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Depression in Tourette syndrome: A controlled and comparison study

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ABSTRACT

Background: Tourette syndrome (TS) is a neurodevelopmental condition characterised by multiple tics and co-morbid behavioural problems. Previous research found that up to 76% of patients with TS experience affective symptoms, with 13% fulfilling diagnostic criteria for depression.
Objectives: We aimed to assess the severity of depression and profile of depressive symptoms in adult patients with TS compared to patients with major depression and healthy controls.
Methods: Depression ratings were collected from patients with TS ($N = 65$) using the BDI-II and from patients with recurrent major depressive disorder (rMDD, $N = 696$) and healthy controls ($N = 293$) using the Beck Depression Inventory (BDI)-IA. Direct comparisons were possible for 14/21 BDI items.
Results: Patients with TS scored significantly higher on the BDI than controls ($P < 0.001$) and all individual symptoms were reported more frequently by patients with TS than by controls ($P < 0.001$). Total BDI score in TS was not significantly different to that in rMDD, however irritability was significantly more frequently reported in the TS group and this remained significant after controlling for age and gender differences between the two groups (OR 5.24, 95% CI 1.97–14.00; $P = 0.001$).
Conclusions: Our findings show that depression is a prominent feature in TS and may present with a more irritable phenotype than rMDD. Patients with TS should be routinely screened for depression to implement treatment as appropriate.

1. Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder characterised by multiple motor and phonic tics [1]. TS is estimated to affect up to 1% of children and adolescents, as well as adults in a less severe form [2]. Symptoms wax and wane in severity over weeks, months and years, but over time patients usually show marked reductions in their symptoms [3], regardless of treatment [4].

TS is associated with a spectrum of behavioural co-morbidities in about 90% of patients [5], particularly attention-deficit and hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), impulse control disorders and affective disorders [6]. Evidence from both controlled and uncontrolled studies suggest that depression is prevalent in TS, with an epidemiological meta-analysis estimating that 13% of patients with TS fulfil diagnostic criteria for depression and 76% experience sub-threshold depressive symptoms [7]. In a large population-based cohort study conducted on 1337 patients with TS, the risk of developing depression was about 5 times higher in the TS population compared to the control cohort [8].

In a sample of children and adolescents with TS, it was found that the presence of affective disorders significantly predicted psychiatric hospitalisation [9]. Moreover, a number of studies showed that depression is associated with significant impairments to health-related quality of life [10,11], in both children [12,13] and adults [14,15] with TS. Recent research has suggested that depressive symptoms, alongside anxiety, moderate the relationship between tic severity and functional impairment in adult patients with chronic tic disorders [16]. Despite extensive research into the behavioural symptoms in young patients with TS, relatively little is known about the clinical presentation of depressive symptoms in adults with TS, apart from a recently identified association between co-morbid depression and increased values of the 'threatened self' or narcissistic vulnerability [17].

The aim of this study was to examine the severity of depression and phenomenology of depressive symptoms in adults with TS in comparison to patients with major depression and healthy controls. We anticipated to find higher depressive symptom severity in patients with TS than healthy controls and partially overlapping affective profiles between TS and major depression, in line with the documented presence of mood disorder and suicidality in patients with 'malignant' TS [18]. This is of particular relevance to clinical practice, as adult patients with TS have been shown to have a greater prevalence of mood disorders than children with TS [19].

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2. Methods

All consecutive adult patients attending the specialist TS clinic at the Department of Neuropsychiatry, BSMHFT and University of Birmingham, UK, were invited to take part in this study. Patients with a lifetime diagnosis of recurrent major depressive disorder (rMDD) and healthy controls were recruited by the multi-centre (Cardiff and Birmingham, UK) Mood Disorders Research Group (MDRG) as part of an ongoing programme of research into the genetic and non-genetic determinants of affective disorders [20]. The MDRG recruited patients with affective disorders and controls via Community Mental Health Teams across the UK and advertisements through GP surgeries, patient support organisations (e.g., Depression Alliance) and local media. Patients with rMDD were recruited when they were judged by their medical team to be well enough to participate. The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision* (DSM-IV-TR) criteria were used for the diagnosis of TS [21], whereas the DSM-IV criteria were applied to the rMDD group [22]. Patients with rMDD were recruited when relatively well and the healthy controls had no personal or family history of psychiatric illness. The studies received both local and national ethics approval and informed consent was obtained from each participant.

The demographic and clinical data of the patients with TS were gathered from participants' medical records. Each patient underwent a comprehensive clinical assessment using the National Hospital Interview Schedule for TS (NHIS-TS) [23]. The NHIS-TS is a detailed semi-structured interview schedule which covers personal and family histories and demographic details. For the diagnosis of various TS-associated psychiatric disorders, the NHIS-TS was originally developed by incorporating the relevant questions and items from the Diagnostic Interview Schedule and WHO criteria to yield a lifetime diagnosis as per DSM-III-R and ICD-10, and was subsequently updated based on the DSM-IV-TR criteria. The treating clinician (AEC) ascertained lifetime recurrent major depression. The Yale Global Tic Severity Score (YGTSS) [24] and the Diagnostic Confidence Index (DCI) [25] were completed as ratings of tic severity and lifetime cumulative symptomatology, respectively. Both the YGTSS and DCI scores range from 0 to 100, with higher scores indicating higher tic severity and diagnostic confidence of TS.

