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Review

Cognitive control over motor output in Tourette syndrome

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ABSTRACT

Tourette syndrome [TS] is a neurodevelopmental disorder characterised by chronic vocal and motor tics. TS has been associated with dysfunctional cognitive (inhibitory) control of behaviour, however the evidence for this, beyond the occurrence of tics, is scant. Furthermore, in recent studies of uncomplicated TS, it has been shown that adolescents with TS exhibit paradoxically enhanced cognitive control of motor output, consistent with the typical developmental profile of increasing control of tics during adolescence. Here we present arguments, together with new data, that run counter to the widely held view that prefrontal cortex (PFC) is the source of inhibitory task-control signals. Instead, we argue that PFC should be viewed as a source of facilitatory signals that bias competition in brain areas more directly involved in motor execution. Importantly, we argue that in TS, over-activation of PFC may contribute to the hyper-excitability of motor regions and the occurrence of tics; and that compensatory changes, leading to enhanced cognitive control in TS, may primarily be implemented by distributed changes in local cortical excitability.

Contents

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1. Introduction

Tourette syndrome [TS] is a developmental neurological disorder that lies at the extreme of the tic disorder spectrum and is characterised by the presence of chronic vocal and motor tics (Leckman, 2002). Tics are involuntary, repetitive, stereotyped behaviours that occur with a limited duration (Leckman, 2002). Motor tics can be simple or complex in appearance, ranging from repetitive movements to coordinated action sequences. Verbal tics can consist of repeating words or utterances (palilalia), producing inappropriate or obscene utterances (coprolalia), or the repetition of another's words (echolalia). Tics occur in bouts, typically many times in a single day, and are the most common form of movement disorder in children (with a prevalence that ranges between 1 and 29% depending upon the precise characteristics of the study population, the diagnostic criteria used, and the study design and methods employed).

Individuals with TS perceive a relatively constant demand to suppress their tics in social situations, and while the voluntary suppression of tics is possible in many cases, individuals with TS report that it can be uncomfortable and stressful to suppress tics, and that the urge to tic becomes uncontrollable after a period of suppression. Importantly, individuals with TS report that their tics are often preceded by 'premonitory sensory phenomena' (PSP) that they describe as uncomfortable cognitive or bodily sensations (e.g., tension, pressure, tickle, etc.), that precede the execution of a tic, and are experienced as a strong urge for motor discharge (Bliss, 1980; Banaschewki et al., 2003). Brain imaging evidence indicates that the source of PSPs may be associated with brain activity within the insular and cingulate motor areas of cortex (Bohlhalter et al., 2006; Jackson et al., 2011b).

While the neurological basis of TS is unclear at this time, it is generally agreed that cortical–striatal–thalamic–cortical (CSTC) circuits are likely to be dysfunctional, and a specific model of basal ganglia dysregulation in TS has been proposed as follows. Subsets of striatal neurons (matrisomes) are thought to become abnormally active in inappropriate contexts, leading to the disinhibition of thalamo-cortical projections that in turn lead to tics. Activity-dependent dopamine inappropriately reinforces such activity leading to stereotyped repetition of behaviour (Albin and Mink, 2006).

A widely held view is that the disinhibition of CSTC circuits gives rise to an impairment of executive or cognitive control of motor behaviour, characterised by a reduced behavioural inhibition (e.g., Channon et al., 2009). While this proposal is consistent with the observation that individuals with TS have difficulties suppressing their tics, there is in fact surprisingly little convincing evidence that individuals with TS are impaired on formal tests of executive function; as behavioural studies of executive function or cognitive control in TS have produced mixed findings (see below). Furthermore, recent studies of cognitive control of motor outputs in situations with high response-conflict demand have in fact shown that individuals with 'uncomplicated' TS (i.e., those without co-morbid disorders such as ADHD) exhibit paradoxically enhanced volitional control over their motor behaviour (Mueller et al., 2006; Jackson et al., 2007, 2011a,b). This finding is consistent with the proposal that the frequent need to actively suppress tics leads to a generalised enhancement in the efficacy of volitional control mechanisms in TS that extends to laboratory tasks of cognitive control of motor output.

1.1. Factors contributing to the mixed findings for cognitive control in TS

In our view the following factors likely contribute to the mixed findings reported thus far on the issue of whether individuals with TS exhibit an impairment of inhibitory or executive control of behaviour. First, previous studies have sought to address this question using a variety of behavioural tasks, for instance the Stroop task (e.g., Ozonoff and Jensen, 1999; Channon et al., 2003a,b), flanker task (e.g., Crawford et al., 2005; Channon et al., 2006), Go-NoGo task (e.g., Ozonoff et al., 1994; Serrien et al., 2005; Watkins et al., 2005), stop-signal task (e.g., Li et al., 2006), and continuous performance task (e.g., Harris et al., 1995). These tasks may differ markedly in the cognitive demands that they impose and the psychological processes or mechanisms involved in efficient task performance. In our view it is extremely unlikely that all of these tasks tap a single behavioural 'inhibition' mechanism or process that is impaired in TS.

Second, studies that do report finding an executive function impairment in individuals with TS, have often failed to exclude individuals presenting with co-morbid conditions such as ADHD (co-morbidity estimated at ~50%) or OCD (co-morbidity estimated at ~40%), that may themselves be associated with executive dysfunction (e.g., Bornstein, 1991; Georgiou et al., 1995; Farber et al., 1999; Dursun et al., 2000). By contrast, when such individuals have been excluded, and studies have been carried out on individuals with 'uncomplicated' TS, then many studies report no behavioural differences between groups (e.g., Ozonoff et al., 1998; Rice & Weyandt, 2000; Mostofsky et al., 2001; Channon et al., 2006), or report significantly enhanced performance in the TS groups (e.g., Mueller et al., 2006; Jackson et al., 2007, 2011a).

Third, studies reporting an executive impairment in individuals with TS have often been based upon sampling only adults with the disorder or mixed samples containing both adults and children (e.g., Silverstein et al., 1995; Farber et al., 1999; Channon et al., 2003a,b, 2009). Such studies may in fact be unrepresentative of the 'typical' presentation of TS for the following reason. TS typically follows a developmental timecourse that is associated with increasing control over tics (Leckman, 2002), and appears to be accompanied by compensatory, neuroplastic, alterations in brain structure and function in many individuals with TS, but not all (Plessen et al., 2004; Mueller et al., 2006; Jackson et al., 2007; Plessen et al., 2009; Jackson et al., 2011a). TS usually first presents during early childhood (~4–7 years), and the severity of tics follow a remitting pattern with increasing age. Tic severity is maximal between 11 and 14 years, but tics typically decrease by early adulthood. Importantly, approximately 70–80% of TS sufferers who present with marked tic severity at around 12 years of age have either mild tics or are free of tics by 18 years of age (Leckman et al., 2006). Importantly then, the majority of individuals with TS appear to develop a means of controlling and effectively suppressing their tics by early adulthood, but a substantial minority continue to have severe tics throughout their adult life. For this reason, studies based on adults with TS, or mixed samples of adults and children with TS, may be unrepresentative of the 'typical' TS presentation.

Fourth, if individuals with TS do follow a developmental timecourse that is accompanied by compensatory, neuroplastic, alterations in brain structure (Plessen et al., 2009; Jackson et al., 2011a) and function (Mueller et al., 2006; Jackson et al., 2007, 2011a) which are associated with increased cognitive control over