Neuroscience and Biobehavioral Reviews 80 (2017) 240–262

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

The puzzling question of inhibitory control in Tourette syndrome: A meta-analysis

Simon Morand-Beaulieu[a,b,c,*], Stéphanie Grot[b,d], Jacob Lavoie[b,c], Julie B. Leclerc[b,e], David Luck[b,c,d,*,&], Marc E. Lavoie[a,b,c,d,*,&]

[a] Cognitive and Social Psychophysiology Lab, Montreal, Qc, Canada
[b] Centre de recherche de l'Institut universitaire en santé mentale de Montréal, Montreal, Qc, Canada
[c] Département de neurosciences, Université de Montréal, Montreal, Qc, Canada
[d] Département de psychiatrie, Université de Montréal, Montreal, Qc, Canada
[e] Département de psychologie, Université du Québec à Montréal, Montreal, Qc, Canada

ARTICLE INFO

Keywords:
Tourette syndrome
Tic disorders
Comorbidity
Attention deficit hyperactivity disorder
Impulsivity
Inhibition
Inhibitory control
Neuropsychology

ABSTRACT

Tourette syndrome (TS) is a neuropsychiatric disorder involving motor and phonic tics. Inhibitory control is a key issue in TS, and many disruptive or impulsive behaviors might arise from inhibitory deficits. However, conflicting findings regarding TS patients' inhibitory performance in neuropsychological tasks have been reported throughout the literature. Therefore, this meta-analysis aimed to evaluate inhibitory control through neuropsychological tasks, and to analyze the factors modulating inhibitory deficits.

To this end, a literature search was performed through MEDLINE and PsycINFO, to retrieve studies including neuropsychological tasks that assessed inhibitory control in TS patients. Of the 4020 studies identified, 61 were included in the meta-analysis, for a total of 1717 TS patients.

Our analyses revealed a small to medium effect in favor of inhibitory deficits in TS patients. This effect was larger in TS + ADHD patients, but pure TS patients also showed some inhibitory deficits. Therefore, deficits in inhibitory control seem to be an inherent component of TS, and are exacerbated when ADHD is concomitant.

1. Introduction

Tourette syndrome (TS) is a neuropsychiatric disorder involving motor and phonic tics. Those tics, are semi-voluntary, sudden and repetitive. Even though tics can be managed though behavioral therapy (Leclerc et al., 2016; McGuire et al., 2014; O'Connor et al., 2016; Wile and Pringsheim, 2013), the presence of such tics leads to think that inhibitory control could be impaired in TS. For example, thinking or talking about tics relates directly to tic onset due to anticipatory vigilance and psychological awareness, suggesting poor inhibition and impulse control in these patients (O'Connor et al., 2014). Furthermore, some individuals with TS have important socially disinhibited tics (Hirschtritt et al., 2016). Various disruptive and impulsive behaviors might also emerge from such impairment in inhibitory control (Stern et al., 2008; Wright et al., 2012).

1.1. Comorbidity and impulsive behavior in TS

In TS, comorbidity is the norm rather than the exception. Among comorbid disorders associated with TS, attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) are the most common (Freeman, 2007; Freeman et al., 2000). It is frequently reported that only 10% of TS patients seen in clinical settings do not present any comorbid disorder (Cavanna et al., 2011; Freeman, 2007; Freeman et al., 2000; Ganos and Martino, 2015). However, this number might be overestimated, since TS patients who seek treatment are those showing more severe symptoms and most associated comorbid disorders. Results from the population-based Avon longitudinal study indicates a 20% prevalence for OCD or ADHD in children with TS (Scharf et al., 2012). Nonetheless, these authors mentioned that the instrument used to diagnose ADHD might underestimate the prevalence. Therefore, 20% should be considered as the minimum prevalence for comorbid ADHD in population-based samples of children with TS, but lower rates were also reported in adults with TS (Burd et al., 2001). Still, ADHD remains an important problem for TS patients seeking treatment, as 61% of children and 39% of adults with TS seen in clinical settings had ADHD (Freeman, 2007). Another issue when diagnosing

* Corresponding authors at: 7331 Hochelaga Street, Montreal, Qc, H1N 3V2, Canada.
E-mail addresses: simon.morand-beaulieu@umontreal.ca (S. Morand-Beaulieu), stephanie.grot@umontreal.ca (S. Grot), jacob.lavoie@umontreal.ca (J. Lavoie), leclerc.julie@uqam.ca (J.B. Leclerc), david.luck@umontreal.ca (D. Luck), marc.lavoie@umontreal.ca (M.E. Lavoie).
& Both senior authors contributed equally to this work.

http://dx.doi.org/10.1016/j.neubiorev.2017.05.006
Received 10 January 2017; Received in revised form 4 May 2017; Accepted 8 May 2017
Available online 11 May 2017
0149-7634/

Table 1
Neuropsychological tests measuring inhibitory control.

