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DOI:
10.1016/j.jns.2023.120725

Journal of the Neurological Sciences 451 (2023) 120725

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Clinical short communication

Neurodevelopmental versus functional tics: A controlled study

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ARTICLE INFO

Keywords:
Functional neurological disorder
Functional tics
Neurodevelopmental tics
Tic disorder
Tourette syndrome

ABSTRACT

Background: An unprecedented increase in newly developed functional tics, mainly in young females, has been reported during the COVID-19 pandemic. We set out to complement existing case series with the largest controlled study to date on the clinical phenomenology of functional tics versus neurodevelopmental tics.
Methods: Data from 166 patients were collected at a specialist clinic for tic disorders during a three-year period overlapping with the COVID-19 pandemic (2020−2023). We compared the clinical features of patients who developed functional tics during the COVID-19 pandemic ($N = 83$) to patients with Tourette syndrome matched for age and gender (N = 83).
Results: Female adolescents and young adults accounted for 86% of the clinical sample of patients with functional tics, who were less likely to report a family history of tic disorders than their matched controls with Tourette syndrome. Co-morbidity profiles were significantly different: anxiety and other functional neurological disorders were more strongly associated with functional tics, whereas attention-deficit and hyperactivity disorder and tic-related obsessive-compulsive behaviors co-occurred more frequently with neurodevelopmental tics. Overall, absence of tic-related obsessive-compulsive behaviors ($t = 8.096$; $p < 0.001$) and absence of a family history of tics ($t = 5.111$; $p < 0.001$) were the strongest predictors of the diagnosis of functional tics. Compared to neurodevelopmental tics, functional tics were more likely to present acutely/subacutely at a later age (21 versus 7 years), without a clear rostro-caudal progression. Coprophenomena, self-injurious behaviors, and complex clinical manifestations such as blocking tics, throwing tics, and tic attacks, were all over-represented in the functional group.
Conclusions: Our findings provide robust confirmation of both patient-related variables and tic characteristics contributing to the differential diagnosis between functional tics developed during the pandemic and neurodevelopmental tics reported by patients with Tourette syndrome.

1. Introduction

Over the last few years, there has been an unprecedented increase in cases of newly developed functional tics, mainly in female adolescents and young adults presenting acutely with repetitive movements and vocalisations that resemble neurodevelopmental motor and vocal tics [1]. Within the broader spectrum of functional movement disorders, functional tics have traditionally been considered to be relatively rare, until the recent outbreak during the COVID-19 pandemic. Aetiological models have included both direct and indirect consequences of the pandemic and pandemic-related restrictions [2], especially increased exposure to social media contents by influencers portraying tic-like behaviors [3]. Reports from different countries [4–6] as well as a multi-national registry collating data from ten specialist centres across North America, Australia, and Europe [7], recently highlighted a number of phenotypical differences between patients with functional tics and patients with primary tic disorders such as Tourette syndrome (TS). These findings are of clinical relevance, however few controlled studies have been conducted to allow direct comparisons between patients with functional tics and patients with neurodevelopmental tics disorders [8–14]. Moreover, controlled studies from individual specialist centres were relatively small, with sample sizes ranging from 9 [10] to 53 [13]

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https://doi.org/10.1016/j.jns.2023.120725
Received 1 May 2023; Received in revised form 30 May 2023; Accepted 28 June 2023
Available online 29 June 2023

patients with functional tics, and in most cases control groups were unmatched, with rare exceptions [8]. Therefore we set out to corroborate and complement existing data with the largest controlled study to date on the clinical phenomenology of functional tics versus neurodevelopmental tics.

2. Methods

We included in the present study all consecutive patients who developed functional tics during the COVID-19 pandemic (April 2020–March 2023) and were referred to the specialist Tourette Syndrome Clinic, Department of Neuropsychiatry, National Centre for Mental Health, Birmingham, United Kingdom. Each patient underwent a comprehensive clinical assessment by a behavioral neurologist with >20 years of clinical experience with both primary tic disorders and functional neurological disorders (AEC). Detailed demographic and clinical data were routinely collected in order to confirm the diagnosis of functional neurological disorder (functional tics) according to DSM-5 criteria [15]. The assessment was based on the National Hospital Interview Schedule for Tourette syndrome [16], a detailed semi-structured interview schedule originally validated in patients with neurodevelopmental tics and adapted for use in patients with functional tics by including key items relevant to functional movement disorders [17]. Demographic and clinical data included gender, age at assessment, age and type of onset, psychological triggers and clinical phenomenology of tics, family history of tic disorder, psychiatric co-morbidities, and treatment interventions.

