



Temporal relationship between premonitory urges and tics in Gilles de la Tourette syndrome

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ARTICLE INFO

Article history:

Received 7 October 2015

Reviewed 9 December 2015

Revised 30 December 2015

Accepted 8 January 2016

Action editor Stefano Cappa

Published online 23 January 2016

Keywords:

Urge

Tic

Gilles de la Tourette syndrome

Premonitory sensation

ABSTRACT

Premonitory urges are a cardinal feature in Tourette syndrome and are commonly viewed as the driving force of tics, building up before and subsiding after the execution of tics. Although the urge-tic interplay is one of the most preeminent features in Tourette syndrome, the temporal relationship between tics and urges has never been examined experimentally, mainly due to the lack of an appropriate assessment tool.

We investigated the temporal relationship between urge intensity and tics in 17 Tourette patients and between urge intensity and eye blinks in 16 healthy controls in a free ticcing/blinking condition and a tic/blink suppression condition. For this purpose, an urge assessment tool was developed that allows real-time monitoring and quantification of urge intensity.

Compared to free ticcing/blinking, urge intensity was higher during the suppression condition in both Tourette patients and healthy controls, while tics and blinks occurred less frequently.

The data show that urge intensity increases prior to tics and decreases after tics in a time window of approximately ± 10 sec. Tic suppression had a significant effect on the shape of the urge distribution around tics and led to a decrease in the size of the correlation between urge intensity and tics, indicating that tic suppression led to a de-coupling of tics and urges.

In healthy controls, urges to blink were highly associated with eye blink execution, albeit in a narrower time frame ($\sim \pm 5$ sec). Blink suppression had a similar effect on the urge distribution associated with eye blinks as tic suppression had on the urge to tic in Tourette patients.

These results corroborate the negative reinforcement model, which proposes that tics are associated with a relief in urges, thereby perpetuating ticcing behaviour. This study also documents similarities and differences between urges to act in healthy controls and urges to tic in Tourette syndrome.

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<http://dx.doi.org/10.1016/j.cortex.2016.01.008>

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1. Introduction

Gilles de la Tourette syndrome (GTS) is a common childhood onset neuropsychiatric disorder. It is characterised by multiple motor and phonic tics (DSM-5, 2013) that can be distinguished from other extra movements mainly because they can be suppressed for some time to a degree. However, suppression is often associated with an increasing discomfort (Jankovic, 1997). Such premonitory urges have been reported in over 90% of adult patients with GTS (Leckman, Walker, & Cohen, 1993; Woods, Piacentini, Himle, & Chang, 2005) and are experienced at the site where a tic is about to be executed or as a generalized inner tension (Miguel et al., 1995). In terms of their sensory quality, urges have been described as pressure-like, a tickling, cold, or warm sensation (Banaschewski, Woerner, & Rothenberger, 2003) and have been likened to the urge to scratch (Lang, 1991; Leckman & Riddle, 2000). Although “premonitory urges” often appear to signalize emerging tics and tics are often experienced as a voluntary reaction to this uncontrollable premonitory sensation to execute the tic (Crossley, Seri, Stern, Robertson, & Cavanna, 2014; Kwak, Dat Vuong, & Jankovic, 2003; Leckman et al., 1993), studies have also shown that urges are not a necessary prerequisite for the ability to suppress tics (Banaschewski et al., 2003; Ganos, Kahl, et al., 2012). Importantly, studies in adult patients with GTS have shown that urges have a negative impact on the quality of life, especially psychological well-being (Crossley & Cavanna, 2013; Eddy & Cavanna, 2014; Kano et al., 2015).

