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Electrophysiological manifestations of stimulus evaluation, response inhibition and motor processing in Tourette syndrome patients

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Abstract

Gilles de la Tourette syndrome (GTS) is a neuropsychiatric disorder with childhood onset presenting with multiple fluctuating motor tics and one or more phonic tics. A significant proportion of people suffering from GTS are still symptomatic in adulthood and present other emotional and cognitive difficulties, along with motor problems that often accompany these comorbid conditions. The nature of these difficulties is still poorly understood and multiple comorbidities are often inadequately controlled. The current study investigates both stimulus evaluation and motor processing in GTS while controlling for comorbidity. Fifteen adults with GTS and 20 control participants were matched on gender, laterality and intelligence. The P300 component, the no-go anteriorization (NGA) as well as the stimulus and response-locked lateralized-readiness potentials (S-LRP, R-LRP) were elicited during a stimulus–response compatibility (SRC) paradigm. The standard version of the Stroop Color–Word Test (SCWT) was also administered. Reaction times showed that participants with GTS processed both the SRC and the SCWT more rapidly than the control group, while producing a delayed P300 peak latency. The GTS group also showed faster S-LRP onset in response to the incompatible and faster processing of interference in the SCWT. There was also a tendency toward a greater frontal shift of the NGA in the GTS group. The P300 latency showed that with GTS patients, stimulus evaluation occurs later whereas the overlapping pre-motor response selection processes occur faster. Our findings are congruent with a probable cortical motor over-activation hypothesis of GTS involving faster motor program selection in processing conflicting SR configuration.

Keywords: P300; NGA; Lateralized-readiness potential; Stimulus–response compatibility; Inhibition; Motor preparation; Stroop task; Pre-motor cortex; Supplementary motor area

1. Introduction

Gilles de la Tourette syndrome (GTS) is a debilitating neuropsychiatric disorder that carries significant social stigma. GTS is diagnosed on the basis of multiple fluctuating motor tics and one or more phonic tics (American Psychiatric Association, 2000). Symptoms usually begin during childhood, and at least 11% of people suffering from GTS remain fully symptomatic as adults (Bloch et al., 2006; Leckman et al., 1998). The manifestation of tics is part of a larger mosaic of collateral symptoms. Freeman et al. (2000) established that anger control problems, sleep difficulties, coprolalia, and self-injurious behavior attain

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high levels in individuals with GTS, particularly those with comorbidity. The most commonly reported comorbidity in GTS is attention-deficit/hyperactivity disorder (ADHD), which is also associated with reduced inhibition at multiple levels in the motor system (Hallett, 2001).

In addition to the numerous behavioral problems cited above, several neuropsychological studies discovered cognitive specificities in GTS such as a deficit in learning for mathematics and written language (Brookshire et al., 1994; Como, 2001), verbal fluency (Bornstein, 1991; Brookshire et al., 1994), fine motor coordination (Bornstein et al., 1983, 1991; Brookshire et al., 1994; Como, 2001; O'Connor et al., 2008) and a non-verbal memory deficit associated with a visuoperceptual integration difficulty in children (Harris et al., 1995; Schuerholz et al., 1996) and adults (Lavoie et al., 2007). Moreover, some studies proposed that GTS children achieved normal performances on tasks evaluating abstract concepts (Bornstein, 1990; Braun et al., 1993; Harris et al., 1995; Schuerholz et al., 1996), planning and response inhibition (Ozonoff and Jensen, 1999), and verbal fluency (Braun et al., 1993; Mahone et al., 2001), while, others proposed other types of executive function impairments (Sutherland et al., 1982; Bornstein et al., 1983; Baron-Cohen et al., 1994; Brookshire et al., 1994; Schuerholz et al., 1996). The lack of consistency in the neuropsychological results could be due to methodological problems considering that, in some cases, studies did not include a control group or did not control for the presence of comorbid disorders, such as ADHD or obsessive–compulsive disorders (OCD). The presence of ADHD or OCD symptoms in children often leads to poorer performance on executive tasks (Bornstein, 1990; Harris et al., 1995). Despite this, there have been consistent reports of deficits in fine motor dexterity and visuo-motor integration in both children and adults with persistent GTS.

Recent etiological studies have all implicated fronto-striato-thalamo-cortical circuits in the cognitive and motor functioning of GTS patients, but assess indirectly cerebral motor functions and the underlying brain structures involved in response processing. A dopaminergic imbalance (Singer and Minzer, 2005; Leckman et al., 2006) has been proposed, as well as a loss of basal ganglia control, a thalamo-cortical neuronal dysrhythmia and a frontal compensation, which impacts on the dysregulation of striatal and thalamo-cortical electrical oscillations (see Leckman et al., 2006). These hypotheses are supported by brain imaging studies reporting volumetric and metabolic reductions in lentiform (Braun et al., 1995; Eidelberg et al., 1997) and caudate nuclei (Hyde et al., 1995; Stoetter et al., 1992; Bloch et al., 2005), while observing larger prefrontal volume (Peterson et al., 2001). Other investigators have shown a metabolic increase reflecting heightened activation in pre-motor cortex and supplementary motor area (SMA) through anatomical (Braun et al., 1993; Eidelberg et al., 1997; Stoetter et al., 1992) or functional magnetic resonance imaging (fMRI) during a finger tapping task (Biswal et al., 1998). More recently, another study showed an increase in alpha EEG coherence in the pre-motor cortex during execution of a go–no-go task in GTS patients (Serrien et al., 2002). In brief, these observations suggest that anomalies in cerebral regions, associated with motor processing and tic generation, are likely to interfere with accurate planning and execution of voluntary movements in GTS.

Despite recent advances in the understanding of GTS etiology, neurobiological and cognitive factors have mostly been addressed independently. For that purpose, the brain event-related potentials (ERPs) offer a useful tool for monitoring cerebral activity, recorded in synchrony with cognitive events. Earlier investigations found anomalies in motor ERPs with patients suffering from GTS and chronic tics. For instance, the *Bereitschaftpotentials* (BP), or readiness potential, reflecting motor preparation, was consistently larger over frontal and smaller over central areas in the GTS group (Rothenberger and Kemmerling 1982; Rothenberger et al., 1986). In a more recent ERP study, chronic tic disorder patients failed to demonstrate a relationship between motor output and preparation of cortical activation (i.e. BP) during a foreperiod reaction time task (O'Connor et al., 2005), supporting the idea that people with tic disorders may not be able to modulate cortical activation optimally when planning and executing motor responses. The BP was nonetheless highly variable in these cohorts, and it might well have reflected overlapping non-motor as well as motor activity. Also, its early onset may have implicated general anticipatory processes rather than the specific cortical preparation preceding movement (Trevena and Miller, 2002). To circumvent this problem, the lateralized-readiness potential (LRP) component, which has its generator sources in the primary motor cortex (Requin and Riehle, 1995), the SMA (Rektor, 2002) and the basal ganglia (Rektor et al., 2003), represents a good candidate measure of motor processing anomalies in GTS. Specifically, the LRP has been shown to be a marker of selective motor activation, representing the differential engagement of the left and right motor cortices in the preparation and initiation of motor responses (Coles, 1989; Kutas and Donchin, 1980). Only one study has investigated this component in a group of patients with GTS, and failed to show any group difference in LRP (Johannes et al., 2001b). However, the LRP was pooled across conditions and analyzed as a non-specific measure of motor