



Specific executive control impairments in Tourette syndrome: The role of response inhibition



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ABSTRACT

Background: Tourette syndrome (TS) is a childhood-onset disorder characterized by motor and vocal tics. While cognitive features of common comorbid conditions such as attention deficit hyperactive disorder and obsessive compulsive disorder have been widely investigated, the cognitive profile of TS patients remains to be precisely defined. In this regard, the executive functions system (EF) is of especial interest.

Aims: The aim of the study was to delineate the various components of executive processes in adult TS patients.

Methods: A sample of 19 adults diagnosed with TS and 19 age-matched control subjects underwent computerized battery of executive tasks, as well as block design and memory tests. All patients received a thorough clinical assessment with an emphasis on illness severity.

Results: There was a marked impairment in response inhibition ability regardless of comorbid conditions. In addition, there was decreased accuracy in set shifting, but not in response time. These results imply that impaired response inhibition in the EF system is the primary cognitive impairment in TS and that many of the previously reported impaired executive functions in TS are secondary to this impairment.

Conclusions: This finding of impaired response inhibition in TS may imply that rehabilitation of this inhibition component could prove to be an important therapeutic strategy in adults with TS.

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What this paper adds?

Here we aimed to resolve recent contrasting reports regarding executive functioning in patients with Tourette Syndrome (TS). We showed a marked impairment in the response inhibition ability in adult TS patients, regardless of comorbid conditions. Thus it appears that response inhibition is a major feature of TS and that other executive abilities previously found to be impaired in the literature are secondary to this impairment. This finding of selective impairment in response inhibition in TS underscores the potential of inhibition component rehabilitation as a therapeutic strategy in TS.

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1. Introduction

Tourette syndrome (TS) is a developmental neuropsychiatric childhood-onset disorder characterized by involuntary and premonitory urge-driven motor and vocal tics (Albin & Mink, 2006). The onset of tics is around 6–7 years, and the diagnosis is made if the symptoms persist for at least 12 months (Leckman et al., 1998; Leckman et al., 2014; Shprecher, Rubenstein, Gannon, Frank, & Kurlan, 2014). The usual pattern begins with motor tics, preceding the vocal tics which usually appear several years later (Robertson et al., 1999). The severity, intensity and frequency of tics usually peak during the second decade of life, at age 11–14 in average, with a significant reduction by the end of the second decade of life (Bloch et al., 2006; Leckman et al., 1998; Leckman, King, & Bloch, 2014) and may remit completely by adulthood (Walkup, Ferrão, Leckman, Stein, & Singer, 2010). However, 20% of patients will continue to show symptoms through adulthood (Bloch et al., 2006; Bloch, State, & Pittenger, 2011).

While the neurological basis of TS is unclear at this time, it is generally agreed that cortical–striatal–thalamic–cortical (CSTC) circuits as well as the basal ganglia are likely to be dysfunctional (Albin & Mink, 2006; Jackson et al., 2011).

Tic regulation and control are widely associated with inhibitory cognitive control processes, which are part of the Executive Function (EF) system (Jackson, Draper, Dyke, Pépés, & Jackson, 2015; Kalsi, Tambelli, Aceto, & Lai, 2015). EF is a complex cognitive processing mechanism requiring the co-ordination of several sub processes to achieve a particular goal (Elliott, 2003). EF includes abilities of goal formation, planning, set shifting, response inhibition, carrying out goal-directed plans, and effective performance (Jurado & Rosselli, 2007).