Until now, formal investigation of premonitory urges has been limited by the lack of an appropriate assessment tool (for reviews of GTS, inhibitory control and premonitory urges please see Ganos, Roessner, & Munchau, 2012; Houghton, Capriotti, Conelea, & Woods, 2014; G. M. Jackson, Draper, Dyke, Pepes, & Jackson, 2015; Leckman & Riddle, 2000; Rajagopal, Seri, & Cavanna, 2013). Assumptions about the temporal relationship between urges and tics have so far been derived from questionnaires and unstructured self-reports of patients. As the name suggests, “premonitory urges” have been assumed to build up prior to a tic to be then transiently relieved by the tic before they build up again (Leckman et al., 1993; Reese et al., 2014). Based on this assumption, it has been proposed that urges maintain ticcing behaviour by creating a negative reinforcement cycle (Capriotti, Brandt, Turkel, Lee, & Woods, 2014; Evers & van de Wetering, 1994; Himle, Woods, & Bunaciu, 2008; Himle, Woods, Conelea, Bauer, & Rice, 2007; McGuire et al., 2015; Specht et al., 2013; Woods et al., 2008). Urges are experienced as highly unpleasant sensations (Eddy & Cavanna, 2014). If tics induce a reduction in urge intensity and patients execute tics to avoid urges, tics become rewarding because of the relief in urge intensity. At the same time, by avoiding urges patients do not learn to tolerate them, which may make them even more aversive, leading to ticcing behaviour to avoid urges. However, the exact temporal relationship between urges and tics has not been systematically examined using an assessment tool that allows a real-time monitoring of their relation.

The aim of the present study was to develop a paradigm capable of capturing fluctuations in urge intensity continuously to address several assumptions and open questions regarding

the nature of the temporal relationship between urge intensity and tics. The first and most important question was how much variance in ticcing behaviour can be explained by fluctuations in urge intensities, i.e., how strongly the two phenomena are associated. The second assumption we tested was that urges increase until they reach a peak, and then, upon execution of a tic, decrease (inverted U-shape). In order to test this assumption, urge intensity levels around tics and blinks were extracted and their shape (peak, width, skewedness, kurtosis) was characterised. The third question addressed in this study was whether urges are also related to bouts of tics because tics have been shown to occur predominantly in bouts or “burst-like” (Peterson & Leckman, 1998). Bouts of tics were extracted using a method adopted from the analysis of spike-trains in single cell recordings and were then analysed in relation to urges. The fourth unresolved question was whether or not urges increase under tic suppression and then decrease (habituate; Capriotti et al., 2014; Specht et al., 2013; Verdellen et al., 2008).

2. Methods and materials

2.1. Participants and clinical assessment

Seventeen patients diagnosed with GTS (DSM-5, 2013) (aged 31 ± 9.9 SD; 14 male), and 16 healthy controls (aged 29 ± 7.5 ; 8 male) were included in this study. One GTS patient was excluded from analyses exceeding simple comparisons between urge levels and tic frequency because he had only eye blinking tics, which were very difficult to distinguish from physiological eye blinking.

Exclusion criteria for healthy controls comprised tics, diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) or Obsessive Compulsive Disorder (OCD). ADHD symptoms were rated on the German short version of the “Wender Utah Rating Scale” (WURS-K; Ward, Wender, & Reimherr, 1993), while OCD symptoms were measured by the “Yale-Brown Obsessive Compulsive Disorder Scale” (Y-BOCS; Goodman et al., 1989). GTS symptom severity was assessed using the clinician-rated Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) and the “Diagnostic Confidence Index” (DCI; Robertson et al., 1999). Overall severity of premonitory urges was assessed using the validated German version of the “Premonitory Urge for Tics Scale” (PUTS; Rössner, Müller-Vahl, & Neuner, 2010).

The study was reviewed and approved by the local ethics committee and conformed to the Declaration of Helsinki. All patients gave their written informed consent prior to the study.

2.2. Experimental design

After arrival in the lab, participants were comfortably seated in front of a laptop on which the real-time urge monitor was displayed (Fig. 1). Participants were introduced to the real-time urge monitor, instructed to indicate the intensity of their current urge continuously and given the opportunity to practise the task for 1min. Patients with GTS were asked to report their urge to tic, healthy controls were asked to report their urge to blink. Each participant was then asked to report

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