p = 0.15$). Likewise, there were no statistically significant differences in age at tic onset (8.3 years, sd 4.5 *versus* 6.2 years, sd 2.2; $p = 0.27$), family history of tics (48.4 *versus* 60.6%; $p = 0.23$), or psychiatric co-morbidities (OCD: 32.3 *versus* 33.0%; $p = 0.94$; ADHD: 29.0 *versus* 41.3%; $p = 0.22$), with the exception of depression (45.2 *versus* 8.3%; $p = 0.01$). The proportion of patients taking pharmacotherapy for their tic disorder was higher in the adult group compared to the children group (54.8 and 35.8%, respectively), although the difference was not statistically significant ($p = 0.06$). Likewise, there were no statistically significant differences in the proportions of patients taking typical antipsychotics (19.4 *versus* 24.8%; $p = 0.53$), atypical antipsychotics (32.3 *versus* 27.5%; $p = 0.61$), and alpha2-agonists (16.1 *versus* 6.4%; $p = 0.09$). Adults with GTS presented with higher tic severity and lower HR-QOL compared to younger patients. Specifically, the adult group had significantly higher YGTSS scores (61.2, sd 15.6 *versus* 50.6, sd 16.6; $p = 0.01$), as well as higher DCI scores (73.2, sd 21.6 *versus* 63.5, sd 16.3; $p = 0.05$), whereas comparison of self-report VAS scores showed that overall satisfaction with life was significantly lower in the adult group (55.2, sd 22.8 *versus* 69.8, sd 21.0; $p = 0.01$).

The adult cohort was characterised by a higher prevalence of headache (48.4 *versus* 22.9%; $p = 0.01$). A further comparison was performed between the group of adults with headache and a subgroup of gender-matched children with headache. With regard to headache type,

tension type headache was significantly more commonly reported by adult patients with GTS (p = 0.02), whereas migraine was significantly more commonly reported by children and adolescents with GTS (p = 0.02). Comparison of the headache characteristics (frequency and duration of headache episodes) between young and adult patients with GTS revealed no statistically significant differences between the two age groups. Adults with GTS and co-morbid headache consistently presented with higher tic severity (p = 0.01) and lower HR-QOL (p = 0.01) compared to children and adolescents with GTS and co-morbid headache (Table I).

TABLE I. *Comparison of young and adult patients with GTS and headache.*

Patient characteristics	Children (n = 16)	Adults (n = 15)	p value
Age (mean, sd)	12.0 (2.7)	31.6 (10.0)	0.01*
Female gender (n, %)	5 (31.2)	5 (33.3)	0.90
Age at tic onset (mean, sd)	6.1 (1.7)	8.9 (5.5)	0.13
Family history of tics (n, %)	9 (56.3)	6 (40.0)	0.37
OCD (n, %)	6 (37.5)	5 (33.3)	0.81
ADHD (n, %)	7 (43.8)	5 (33.3)	0.55
Depression (n, %)	3 (18.8)	6 (40.0)	0.19
Pharmacotherapy (n, %)	10 (62.5)	11 (73.3)	0.52
- Typical antipsychotic (n, %)	3 (18.8)	5 (33.3)	0.35
- Atypical antipsychotic (n, %)	8 (50.0)	7 (46.7)	0.85
- Alpha2-agonist (n, %)	1 (6.2)	4 (26.7)	0.12
YGTSS total (mean, sd)	47.8 (12.6)	60.8 (14.4)	0.01*
GTS-QOL VAS (mean, sd)	75.4 (19.7)	52.3 (22.1)	0.01*
DCI (mean, sd)	64.3 (19.5)	74.6 (20.2)	0.23
Headache type			
Migraine	11 (68.8)	4 (26.7)	0.02*
- Migraine with aura	3 (18.8)	1 (6.7)	0.25
- Migraine without aura	8 (50.0)	3 (20.0)	0.08
Tension type headache	5 (31.2)	11 (73.3)	0.02*
Headache frequency			
< 1/month	2 (12.5)	1 (6.7)	0.58
1-3/month	4 (25.0)	4 (26.7)	0.92
1/week	3 (18.8)	5 (33.3)	0.36
2-3/week	6 (37.5)	2 (13.3)	0.12
> 3/week	1 (6.2)	3 (20.0)	0.26
Headache duration			
< 30 minutes	3 (18.8)	2 (13.3)	0.68
30-60 minutes	3 (18.8)	2 (13.3)	0.68
1-2 hours	5 (31.2)	1 (6.7)	0.08
3-5 hours	2 (12.5)	3 (20.0)	0.57
6-12 hours	2 (12.5)	5 (33.3)	0.17
13-24 hours	1 (6.2)	2 (13.3)	0.50

**p < 0.05*

Abbreviations: GTS, Gilles de la Tourette syndrome; OCD, obsessive-compulsive disorder; ADHD, attention-deficit and hyperactivity disorder; YGTSS, Yale Global Tic Severity Scale; GTS-QOL VAS, Gilles de la Tourette Syndrome-Quality of Life Visual Analogue Scale; DCI, Diagnostic Confidence Index.

Discussion

The results of our study confirmed that headache is a relatively common problem in patients with GTS, particularly in adults seen at specialist clinics [6-8]. In our clinical samples, headache was reported in about 48% of adults with GTS and 23% of children and adolescents with GTS, suggesting that screening for headache and treatment interventions might be appropriate in this patient population across the lifespan.