Out of a clinical sample of 538 patients from the same Clinic, we identified a group of age- and gender-matched controls who fulfilled current diagnostic criteria for TS (persistent motor and vocal tics with onset in childhood or adolescence). The assessment of the patients with TS was also based on the National Hospital Interview Schedule for Tourette syndrome [16]. The control group of patients with neurodevelopmental tics was selected consecutively from the clinic database by the same researcher (AEC), who conducted both the clinical assessments and the relevant data extraction. We did not include patients with neurodevelopmental tics in the context of a primary tic disorder who subsequently developed co-morbid functional tics (functional overlay), as the clinical characteristics of this group of patients might differ from those of patients with neurodevelopmental tics only [18]. Patients with a limited understanding of English and patients with severe autism spectrum disorder/learning disability were also excluded from our analysis. All patients provided informed consent to participate in the study, which was approved by the local section of the National Research Ethics Service.

Anonymized data were stored on Microsoft Excel 2019. The Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago, IL, USA, version 25) was used to perform all statistical analyses. This retrospective study was conducted using descriptive statistics to illustrate the demographic and clinical characteristics of the participants. Moreover, we used Fisher's exact test for dichotomous variables and the *t*-test for continuous variables to assess possible differences between functional and neurodevelopmental tics. Finally, the strength of the association between each demographic and clinical variable and the diagnosis of functional tics was quantified by building a stepwise logistic regression model.

3. Results

A total of 83 patients assessed at the specialist Tourette syndrome Clinic developed functional tics in the absence of a pre-existing primary tic disorder during the COVID-19 pandemic. Demographic and clinical data of 83 age- and gender-matched controls were extracted from an existing database of 538 patients with TS from the same Clinic. The characteristics of the two clinical samples are compared in Table 1.

The average age of the patients with functional tics at the time of the assessment was 23 years (range 13–63 years). The vast majority of patients (71%) were females, and female adolescents and young adults accounted for 86% of the whole sample. As for the controls, after removal of patients with functional overlay from the whole database, 157/515 patients with TS (30%) were females. A family history of tic disorders was reported by 7% of patients with functional tics and 55% of patients with TS from the extracted control group. Co-morbid psychiatric disorders were diagnosed in the vast majority of patients, regardless of the clinical group (90.4% of patients with functional tics and 91.6% of patients with TS). Anxiety was diagnosed more frequently in patients with functional tics compared to patients with TS (70% versus 39%). Approximately one third of patients fulfilled diagnostic criteria for an affective disorder in both groups. Co-morbid neurodevelopmental conditions were less common, with autism spectrum disorder affecting 25% of patients with functional tics and 10% of patients with TS. The prevalence of both attention-deficit and hyperactivity disorder and obsessive-compulsive disorder was higher in patients with TS (30% and 19%, respectively). Similarly, tic-related obsessive-compulsive behaviors were reported considerably more commonly in association with neurodevelopmental tics than functional tics (74% versus 7%). Almost half of the patients with functional tics – but none of the patients with TS – had at least another functional neurological disorder. There were no significant differences across the two groups in the rates of patients receiving pharmacotherapy and psychotherapy. According to the results of the stepwise logistic regression analysis, absence of tic-related obsessive-compulsive behaviors ($t = 8.096$; $p < 0.001$) and absence of a family history of tics ($t = 5.111$; $p < 0.001$) were the strongest predictors of the diagnosis of functional tics.

Table 1
Demographic and clinical characteristics of patients with functional tics ($N = 83$) and age- and gender-matched patients with Tourette syndrome ($N = 83$).

