

The prognosis of Tourette syndrome: implications for clinical practice

Nadiya Hassan^a

Andrea E. Cavanna, MD, PhD^{a,b}

^a The Michael Trimble Neuropsychiatry Research Group, Department of Neuropsychiatry, University of Birmingham and BSMHFT, Birmingham, UK

^b Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology and UCL, London, UK

Corresponding author: Andrea E. Cavanna,
Department of Neuropsychiatry
University of Birmingham and BSMHFT
The Barbary National Centre for Mental Health
25 Vincent Drive
Birmingham B152FG
United Kingdom
Email: cavanna77@tin.it

Summary

Tourette syndrome (TS) is a childhood-onset neuropsychiatric condition characterised by multiple motor and phonic tics. Comorbid behavioural problems are common, especially attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). Little is known about the long-term prognosis of TS, despite the need to inform patients about their possible clinical course and advise health care providers on clinical resource allocation strategies. This paper reviews the scientific literature on the prognosis of TS spanning the period 1990-2010. After searching three scientific databases, we identified seven original studies investigating the prognosis of TS. It is suggested that tic frequency and severity decline with age in a large proportion of patients (59-85%). Predictors of increased tic severity in adulthood include higher childhood tic severity, smaller caudate volumes and poorer fine motor control. Furthermore, the presence of untreated comorbid psychopathology, such as ADHD and OCD, can adversely affect the long-term outcome of patients with TS. Future studies on the prognosis of TS should be conducted on larger samples, both in community and clinical settings.

KEY WORDS: behaviour, outcome, prognosis, tics, Tourette syndrome

Introduction

Tourette syndrome (TS) is a childhood-onset neuropsychiatric disorder characterised by multiple motor tics and at least one phonic tic that last for more than one year (1). It is estimated that TS affects up to 1% of school-age children, with a male:female ratio of approximately 4:1 (2,3). Tics are defined as sudden, intermittent, repetitive vocalisations (phonic tics) or movements (motor tics)

(4). Multiple tics, together with coprolalia (the inappropriate utterance of swear words) and echolalia (the repetition of what other people say) form the pathognomonic triad of symptoms originally described by Dr Georges Gilles de la Tourette in 1885 (3). However, more recent clinical studies have shown that coprolalia is reported in only about one third of patients seen in specialist TS clinics and in a smaller proportion of patients in the community (5).

The aetiology of TS has been explained by both genetic factors and, to a lesser extent, environmental influences (6). These explanations are based on the vertical transmission of TS (7) and emerging evidence concerning the aetiological significance of perinatal difficulties (8) and immunological abnormalities (9) respectively. Patients with TS identify stress, anxiety and fatigue as factors that worsen tics, in contrast to focusing on fine-motor movements, such as playing an instrument or dancing, which are thought to alleviate tic severity (5). In addition, tics may improve as a result of treatment, for example educational interventions, behavioural therapy, medications and functional neurosurgery (10).

It is estimated that up to 90% of patients with TS have concomitant psychopathology (3) with the most common comorbidity in children being attention deficit hyperactivity disorder (ADHD) (3). Epidemiological studies report that over 50% of individuals with TS experience ADHD (11) and document lower rates for other comorbid conditions such as obsessive-compulsive disorder (OCD) (12). In view of the fact that ADHD is responsible for adverse behavioural, social and academic performance in children with TS (13), the former diagnosis may be of greater clinical significance with regard to the treatment and management of children with TS (14).

The prognosis of TS has been extensively researched in the 127 years that have elapsed since its first description in the medical literature. Data gathered from longitudinal studies underpin our understanding of the typical clinical course of TS. Prognostic indicators carry clinical significance in terms of helping to inform patients of the long-term outcomes of their disorder, and directing their follow up and management. Moreover, such information would be of great value from the perspective of advising health care providers on clinical resource allocation strategies. This article reviews the published scientific literature concerning the prognosis of TS, focusing particularly on implications for clinical practice.

