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Review article

Neuropsychological aspects of Tourette syndrome: A review

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Abstract

Tourette syndrome (TS) is assumed to result from frontostriatal dysfunction, which would be expected to result in impairments in neuropsychological functions. This possibility has been explored in a number of studies that have assessed the performance of patients with TS within major cognitive domains and on tests involving executive functioning. We aim to summarize the main findings of these studies while evaluating the influence of task limitations and potentially critical confounding factors such as the presence of comorbidity. Although there is clearly a need for improved study design, we tentatively suggest that there is considerable evidence for cognitive impairment in a subgroup of patients, and that some difficulties seem to be intrinsic to TS. These impairments may reflect dysfunction of the anterior cingulate network within the frontostriatal pathway.

Keywords: Tourette syndrome; Neuropsychology; Executive functions; Cognition

Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder that is most commonly diagnosed in childhood or early adolescence [1]. The core symptoms of TS include multiple motor tics and one or more phonic tics, which last for more than a year. The tics may be simple or complex in nature and vary in number, frequency, and severity over time. Comorbid disorders include anxiety, depression, learning difficulties, and sleep disorders, although attention deficit/hyperactivity disorder (ADHD) and obsessive–compulsive disorder (OCD) are most common [2].

Tics may reflect changes in striatal functioning [3], and studies of patients with TS have indicated structural changes within the basal ganglia such as decreased volume of the left side of the caudate, putamen, and globus pallidus [4], and decreased striatal metabolism [5]. Striatal changes may result in dysfunction within frontostriatal circuits, which are formed through connections between the striatum and different regions of the frontal cortex [6]. Dysfunction within circuits involving cortical motor regions is likely to lead to tics. However, three of these parallel circuits involve frontal areas that are likely to subserve cognitive functions—the lateral orbitofrontal cortex, the dorsolateral prefrontal cortex, and the anterior cingulate cortex—and dysfunction within these circuits may lead to cognitive impairments [7]. Support for frontal dysfunction in TS has been provided by studies indicating changes in the activity and metabolism of this region [5,8,9].

Frontostriatal dysfunction has been associated with significant deficits in cognitive functions in other disorders of the basal ganglia such as Parkinson's disease [10–12] and Huntington's disease [13,14]. A considerable number of studies have similarly shown patients with TS to have related cognitive impairments. However, the exact nature of the

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deficits attributable to TS, rather than to comorbid disorders, has yet to be elucidated.

This review will summarize findings in core domains (visual perceptual, motor, attention, memory, and learning) and will then discuss patients' performance on tasks involving higher cognitive or executive functions (working memory, fluency, planning, shifting, and inhibition). The discussion will focus on the possible implications of patients' deficits on dysfunction within three specific frontostriatal pathways involving the dorsolateral prefrontal, orbitofrontal, and anterior cingulate cortices. The dorsolateral prefrontal cortex is implicated in cognitive flexibility [15], memory [16], and attentional processes [17]; orbitofrontal dysfunction is more selectively associated with deficits in reinforcement and reversal learning tasks [18]; and the anterior cingulate cortex is important for conflict monitoring and resolution [19] and is active during tasks involving response inhibition [20].

Recent factor analytic studies [21] have shown that there may be more than one TS phenotype. Among these, the "pure TS" phenotype (patients with "uncomplicated" TS, i.e., without comorbid psychiatric conditions) has been consistently replicated [2,22,23] and accounts for about 10% of patients diagnosed with TS in both community [24] and clinical [25] settings. Due to the high rates of comorbidity in TS, many studies have included patients with symptoms of ADHD or OCD. Patients with ADHD alone may exhibit deficits in response inhibition [26], working memory [27], and cognitive flexibility [28], while OCD has been associated with poor reversal learning [29] in addition to inhibitory dysfunction [30]. Special attention has been paid to the issue of comorbidity, although we will consider the potential influence of other sample and task limitations. Despite these difficulties, some preliminary conclusions about the nature and basis of cognitive impairment in TS can be drawn.

Perceptual, motor, and visuomotor performance

The most relevant studies providing support for difficulties in fine-motor, perceptual, and visuomotor skills are shown in Table 1. A number of studies have reported that children with TS exhibit deficits in visuomotor integration skills based on performance on the Beery Visual Motor Integration Test (Beery VMI) [31], although one study reported no impairment [32]. Furthermore, some of these studies have indicated that patients' deficits are unlikely to be due to comorbid ADHD [33,34]. The results of studies that have assessed performance on design-copying tasks, such as the Rey Osterreith Complex Figure Test (ROCFT), are more varied. Harris et al. [35] found evidence for a deficit in children with TS and comorbid ADHD, but not in those with TS only. In contrast, another study [34] showed that TS patients without ADHD exhibited impairment similar to the impairment exhibited by those with comorbid ADHD, and that these difficulties were unrelated to poor attention or motor inhibition. Other studies, however, failed to reveal significant deficits in groups of TS patients, including "uncomplicated" cases [32,33,36].

Poor performance on visuomotor integration tasks could reflect deficits in either the component skills that contribute to task performance or the combination of these abilities; thus, research has addressed performance within perceptual and motor domains. In a study of monozygotic twins, Randolph et al. [36] found that greater tic severity was associated with poorer performance on a face perception task. However, the children with TS in this study did not exhibit deficits on a block-design task, and comorbid ADHD may have influenced some patients' performance. Children with TS also performed poorly on a motor free visual perception test in one study [37], and there are also indications of perceptual deficits on performance IQ tests in children [38] and adults [39] with TS. Other studies have reported intact performance on perceptual integration [35] and line orientation [31] tasks.

There is stronger evidence of disrupted motor performance in TS. While research has revealed little evidence of changes in motor speed performance during finger-tapping tasks [40–42], many studies have highlighted impairments in motor skills on the Purdue Pegboard [33,36,43], but few have controlled for comorbid ADHD [33,34]. Subjects with TS have also been shown to perform poorly on the Grooved Pegboard [40,42], although one study [31] found only a trend for poorer performance in the TS group. These motor impairments are perhaps likely to reflect basal ganglia dysfunction, and some similar deficits have been reported in Parkinson's disease [44]. Schultz et al. [34] suggested that deficits in TS on these tasks could lie in the synthesis of perceptual and motor inputs, whereas Margolis et al. [43] suggested that poor performance may reflect poor motor integration across the hemispheres, and that changes in interhemispheric connectivity in TS may also explain the increased corpus callosum sizes exhibited by their patient sample. Support for this claim may be provided by other studies that have reported abnormalities of the corpus callosum in TS [45].

In summary, the evidence for deficits in perceptual processes in "uncomplicated" TS is certainly limited, and while difficulties in motor skills may contribute to impairments reported on visuomotor integration tasks, further research is needed to establish whether such difficulties are independent of comorbid ADHD.

Attention

A number of studies have provided evidence for the presence of attentional deficits in TS, and the most relevant findings are listed in Table 2. The presence of comorbid ADHD plays a central role in the investigation of possible attentional impairment in TS. Channon et al. [46] found