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Unique saccadic abilities associated with tourette syndrome: Pure and comorbid groups a controlled study

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ABSTRACT

Tourette Syndrome (TS) is a childhood onset disorder characterized by motor and vocal tics. TS often co-occurs with Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive-Compulsive Disorder (OCD). Since neural networks associated with TS overlap with that of saccadic eye movements, saccadic performance may reflect psychopathology underlying TS+comorbidity. The aims of the present study were to determine whether heterogeneity in TS samples and use of various saccadic conditions are responsible for inconsistent findings. We examined: (1) saccadic behaviour in children groups: TS-only, TS+ADHD, TS+ADHD+OCD and healthy Controls; (2) the effect of different saccadic conditions. Participants (8–16 years) either looked towards (prosaccade) or in the opposite direction (antisaccade) of a peripheral visual stimulus in three conditions: fixation dot disappeared simultaneously (standard), 200 ms prior to (Gap200) and 800 ms following (Overlap800) stimulus onset. The findings demonstrated that sample heterogeneity and use of various saccadic conditions contribute to inconsistent findings. The TS+ADHD+OCD group displayed an enhanced saccadic ability substantiating the hypothesis of an enhanced adaptive cognitive control in certain groups of children with TS. The TS+ADHD group displayed significantly higher rates of antisaccade errors and unable to reduce their error rates. These findings lend further support to the nosological hypothesis.

1. Introduction

Tourette Syndrome (TS) is a childhood onset disorder characterized by the presence of multiple motor tics and one or more phonic tics. A tic is a sudden and recurrent motor movement or vocalization (Sandor 1993; DSM IV, 2000). TS often occurs together with Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive-Compulsive Disorder (OCD). TS and OCD appear to share certain clinical characteristics (Sheppared & Bradshaw, 1999). Both disorders involve repetitive acts/urges that are considered involuntary and increased tension is felt if such behaviour/urges are inhibited (Sheppared & Bradshaw, 1999). In fact OCD has been described as the "cognitive" counterpart to "TS" (Sheppard & Bradshaw, 1999). Genetic studies have confirmed that an early onset form of OCD shares common genetic factors with TS (O'Rourke, Scharf, Yu & Pauls, 2009).

Deficits within the basal ganglia and the areas of the frontal cortex to which the basal ganglia project to through the thalamocortical pathways are implicated in the pathophysiology of TS (Fredericksen et al., 2002; Segawa, 2003; Sweeney, Takarae, Macmillan, Luna & Minshew, 2004; Plessen, Royal & Peterson, 2007; Swain, Scahill, Lombroso, King & Leckman, 2007; Sowell et al., 2008; Makki, Govindan, Wilson, Behen & Chugani, 2009). These structures are also part of the neural circuitry involved in the generation of eye movements. Thus, oculomotor studies provide a simple and non-invasive method of examining the integrity of the neural circuitry underlying TS pathophysiology.

Saccade eye movements are high velocity eye movements used to scan the visual world (Leigh & Zee, 2006). The two tasks commonly used in oculomotor research are the prosaccade and the antisaccade tasks. In the prosaccade task, participants look toward a peripheral visual stimulus (a reflexive task), but in the antisaccade task they look in the opposite direction of the stimulus. The antisaccade task is sensitive to inhibitory control (Hallett, 1978; Munoz & Istvan, 1998; Fukushima, Hatta, & Fukushima, 2000) and working memory resources (Roberts, Hager,& Heron 1994; Malone & Iacono, 2002). Hence, data are commonly reported separately for each task.

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Research exploring saccade eye movements of children with TS is very sparse and findings are inconsistent. Earlier reports have indicated longer saccade latencies (Straube, Mennincken, Riedel, Eggert, & Muller, 1997; LeVasseur, Flanagan, Riopelle, & Munoz, 2001; Munoz, LeVasseur, & Flanagan, 2002) normal saccade latencies (Bollen et al. 1988) and faster saccade latencies (Jackson, Mueller, Hambleton & Hollis, 2007) in children with TS relative to those of healthy Controls. There have also been reports of children with TS committing significantly more error saccades (generating a saccade prior to the offset of the fixation dot) (Nomura, Fukuda, Terao, Hikosaka & Segawa, 2003) and significantly fewer errors in saccade generation relative to healthy children (Mueller, Jackson, Dhalla, Datsopoulos & Hollis, 2006; Jackson et al., 2007).

Two factors may be contributing to these inconsistent findings: (1) different oculomotor task/conditions have been used in studies; (2) the TS samples have been heterogeneous between studies, consisting of various composition of TS+comorbid disorders. Mostofsky et al. (2001) investigated eye movements of children with TS with and without the comorbid ADHD and reported increased number of antisaccade errors observed in TS+ADHD relative to those of TS-only group. Hence, comorbidity in TS may be an important factor to examine. The samples of children with TS in the above mentioned studies either consisted of participants with different combinations of TS+comoribid conditions, or were not assessed for the comorbid conditions with the exception of Muller et al. (2006) and Jackson et al. (2007) who excluded participants with the diagnosis of ADHD. Hence, the impact of comorbid conditions on oculomotor ability of TS participants requires further investigation.

The aims of the present study were to: (1) examine the effect of the comorbid conditions; and (2) the effect of oculomotor task/conditions on saccades of children with TS and to determine whether these factors contribute to inconsistent findings. Hence we hypothesized that the participants' performance would be moderated as a result of "Condition" and the presence of "comorbid" conditions. In terms of Group differences, based on the findings of the previous studies, we hypothesized that the TS+ADHD group would display greater antisaccade error rates than the TS-only group. We also hypothesized that the TS+ADHD+OCD group would display the greatest oculomotor problems because the behavioural data indicate greater behavioural and educational problems in this group (Debes, Hjalgrim & Skov, 2010).