Methods

A computerised literature search was conducted using three databases (PsychINFO, Medline and EMBASE) accessed via the Birmingham and Solihull Mental Health NHS Foundation Trust online library resources. Searches were conducted using the following search terms: "Tourette*" or "tic disorder", and "prognosis", "outcome",

“longitudinal studies,” “follow-up studies,” or “disease course.” The titles and abstracts of all retrieved articles were reviewed by the authors and all irrelevant papers were excluded. In addition, papers published before 1990 and those not written in English were eliminated. Finally, the references of all eligible full-text articles were examined for potentially relevant studies.

Results

Our initial database search yielded 125 articles. After reviewing all the abstracts, 106 papers were excluded as irrelevant to the purpose of this review. A further 12 articles were not eligible as they were written in a language other than English or published before 1990. Therefore

we identified seven relevant original studies on the prognosis of TS, which are described in Table 1. A few additional studies retrieved from the reference lists of the original articles are cited in the Discussion section.

Discussion

Tics

Our understanding of the prognosis of TS has developed gradually over the last two decades owing to longitudinal research, which has highlighted the typical clinical course of TS, focusing particularly on the longitudinal course of tic symptoms.

Table 1 - Original studies on the prognosis of Tourette syndrome (1990-2010).

Study	Population	Methodology	Main findings
Gorman et al., 2010 (15)	65 individuals with TS (identified in childhood) and 65 matched controls without tic or OCD symptoms	Controlled study; assessment of psychosocial functioning and psychiatric symptoms at 18 years of age.	Higher rates of psychopathology in patients with TS compared to controls. Poorer psychosocial outcomes associated with greater tic, ADHD and OCD severity.
Bloch et al., 2006 (16)	46 children with TS	Prospective cohort study; clinical evaluation before age 14 years and follow up 7.6 years later.	Reduction in tic symptoms during adolescence reported by 85% of patients.
Bloch et al., 2005 (17)	43 children with TS	Prospective longitudinal study; measurement of basal ganglia volume before age 14 years and follow up after age 16 years.	Caudate volumes are inversely proportional to severity of tic and OCD symptoms in early adulthood.
Hoekstra et al., 2004 (18)	52 paediatric and adult patients with tic disorders	Prospective longitudinal study; administration of weekly questionnaire comparing incidence of small life events with tic severity.	Weak positive association between small stressful life events and tic severity ($r=0.268$, $p<0.001$).
Pappert et al., 2003 (19)	31 patients with TS (first recruited as children)	Longitudinal study; videotape assessment of each patient in childhood and in adulthood.	90% of patients retained their tics, however tic frequency and severity improved.
Burd et al., 2001(20)	39 patients with TS	Prospective longitudinal study; patient interviews with 507 person-years of follow up.	44% of patients were symptom-free at follow up.
Carter et al., 1994 (21)	34 children without tics but with first-degree relatives with TS.	Prospective longitudinal study; assessment of diagnostic status, family functioning and social-emotional functioning.	Demonstration of increased rates of tic disorders. Poor family functioning associated with anxiety disorders and lower self-esteem.

Abbreviations: TS=Tourette syndrome; OCD=obsessive-compulsive disorder; ADHD=attention deficit hyperactivity disorder

Tic symptomatology

Tics are defined as sudden, non-rhythmic, stereotyped motor movements or vocal productions that are performed repetitively by patients with TS (22). Tics are reported to begin in the first decade of life. Motor tics typically present between 4 and 6 years of age (23), whilst phonic tics tend to develop one to two years after the first motor tic (6). Tics characteristically vary in type, severity, frequency and localisation (4). For example, in a prospective study by Burd et al. (20), 15% of patients with TS reported that tics were most severe in the afternoon, although 46% were unable to identify a temporal pattern of their tics.