	Patients with functional tic disorder	Patients with Tourette syndrome	***p*-value**
Female gender	59 (71.1%)	59 (71.1%)	1
Age at assessment	23.2 (±10.7) years (range 13–63 years)	23.5 (±10.5) years (range 13–63 years)	0.868
Family history of tic disorder	6 (7.2%)	46 (55.4%)	**<0.001**
Obsessive-compulsive disorder	3 (3.6%)	16 (19.2%)	**0.002**
Obsessive-compulsive behaviors	6 (7.2%)	61 (73.5%)	**<0.001**
Attention-deficit and hyperactivity disorder	9 (10.8%)	25 (30.1%)	**0.004**
Autism spectrum disorder	21 (25.3%)	8 (9.6%)	**0.013**
Affective disorder	32 (38.6%)	33 (39.8%)	1
Anxiety disorder	58 (69.9%)	32 (38.6%)	**<0.001**
Functional neurological disorder	39 (47.0%)	0 (0%)	**<0.001**
Non-epileptic attack disorder	31 (37.3%)	0 (0%)	**<0.001**
Other functional movement disorder	17 (20.5%)	0 (0%)	**<0.001**
Pharmacotherapy	47 (56.6%)	45 (54.2%)	0.876
Psychotherapy	32 (38.6%)	27 (32.5%)	0.517

The clinical characteristics of functional tics and neurodevelopmental tics are compared in Table 2.

There was a significant difference between the average age of patients at the onset of their functional tics (21 years) and neurodevelopmental tics (7 years). Moreover, the onset of functional tics was acute or subacute (peak of severity reached within one week or one month, respectively) in over three quarters of patients in the functional tics group, whereas all patients with TS reported a more gradual development of their symptoms. The acute onset of functional tics was related to a specific psychological trigger - typically stress or anxiety - in three quarters of patients. The rostro-caudal distribution that

Table 2
Clinical phenomenology of functional tics (N = 83) versus neurodevelopmental tics (N = 83).

	Functional tics	Neurodevelopmental tics	*p*-value
Age at onset	21.2 (±10.9) years (range 11–61 years)	6.5 (±3.7) years (range 1–16 years)	**<0.001**
Acute/subacute onset	65 (78.3%)	0 (0%)	**<0.001**
Psychological trigger	62 (74.7%)	0 (0%)	**<0.001**
Rostro-caudal distribution	13 (15.7%)	77 (92.8%)	**<0.001**
Suppressibility	37 (44.6%)	79 (95.2%)	**<0.001**
Distractibility	54 (65.1%)	76 (91.6%)	**<0.001**
Premonitory urges	28 (33.7%)	80 (96.4%)	**<0.001**
Simple motor tics	72 (86.7%)	83 (100%)	**<0.001**
Complex motor tics	67 (80.7%)	66 (79.5)	1
Blocking tics	12 (14.4%)	0 (0%)	**<0.001**
Throwing tics	16 (19.3%)	0 (0%)	**<0.001**
Simple vocal tics	65 (78.3%)	83 (100%)	**<0.001**
Complex vocal tics	65 (78.3%)	46 (55.4%)	**0.003**
Coprolalia	44 (53.0%)	27 (32.5%)	**0.012**
Copropraxia	15 (18.1%)	4 (4.8%)	**0.013**
Forced touching	8 (9.6%)	24 (28.9%)	**0.003**
Tic-related self-injurious behaviors	27 (32.5%)	6 (7.2%)	**<0.001**
Tic attacks	32 (38.6%)	0 (0%)	**<0.001**

characterises neurodevelopmental tics was absent in 86% of patients with functional tics. Tic suppressibility, distractibility, and premonitory urges were reported by over 90% of patients with TS, more frequently than by patients with functional tics. Patients with functional tics were less likely to have simple motor and vocal tics, as well as forced touching, but more likely to have coprophenomena and tic-related self-injurious behaviors. Variable proportions of them also reported complex clinical manifestations (blocking tics: 14%, throwing tics: 19%, tic attacks, defined as lengthy paroxysms of non-suppressible motor and vocal tics: 39%), which were not reported by patients with TS.

4. Discussion

To the best of our knowledge, we presented data from the largest study to date comparing the clinical characteristics of patients who developed functional tics during the COVID-19 pandemic with those of patients with neurodevelopmental tics (TS). In addition to their relatively smaller sample sizes, previous controlled studies from single-centre case series were characterised by considerable heterogeneity in the type of information collected [8–14] (Table 3).