Test	Description	Outcome measure of inhibitory control
Circle tracing task	The participant must draw over a circle as slowly as possible. Faster drawing reflects a lack of inhibitory control (Bachorowski and Newman, 1985, 1990).	Latency
Continuous performance test (CPT)	In this task, participants are presented with a repetitive set of stimuli and they must maintain their attention over time in order to respond to target stimuli and to inhibit their responses when requested. Participants must press a key every time the letter "X" is presented (or when the letter "X" is preceded by the letter "A", in the AX variant) (Rosvold et al., 1956). More commission errors (i.e.: responding to any other letter than "X") and longer RT represent poor inhibitory control (Moeller et al., 2005; Shucard et al., 1997).	Commission errors & RT
Go/No-Go	Stimuli are presented to a participant; Go and No-Go. The participant must press a key every time a Go stimulus is presented, and must inhibit his response when a NoGo stimulus is presented. Commission errors (i.e.: pressing the key to a No-Go stimulus) and longer RT reflect poor inhibitory control (Bezdjian et al., 2009).	Commission errors & RT
Sentence completion	In sentence completion tests, such as the Hayling test, the examiner read a sentence aloud, with the last word missing. In the first part, the participant is simply asked to complete the sentence. In the second part, the participant must complete the sentence with a word that is not connected to the sentence. He must therefore inhibit his automatic response (Burgess and Shallice, 1997). More errors and longer latencies in sentence completion tasks reflect poor inhibitory control (Christodoulou et al., 2006).	Numbers of errors & latency
Stimulus-response compatibility paradigms	This group includes various tasks (Eriksen flanker task, Simon task, etc.) where the congruency between the stimulus and the response varies. These tasks include a compatible and an incompatible condition. In the compatible condition, the participant gives a response that is congruent with the stimulus. The incompatible condition creates a conflict between the stimulus and the response. For example, in a Simon task, a blue arrow pointing to the right would require a left-hand response. The participant must inhibit the automatic response (a right-hand response) (Eriksen and Eriksen, 1974; Simon and Wolf, 1963). More errors and longer RT in the incompatible condition represent deficits in inhibitory control (Wylie et al., 2012).	Accuracy & RT during the incompatible condition
Stop-signal task	The stop-signal task involves the ability to stop an already ongoing response. When stimuli are presented, the participant must press a key. On some trials, a stop-signal will appear, indicating the participant to stop the response that he just initiated (Logan, 1981). Less accuracy and longer SSRT are associated with poor inhibitory control (Castro-Meneses et al., 2015; Logan et al., 1997).	Accuracy & SSRT
Stroop	This test has three conditions. The first two conditions, where the participant must name colors and read words designating colors, serve as baseline measures. In the third (interference) condition, the words are printed in a color that does not match their significance (i.e.: "red" printed in green). The participant must name the color of the word without reading the word. (Stroop, 1935). Accrued latency in the interference condition reflects deficits in inhibitory control (Zaparniuk and Taylor, 1997).	Latency of the interference condition

***Note*:** SSRT: stop-signal reaction time; RT: reaction time

ADHD in TS patients is that some inherent features of TS might cause ADHD-like symptoms. Indeed, the ability to maintain attention could be impaired by the tics themselves, by efforts to inhibit the tics, or by distractions from comorbid anxiety or OCD (Erenberg, 2005).

TS also has a high rate of comorbidity with impulse control disorders, such as intermittent explosive disorder (IED), sexually inappropriate behavior, trichotillomania, self-injurious behavior or compulsive buying disorder (Frank et al., 2011; Freeman, 2007; Mathews et al., 2004; Wright et al., 2012). However, these disorders might not be solely impulsive disorders, but could also feature some compulsivity (Arzeno Ferrao et al., 2006; Flessner et al., 2012; Starcevic, 2015; Stein et al., 2002). For example, trichotillomania shares impulsive (pleasure and gratification obtained from hair pulling) and compulsive (hair pulling in response to negative affect) features (Flessner et al., 2012). This mix of impulsivity and compulsivity might explain why such disorders are often found in TS, which is a disorder characterized by both symptom clusters (Palumbo and Kurlan, 2007).

Impulsive behaviors are also common among TS patients, especially those with concomitant ADHD (Palumbo and Kurlan, 2007) or OCD (Budman et al., 2000; Freeman et al., 2000). These behaviors include argumentativeness, kicking and explosive outbursts (EO) (Alsobrook and Pauls, 2002). EO might be one of the most disturbing behaviors TS patients can experience. They consist of recurrent episodic rage attacks that seem unpredictable and lead the child to react in a disproportionate manner to a trigger stimulus (Budman et al., 2003; Stephens and Sandor, 1999; Sukhodolsky et al., 2003). These outbursts are similar to IED, but occur more frequently in TS patients than in the general population (Chen et al., 2013). Indeed, they affect between 25% and 70% of TS patients and occur more frequently in children than in adults (Budman et al., 2000), causing distress to both the patient and his surroundings (Budman et al., 2003). EO symptoms can take the form of a refusal (quickly gets angry), a lack of tolerance to frustration, a struggle in self-control, a social immaturity, and a disruptive behavior (Khalifa and von Knorring, 2006). The co-occurring presence of ADHD (Chen et al., 2013) or OCD (Budman et al., 2000) increases the risk of having such outbursts. While impaired impulse control is a factor favoring the occurrence of EO, they might also emerge from a deficit in emotional regulation (Fettich et al., 2015).

1.2. Inhibition and its relation to impulsivity: a neuropsychological perspective

Impulsivity is often conceptualized in three distinct dimensions: (1) the inability to use the available information to evaluate the consequence of someone's actions; (2) the inability to refuse an immediate smaller reward in favor of a delayed larger reward; (3) and impairment in suppressing prepotent motor responses (i.e.: lack of inhibitory control) (Bari and Robbins, 2013; Chamberlain and Sahakian, 2007; Torregrossa et al., 2008).

Neuropsychological tasks involving inhibitory control do not give a full picture of impulsivity, but they represent an objective assessment which is, at least in part, related to impulsivity. Furthermore, response inhibition deficits in neuropsychological tasks have been commonly found in ADHD, trichotillomania and substance abuse disorder, which represent archetypal impulsivity disorders (Chamberlain and Sahakian, 2007; Moeller et al., 2005; Swann et al., 2009). Poor response