Factors affecting tic severity

The frequency and intensity of tic symptoms spontaneously wax and wane over time (24). Moreover, it is reported that tics are exacerbated by many factors, predominantly fatigue, anxiety and stress (6). However, the relationship between the latter factor and tic severity is under-researched and largely based on patients' subjective reports (18). For instance, a questionnaire-led longitudinal study conducted by Hoekstra et al. (18) recorded the occurrence of stressful life events and self-ratings of tic severity on a weekly basis. The authors concluded that life events do not account for changes in tic severity (18). Increased core body temperature has been reported as an alternative cause of tic exacerbation (25,26). By contrast, tics typically improve upon undertaking fine motor movements, for example, playing a musical instrument or dancing (6). Additionally, there is evidence to suggest that tics can be voluntarily controlled through active suppression (27). This may result in the accumulation of "inner tension", as it is known, which in turn leads to rebound in tic severity (24).

Clinical course of tics

The clinical course of tic severity has been shown to worsen throughout childhood with a peak occurring at approximately 10 years of age on average. This is usually followed by a steady decline in tic severity usually during the second decade of life (28). Therefore, the majority of TS patients have positive prognoses with respect to tic symptoms. A complete remission of tics is documented by several studies, including a study by Burd et al. (20), in which 44% of the recruited patients were essentially symptom-free at follow up in early adulthood. More recently, Pappert and colleagues reported that 10% of a cohort of patients with TS followed up from childhood to adulthood experienced complete tic remission (19).

Longitudinal research has shown that some patients do not demonstrate complete tic remission but, alternatively, experience a decline in tic frequency and severity over time. Between 59% and 85% of patients with TS are estimated to experience a decline in tic symptoms according to follow-up studies by Bloch et al. (16), Burd et al. (20), Erenburg et al. (29) and Zausmer et al. (30). Typically, motor tics tend to show significant improvement (19), and males demonstrate more improvement than females (20). The reported differences in tic improvement may be attributable to the fact that subjects

were from different geographical locations, were taking different medications and were assessed using different psychometric instruments, including self-report rating scales.

Although the majority of patients experience an improvement or even complete remission of tic symptoms, a proportion of them develop increased tic severity. In a prospective study, Burd and colleagues (20) found that 10.3% of patients with TS experienced greater tic severity at follow up. It has been shown that higher tic severity during childhood is significantly associated with increased tic severity at follow up in adulthood, suggesting that this factor plays a role in the prognosis of TS (16).

Prognostic indicators of adult tic severity

Several studies have attempted to ascertain whether other clinical or physiological measures can be used as prognostic indicators for children with TS. In one recent prospective longitudinal study, it was hypothesised that the volume of the caudate nucleus during childhood can determine the course of tic and OCD symptoms into adulthood (17). The authors concluded that the caudate volumes in childhood were inversely proportional to the severity of early adulthood tic and OCD symptoms (17). A further potential prognostic factor is fine motor control, which is thought to be related to the activity of the caudate nucleus (31).

Comorbid conditions

Tourette syndrome is recognised as a condition that frequently co-occurs with behavioural problems, with approximately 90% of patients having comorbid conditions such as ADHD, OCD, anxiety and self-injurious behaviours (32).

PRESENTATION OF COMORBID CONDITIONS

In one prospective study, it was reported that 41% of the TS cohort had experienced at least moderate OCD symptoms at one time (16). These OCD symptoms were reported to have presented in late childhood or early adolescence, with their peak severity occurring approximately two years after the peak tic severity. This finding highlights the importance of thorough clinical follow up of all patients even when tic severity declines.

Although TS is rarely described as a life-threatening condition, Cheung and co-workers estimated that 5% of patients referred to specialist TS clinics have critical symptoms (12). It is hypothesised that these individuals, who suffer from what is referred to as "malignant TS", are at higher risk of developing severe tic symptoms due to possessing at least two behavioural comorbidities (12). Specifically, OCD has been identified as a risk factor for malignant TS, thus highlighting the extent to which this comorbid condition can influence tic severity (12). Similarly, in a recent case report of a child with TS and OCD who developed the delusional belief that he had caused a major catastrophic event, it was suggested that comorbid OCD worsens the prognosis of TS (33). Hence, it is essential to monitor all patients with TS for comorbidities as part of their routine clinical assessment.