In a further retrospective cross-sectional study, 89 patients presenting to a pediatric movement disorders clinic with a new diagnosis of functional tics were compared with a randomly selected cohort of 89 youth with TS [19]. This controlled study focused on the functional impact and level of impairment, without data on the clinical phenotypes: compared to patients with TS, patients with functional tics were found to be more commonly associated with reported visits to the emergency department, mental health service utilization, physical injury, and home schooling.

In order to facilitate direct comparison of their clinical characteristics and tic phenomenology, we matched patients with functional tics and patients with TS for both age and gender – a procedure that was followed by only one previous study with a sample size of 13 patients [8]. The control group selection process confirmed key differences in the gender pattern, with functional tics being strongly associated with female adolescents [9–13] and – to a lesser extent – young adults [14]. These findings are broadly in line with previous observations across the whole spectrum of functional movement disorders [20]. The only exception was the study by Paulus et al., which included only those patients ($N = 13$) who stated that their symptoms had started after the consumption of social media videos from a particular YouTube channel

Table 3
Selected findings from controlled studies comparing the clinical characteristics of functional and neurodevelopmental tics (statistically significant differences in bold).

Study	N of patients with functional tics vs neurodevelopmental tics (gender)	Family history of tics	Anxiety	Depression	ASD	ADHD	OCD	Age at onset	Abrupt onset	PU	Coprolalia	**SIB**
Paulus et al., 2021 [8] (Germany)	13 (38% F) vs 13 (matched)	8% vs 31%	NA	NA	8% vs 0%	8% vs 15%	23% vs 31%	**15 vs 5**	**100% vs 0%**	83% vs 92%	38% vs 8%	NA
Pringsheim et al., 2021 [9] (Canada)	20 **(95% F)** **vs** 270 **(21% F)**	NA	**75% vs 19%**	**55% vs 4%**	0% vs 6%	25% vs 44%	5% vs 19%	**14 vs 6**	100% vs NA	NA	55% vs NA	70% vs NA
Pringsheim and Martino, 2021 [10] (Canada)	9 **(100% F)** **vs** 24 **(25% F)**	NA	56% vs 25%	44% vs 8%	NA	22% vs 25%	0% vs 33%	**15 vs 10**	100% vs NA	100% vs NA	**67% vs 4%**	NA
Han et al., 2022 [11] (Australia)	22 **(100% F)** **vs** 163 **(28% F)**	14% vs 21%	**95%*** **vs** **41%***	**95%*** **vs** **41%***	9% vs 17%	14% vs 37%	23% vs 17%	**14 vs 7**	100% vs NA	NA	**77% vs 10%**	**50% vs 4%**
Trau et al., 2022 [12] (United States)	31 **(97% F)** **vs** 113 **(35% F)**	19% vs 43%	**90% vs 69%**	NA	NA	68% vs 81%	58% ^ vs 57% ^	**14 vs 5**	**100% vs 0%**	77% vs 67%	**26% vs 2%**	**61% vs 1%**
Anderson et al., 2023 [13] (Denmark)	53 **(94% F)** **vs** 200 **(31% F)**	**11% vs 33%**	26% vs 7%	NA	13% vs 8%	19% vs 16%	19% vs 8%	**14 vs 6**	NA	NA	**30% vs 2%°**	**43% vs 5%°**
Baizabal-Carvallo et al., 2023 [14] (United States)	21 **(48% F)** **vs** 156 **(22% F)**	NA	NA	NA	NA	**14% vs 44%**	**24% vs 57%**	**32 vs 9**	NA	19% vs NA	NA	0% vs 15%

Abbreviations: ASD, autism spectrum disorder; ADHD, attention-deficit and hyperactivity disorder; OCD, obsessive-compulsive disorder; PU, premonitory urge; SIB, self-injurious behavior; F, female gender; NA, not available.

* anxiety or depression.

^ obsessive-compulsive behavior.

° analysis conducted on a sub-set of 87 patients.

where a popular male influencer portrays himself as having TS - or other videos allegedly featuring TS on platforms such as TikTok [8]. Of note, onset of functional tics following exposure to social media was explicitly excluded only in the study by Baizabal-Carvallo et al. [14]. Interestingly, the previously reported trend for patients with functional tics to be less likely to report a family history of tic disorders than patients with TS reached statistical significance in our larger sample, and absence of a family history of tics was the second strongest predictor of the diagnosis of functional tics according to our linear regression model [8,11–13].