The relationship between EF and TS is not clear. While some studies showed no differences in EF between TS patients and normally developing individuals (Bornstein, 1991; Verté, Geurts, Roeyers, Oosterlaan, & Sergeant, 2005), others did find EF impairments in TS patients (for example, Channon et al., 2009; Eddy et al., 2012). In addition, and contrary to these findings, Mueller et al. reported increased levels of cognitive control in a group of young TS patients (under 18 years old) compared to an age-matched control group (Mueller, Jackson, Dhalla, Datsopoulos, & Hollis, 2006). These findings have led Jackson et al. to speculate that some young TS patients show reorganization of pre-frontal areas to allow for enhanced EF as a compensation mechanism of the syndrome (Jackson et al., 2011). In another study, an enhanced shifting ability, a central component of EF, was found in young TS subjects compared to a control group. Interestingly, individuals with TS, who did not show better EF performance, had higher tic severity than the subjects with TS who did show enhanced shifting ability (Jung, Jackson, Nam, Hollis, & Jackson, 2014). A recent review of these and other findings suggested that this better performance can be attributed to increases in gamma-Aminobutyric acid (GABAergic) ‘tonic’ inhibition in motor regions related to motor planning which results in reduction in motor excitability (Jackson et al., 2015).

It seems that there are several reasons for these contradictory findings. First, comorbid conditions such as attention-deficit/hyperactivity disorder (ADHD) and Obsessive-compulsive disorder (OCD) are highly prevalent in TS patients (Jackson, Mueller, Hambleton, & Hollis, 2007). Both these conditions are associated with changes in EF. Thus deficits in cognitive flexibility, which is a major part of EF, are seen in OCD (Gu et al., 2008), and deficits in cognitive control are commonly associated with ADHD (Barkley, 1997). Thus, Ozonoff et al. found that patients who were not diagnosed with any other comorbid condition (‘uncomplicated TS’), performed similarly to typically developed individuals on executive measures (Ozonoff et al., 1998). However, this study also found that TS patients with high tic severity, showed executive impairments, regardless of comorbidity. Another study found positive correlations between explosive outbursts, described as impulsive behaviors, and the number of comorbid conditions (Budman, Bruun, Park, Lesser, & Olson, 2000). Taken together with recent studies which found executive impairments in uncomplicated TS patients (Channon et al., 2009; Eddy et al., 2012), the overall picture remains unclear.

Yet another source for these conflicting results is the subjects’ age. While the majority of studies reporting enhanced EF abilities based their findings on young TS patients (Jackson et al., 2007; Jackson et al., 2011; Jung et al., 2014; Mueller et al., 2006), studies which tested adult patients reported impaired EF abilities (for example, Channon et al., 2009; Eddy et al., 2012). Moreover, the previously mentioned study reporting executive impairments only for TS patients with comorbid conditions, recruited young subjects (Ozonoff et al., 1998), and studies that found EF impairments in uncomplicated TS based their findings on adults (Channon et al., 2009; Eddy et al., 2012; Goudriaan, Oosterlaan, de Beurs, & van den Brink, 2006). This discrepancy has led some researchers to view the adult form of TS to be a unique condition (Jackson et al., 2015). A recent study examined cortical motor excitability in TS patients at different ages, and found increased motor threshold, increased motor evoked potential (MEP) variability, and reduced increase in motor excitability in children, but not in adults TS (Pépés, Draper, Jackson, & Jackson, 2016). The authors suggest that this is due to a developmental delay in the maturation process of certain brain networks related TS symptoms (Pépés et al., 2016).

One more explanation for the inconsistent findings regarding EF is the use of different cognitive tasks for measuring EF abilities. The findings mentioned above were based on different tasks and measures such as the Stroop task (Channon et al., 2009), flanker task (Channon et al., 2009), Go-No Go (Thomalla et al., 2014) stop-signal task (Ganos et al., 2014), set shifting task (Watkins et al., 2005) and oculomotor switching task (Mueller et al., 2006). Apparently, these tasks explore different executive processes (Kalsi et al., 2015), although the majority of studies describe their findings as global undifferentiated cognitive traits such as *cognitive control* or *executive control*.

It appears seems that some of the executive abilities which were traditionally related to TS, such as response inhibition and set shifting, correlate with one another, are separable to some extent although highly inter-correlated (Miyake et al., 2000). In this comprehensive framework, most of the EF system was fitted to a 3 factor model, including 9 different executive

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