The 21-item Beck Depression Inventory (BDI) is a widely used self-report scale which measures the psychological and biological symptoms of depression over the week prior to completion. The first edition (BDI-IA) was amended to simplify the scoring structure [26], with the second edition (BDI-II) subsequently developed to reflect DSM-IV criteria for affective disorders [27]. A study comparing self-report scales for affective symptoms proposed the BDI-II as the instrument of choice for assessing depression in patients with TS [28]. In our study, all patients with TS completed the BDI-II, whilst patients with rMDD and controls completed the BDI-IA, as their recruitment preceded the enrolment of patients with TS. In developing the BDI-II, 4 items (self-image, occupational functioning, weight loss and hypochondriasis) were removed from the original BDI-IA list and replaced with questions addressing agitation, feelings of worthlessness, loss of energy and concentration difficulty. These items were excluded from our analysis, along with the items on self-dislike, sleeping pattern and appetite, because the scoring anchor points were different between the two BDI versions. The remaining 14 items had minor wording changes with intact anchor points, which allowed reliable comparisons of symptom severity. Total BDI-II scores from the TS sample were converted to BDI-IA scores using the recommended equipercentile equating method [27]. With scoring adjustments, the BDI-IA and BDI-II self-reports have previously been compared in psychiatric outpatients [29]. In the present study, to compare the frequency of different BDI items across the diagnostic groups, we assigned '0' and '1' responses as non-clinically significant ('absent'), with '2' and '3' being clinically significant ('present').

Statistical analyses were performed using the SPSS statistical package version 20.0 (IBM, Armonk, NY, USA). Continuous variables (e.g., total BDI score) were compared between diagnostic groups using Kruskal-Wallis tests (*KWH*) followed by pairwise post-hoc comparisons using Mann-Whitney tests (*MWU*). Categorical variables (e.g., presence/absence of each BDI symptom) were compared between diagnostic groups using X^2/Fisher's exact tests. Within group associations between continuous variables (e.g., between total BDI score and age) were explored using correlation analyses (Spearman's rho; ρ). The Bonferroni method was used to adjust the cut-off for a significant P value to 0.025 and control for α-inflation by multiple testing. We also carried out logistic regression analyses (enter method) to explore i) whether BDI total score and ii) which combination of BDI symptoms was/were associated with diagnostic group after controlling for demographic differences between groups (gender, age).

3. Results

A total of $N = 1054$ participants were included in the study. Demographic data for the three groups are illustrated in **Table 1**. The TS group was significantly younger ($KWH = 106.03$, $P < 0.001$), and comprised significantly more males $X^2 = 58.26$, $P < 0.001$), than the rMDD and control groups, reflecting the higher male:female ratio in TS populations. The vast majority of participants in all groups were White British.

The TS group was representative of a clinic population with characteristic symptoms (median TS DCI score 68.0% [range 33.0–100.0]) and moderate-to-marked tic severity (median YGTSS tic severity score 25.0/50 [range 11.0–46.0], with overall impairment score 20.0/50 [range 10.0–50.0]). Co-morbid diagnoses included depression (40.0%), ADHD (24.6%), OCD (23.1%, with 49.2% of patients presenting obsessive-compulsive symptoms of different degrees of severity) and bipolar disorder (7.7%). With regards to pharmacotherapy, patients were mainly treated with neuroleptics (46.2%), clonidine (21.5%) and antidepressants (30.8%). A family history of affective disorders was present in 24.6% of patients with TS.

As illustrated by **Fig. 1A**, there was a significant difference in total BDI score across diagnostic groups ($KWH = 411.52$, $P < 0.001$). Pairwise comparisons between TS and control and rMDD groups identified a statistically significant difference between TS and controls ($P < 0.001$) with TS patients scoring significantly higher than controls, but not between TS and rMDD ($P = 0.030$). **Fig. 1B** illustrates the frequencies of participants reporting the presence of each BDI symptom in each diagnostic group. There was a significant difference between groups for every symptom (all $P < 0.001$). Pairwise X^2 comparisons showed significantly higher reporting of every symptom in the TS and rMDD groups compared to controls (all $P < 0.001$). When comparing the TS and the rMDD groups, the only significant differences were that sadness ($P = 0.005$) and loss of libido ($P = 0.008$) were more frequently reported in the rMDD group, and irritability ($P = 0.006$) was more frequently reported in the TS group.

Logistic regression showed that, after controlling for age and gender, total BDI score was predictive of a diagnosis of TS compared to controls (odds ratio [OR] 1.50, 95% confidence intervals [CI] 1.33–1.69; $P < 0.001$), but not compared to rMDD. Further analysis showed that, after controlling for age and gender, the only BDI symptom that

Table 1
Demographic characteristics of the study participants.

	Controls	TS	rMDD
***N* (% female)**	293 (60.8)	65 (32.3)	696 (71.7)
Age – median (range) years	50.0 (24.0–63.0)	26.0 (16.0–65.0)	48.0 (18.0–65.0)
Ethnicity – %			
White British	100.0	89.2	97.7
White Other	–	3.1	2.2
Asian	–	6.2	–
African	–	1.5	0.1

Abbreviations: TS, Tourette syndrome; **rMDD**, recurrent major depressive disorder.