2. Method

2.1. Subjects

Ten typically developed children 10–16 years of age ($M=12.8$, SD=2.3) and 22 children with Tourette syndrome 8–16 years of age ($M=12.1$, SD=2.3) participated in this study. Healthy children were recruited through e-mail advertisements posted on the list serve for all staff working at the Toronto Western Hospital and also on the advertisement boards present throughout the hospital. The children with TS were recruited from the Neurodevelopmental clinic at the Toronto Western Hospital. The parents of patients who were within the age-range of interest were contacted by one of the experimenters, the study was briefly explained to them over the phone and if they expressed interest in having their child participate in the study, a data collection appointment was booked for them on the same day as their clinic appointment at the hospital. The children with TS were divided into three subgroups: TS-only ($n=6$; $M=10.7$, SD=1.6), TS+ADHD ($n=9$; $M=11.8$, SD=2.5), and TS+ADHD+OCD ($n=7$; $M=13.9$, SD=1.6). For participants' demographic and medication information see Tajik-Parvinchi and Sandor (2011).

In order to substantiate the diagnoses of each group, an independent practitioner reviewed the patients' files and provided independent diagnoses of each patient participant. An inter-rater reliability analysis suing Kappa statistics was carried out in order to examine the consistency between the diagnoses concluded by the two physicians. The result of this analysis revealed the inter-rater reliability to be Kapp=0.861 ($p<0.001$)

The participants with TS were diagnosed according to DSM III R diagnostic criteria by an experienced neuropsychiatrist. Tic severity was assessed retrospectively, based on review of the clinical information by the same neuropsychiatrist. Life-time tic severity was rated on a 3-point scale (1-mild, 2-moderate and 3-severe) (Fig. 7). The participant's ADHD symptom severity was assessed retrospectively using the Clinical Global Impression of ADHD symptoms (CGI) both for life time and at the time of data collection (Fig. 7). The rater was not aware of the oculomotor performances of the participants when making the ratings. All control participants, by parental report, had no history of TS, OCD or ADHD, vestibular, ocular motor anomalies, or any type of surgery. Written informed assent was obtained from the participants and written informed consent was obtained from parents of the participants. This study was approved by the University Health Network Research Ethic Board and complied with the tenets of the Declaration of Helsinki.

2.2. Apparatus

Horizontal eye movements were recorded binocularly using a video-based cornea/pupil tracking system (El-Mar Series 2020 Eye Tracker, Toronto, Canada). This system is free from drifts and has a maximum resolution of 0.1 degree of visual angle. It has a linear range of ± 25 deg in the vertical meridian and greater than ± 30 deg in the horizontal meridian. Eye movements were sampled at 120 Hz. The head was stabilized by a chin-rest. Participants were seated in a chair, which was especially crafted to adjust to different heights to allow children's eyes to be aligned with the centre of the screen, which was located 200 cm in front of the participants. The stimuli were back projected onto this screen. The size of the stimuli extended about 0.25°. The room was dimly illuminated to encourage larger pupils for better data acquisition. Prior to data collection the eye tracker was calibrated binocularly for each participant by recording eye position at 7 locations horizontally and vertically with a range of $\pm 10°$. The data for the eye with the better calibration data was selected for further analyses.

2.3. Procedure

The prosaccade and antisaccade tasks were presented in separate blocks of trials in three conditions: Standard, Gap200 and Overlap800. Hence, each participant was assigned 6 blocks of trials. Each block consisted of 25 trials, making up 150 trials per participant. The order of presentation of blocks of trials was randomized. The fixation dot was presented in the centre of the screen and the peripheral stimuli were presented at ± 5, ± 10 and ± 15 relative to the fixation point in a random order.

In the Gap200 condition, the fixation dot disappeared 200 msec prior to stimulus presentation. In the Overlap800 condition, the fixation dot remained on for 800 msec following stimulus onset. The Standard condition consisted of the fixation dot disappearing simultaneously as the peripheral stimulus appeared. The duration of the stimulus presentation varied randomly from 1000 msec to 1500 msec.

Children were instructed prior to the presentation of each block of trials and the experiment continued when the child expressed understanding of the task instructions. In the prosaccade tasks, children were told to look towards the peripheral target as soon as it appeared. In the antisaccade tasks, they were instructed to look in the opposite direction of the peripheral target but mirror distance from the fixation dot. Data collection was incomplete for 6/32 children (1 in the Control, 2 in the TS-only, 1 in the TS+ADHD and 2 in the TS+ADHD+OCD groups). The reasons consisted of fatigue and technical difficulties.

3. Calculation

Eye movements with peak velocities greater than 50 deg/sec were marked as saccades by a custom-designed software program (AnYZll 3.3). The onset of a saccade was determined as the time at which its velocity surpassed 10°/sec. Eye blinks were filtered out by AnYZll 3.3, however, the experimenter viewed the marked saccades as well to ensure that these were not blink artifacts. The first saccade generated within 100–1000 msec of the target onset was selected for further analysis. The saccades outside of this time frame were considered anticipatory, secondary or not in response to the stimulus and therefore were excluded from further analyses. The digitized information of each saccade including time of onset and direction was imported into an excel sheet where the rest of the calculations were carried out. Saccade Latency was calculated by subtracting the time of target onset from that of the saccade onset. In the antisaccade task, a saccade was considered an antisaccade error, if it was generated in the same direction as the peripheral target. Hence, Error rates indicated the percentage of direction errors committed in a block of trial. Saccades, which were considered direction errors, were not included in the calculations of Latency.