EDUCATIONAL IMPLICATIONS OF COMORBID PSYCHOPATHOLOGY

In addition to the tic symptomatology and behavioural problems exhibited by patients with TS, it is important to assess the cognitive status of children with tic disorders. Although most investigators described a decline in tic severity during adolescence, it cannot be assumed that there will automatically be a congruent improvement in academic ability. In fact, the authors of one follow-up study reported that just over a half of their cohort experienced educational or social dysfunction during adolescence or adulthood (19). However, all the subjects completed high school and approximately three-quarters subsequently entered full-time higher education or employment (19). In the presence of comorbidities, academic performance may suffer more. For instance, a recent review of the existing literature on TS showed that patients with TS and comorbid ADHD, compared with patients without ADHD, are more likely to display signs of cognitive dysfunction, leading to impaired school performance (4). This observation has implications as regards the degree to which the academic development of young patients with TS and comorbid ADHD should be monitored.

PSYCHOSOCIAL IMPLICATIONS OF COMORBID PSYCHOPATHOLOGY

As well as cognitive and academic dysfunction, it is noteworthy that patients with TS can also develop psychological, social and emotional problems. There is evidence to suggest a relationship between TS symptom severity and psychosocial functioning with greater tic, OCD and ADHD severity being associated with poorer psychosocial outcome (15). In addition, a study by Carter et al. (21) found a significant difference between children with tic disorders and unaffected children in two socio-emotional domains. In this study, perceived physical attractiveness was given lower ratings by patients with TS compared with unaffected children; moreover, the family unit was shown to influence the emotional state of patients with TS, with children in families with low cohesion being more likely to exhibit affective difficulties (21). Finally, the multi-dimensional construct of health-related quality of life has recently been shown to be profoundly affected by TS (34-36). This emphasises the need to provide a complete assessment of TS, which incorporates the psychosocial, emotional, behavioural and physical symptoms of the condition.

Limitations and suggestions for further research

The prospective studies reviewed in this paper have numerous limitations. For instance, various studies obtained data using self-report measures, which can introduce bias as a result of the possible inconsistency of patients' subjective estimates. Indeed, Pappert et al. (19) found that 50% of their patients who considered themselves tic-free actually demonstrated multiple tics on videotape. Therefore, there is a need for further studies to document tic severity over time using objective measures. Moreover, future research should aim to increase sample sizes and longitudinal follow-up duration. The body of literature concerning TS suggests that there is a need for further research on specific aspects of tic

symptomatology. In particular, there is a need for research that aims to identify reliable clinical measures, which can be used as prognostic indicators for children with TS who present with increased tic severity at follow up. Additionally, clinical practice may benefit from future research to confirm preliminary observations regarding differences in prognosis between male and female patients with TS. Finally, timely diagnosis of the rare cases of malignant TS is extremely important clinically; further research is needed to establish the risk factors associated with this subgroup of patients.

Concluding remarks

Longitudinal studies have reliably found that the majority of TS patients will experience an improvement in tic severity, and that those patients with chronic motor or vocal tic disorders alone will have more favourable outcomes (16,20,29,30). However, comorbid psychopathology is very common in TS populations. In fact, "...tics alone are the exception rather than the rule" (24), and it is the presenting psychiatric comorbidities, namely ADHD or OCD, that often determine the overall outcome of TS (24). This review suggests that tic severity is influenced by stressful life events, active suppression, caudate nucleus volume and fine motor control, in addition to behavioural comorbidities. It is important to highlight the implications that our greater understanding of the prognosis of TS has for clinical practice and health resource allocation. To this end, it is imperative for clinicians to thoroughly follow up patients in order to tailor therapeutic approaches to their early prognostic indicators and to recognise the development of any comorbid conditions. Ultimately, this may pave the way for improved clinical care of patients with TS in the future.

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