In our study, the higher prevalence rate of headache (especially tension-type headache) in older patients could be related to the higher tic severity in the adult group. Overall, specialist clinics for adult patients with GTS tend to be accessed by the subpopulation of patients with persistently severe GTS throughout adulthood. Moreover, the smaller sample size in the adult group could have led to an overestimation of the prevalence of headache in this age group. Finally, our adult sample reported poorer HR-QOL and showed a trend towards a higher prevalence of co-morbid affective symptoms, compared to the younger sample. Our findings could complement the results of a recent study on a large sample of 401 patients with headache suggested that psychiatric symptoms and social stressors were associated significantly more often with tension-type headache than with migraine [14].

Our findings are in line with the results of previous studies suggesting a possible association between GTS and migraine. The hypothesis of a shared pathophysiological basis is in line with the available evidence of altered serotonin metabolism in both conditions [6 7]. A shared disturbance in the extrapyramidal system has also been proposed, based on neuroimaging findings about the involvement of basal ganglia-thalamocortical circuitries [15]. More recently, large scale genetic studies have found evidence for shared hereditability of GTS and migraine [16 17].

The main limitations of the present study include sample size (relatively small in both groups), generalisability (limited by referral bias across specialist clinics), and inter-rater reliability (potentially sub-optimal). Our findings prompt further research into the link between GTS and headache. Specifically, replication of our results on the differential prevalence and characteristics of headache in patients with GTS across the lifespan could inform more targeted screening and treatment interventions. This is particularly relevant as pharmacological studies have identified medications, such as the antiepileptic drug topiramate, that are effective in the treatment of both headache (migraine prophylaxis) and GTS (tic control) [18]. Finally, further research is needed to test the existing hypotheses on the possibility of shared underlying mechanisms between GTS and headache.

Acknowledgments

The authors are grateful to Tourettes Action-UK, Tourette Association of America, and Associazione Tincontro for their support.

Conflicts of interest

The Authors declare to have no conflict of interest.

References

1 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders* (5th ed.) Washington, DC: 2013.

2 Cavanna AE, Seri S. *Tourette's syndrome*. BMJ 2013;347:f4964.

3 Cavanna AE. *Gilles de la Tourette syndrome as a paradigmatic neuropsychiatric disorder*. CNS Spectr 2018;23:213-8.

4 Semerci ZB. *Neurological soft signs and EEG findings in children and adolescents with Gilles de la Tourette syndrome.* Turk J Pediatr 2000;42:53-5.

5 Wong LC, Huang HL, Weng WC, et al. *Increased risk of epilepsy in children with Tourette syndrome: a population-based case-control study.* Res Dev Disabil 2016;51-52:181-7.

6 Barabas G, Matthews WS, Ferrari M. T*ourette's syndrome and migraine.* Arch Neurol 1984;41:871-2.

7 Kwak C, Vuong K, Jankovic J. *Migraine headache in patients with Tourette syndrome.* Arch Neurol 2003;60:1595-8.

8 Ghosh D, Rajan PV, Das D, et al. *Headache in children with Tourette syndrome.* J Pediatrics 2012;161:303-7.

9 Robertson MM, Banerjee S, Kurlan R, et al. *The Tourette syndrome Diagnostic Confidence Index: development and clinical associations.* Neurology 1999;53:2108-12.

10 Leckman JF, Riddle MA, Hardin MT, et al. *The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity*. J Am Acad Child Adolesc Psychiatry 1989;28:566-73.

11 Cavanna AE, Schrag A, Morley D, et al. *The Gilles de la Tourette syndrome-quality of life scale (GTS-QOL): development and validation.* Neurology 2008;71:1410-6.

12 Cavanna AE, Luoni C, Selvini C, et al. *The Gilles de la Tourette Syndrome-Quality of Life Scale for Children and Adolescents (GTS-QOL-C&A): development and validation of the Italian version*. Behav Neurol 2013;27:95-103.

13 Headache Classification Committee of the International Headache Society. *The International Classification of Headache Disorders (3rd edition).* Cephalalgia 2018;38:1-211.

14 Eidlitz-Markus T, Zolden S, Haimi-Cohen Y, et al. *Comparison of comorbidities of migraine and tension headache in a pediatric headache clinic.* Cephalalgia 2017;37:1135-44.

15 Barbanti P, Fabbrini G. *Migraine and the extrapyramidal system.* Cephalalgia 2002;22:2-11.

16 Tsetsos F, Padmanabhuni SS, Alexander J, et al. *Meta-analysis of Tourette syndrome and attention deficit hyperactivity disorder provides support for a shared genetic basis*. Front Neurosci 2016;10:340.

[17] Brainstorm Consortium. *Analysis of shared heritability in common disorders of the brain.* Science 2018;360:eaap8757.

[18] Jankovic J, Jimenez-Shahed J, Brown LW. *A randomised, double-blind, placebo-controlled study of topiramate in the treatment of Tourette syndrome*. J Neurol Neurosurg Psychiatry 2010;81:70-3.

How to cite this article: Cavanna AE, Bandera V, Bartoli B, et al. *Headache in paediatric and adult patients with Gilles de la Tourette syndrome*. Journal of Psychopathology 2019;25:190-4.