Co-morbidity profiles differed significantly between the two groups. In addition to the established link with anxiety [9,11,12], we confirmed the association between functional tics and other functional neurological symptoms, especially non-epileptic attacks [12]. The trend for affective disorders to be more strongly associated with functional tics than with neurodevelopmental tics [9–11] was not confirmed, possibly because our control matching process resulted in the inclusion of a disproportionately higher percentage of female patients with TS, who are known to be at higher risk for the development of depression [21]. Moreover, patients with TS had a considerably younger age at onset: the longer duration of their chronic condition might also have contributed to their relatively high rate of affective disorders. In our larger sample, both attention-deficit and hyperactivity disorder [8–12,14] and tic-related obsessive-compulsive behaviors/disorder [8–10,14] co-occurred more frequently with TS, thus allowing previously reported trends to reach statistical significance. Specifically, the absence of tic-related obsessive-compulsive behaviors was the strongest predictor of the diagnosis of functional tics according to our linear regression model. Previous findings on co-morbid autism spectrum disorder have been more contradictory [8,9,11,13]: the known association with male gender, together with the exclusion of patients with severe autism spectrum disorder/learning disability from our analysis, might have contributed to the relative under-representation of pervasive developmental disorders in the TS group [22]. Little is known about the association between autism spectrum disorder and functional tics, although a previous study on young patients with functional seizures found similar co-morbidity rates [23].

Our findings provided confirmation of significant differences in the clinical phenomenology between functional and neurodevelopmental tics [4–6]. We found a considerable gap between the age at onset of neurodevelopmental tics (7 years; 5–10 years in previous controlled studies) and the age at onset of functional tics (21 years; 14–15 years in previous controlled studies) [8–12,14]. This latter figure is likely to reflect our clinical setting, which spans the whole lifetime. One of the key differences between functional and neurodevelopmental tics was the acute/subacute onset, often triggered by stress or anxiety, in the absence of a clear rostro-caudal progression of symptoms in the vast majority of patients with functional tics of patients with functional tics. This is in striking contrast with the gradual development of motor and, subsequently, vocal neurodevelopmental tics, which can spread from the cephalic district to the rest of the body over the course of months to years, typically throughout childhood and adolescence [24,25]. In a recent study on 10 patients with both neurodevelopmental and functional tics (TS with functional overlay developed during the COVID-19 pandemic), within-subject comparison showed that age and modality of tic onset, as well as rostro-caudal distribution, were the only features that differed significantly between the two types of tics [18]. Tic suppressibility, distractibility, and premonitory urges were reported by over 90% of patients with TS: these figures were significantly higher than those reported by patients with functional tics, despite somewhat contradictory findings from previous controlled studies [8,10,12].

Finally, our data provided ample confirmation to the observation that patients with functional tics are less likely to have simple motor and vocal tics than patients with TS [8–14]. Specifically, coprophenomena, self-injurious behaviors, and complex clinical manifestations such as blocking tics, throwing tics, and tic attacks, were all over-represented in the functional group [12,14]. Conversely, forced touching was more commonly reported by patients with TS, possibly reflecting the more violent nature of functional tics involving interaction with the environment (e.g. hitting, banging, slapping).

Our study has limitations. The sample originated from a single specialist centre and included native English speakers only. Therefore, our findings cannot be considered representative of the different world regions in which this clinical phenomenon has been reported. The generalizability of our results is further limited by referral bias, as all patients were recruited from a tertiary referral centre, where more severe and/or complex cases are seen. Finally, controls were matched with patients with functional tics for both age and gender, resulting in a TS group characterised by an over-representation of female patients.

Despite these limitations, findings from the largest controlled study to date provide robust confirmation of specific clinical features contributing to the differential diagnosis between functional tics developed during the COVID-19 pandemic and neurodevelopmental tics reported by patients with TS. These include both patient-related variables (especially demographic characteristics, family history, and co-morbidity profiles) and tic characteristics (ranging from the clinical phenomenology to the clinical course of tics). Several open questions remain, particularly with regard to the underlying aetiology, the possible role of increased time spent on social media during the pandemic, and the implementation of tailored treatment interventions. Further research is needed, including longitudinal follow-up studies assessing the long-term outcome of functional tics. In consideration of the global impact of this condition, active monitoring is recommended during the post-pandemic era.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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