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Functional brain asymmetry, attentional modulation, and interhemispheric transfer in boys with Tourette syndrome

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Abstract

We tested the hypothesis that children with Tourette syndrome (TS) would exhibit aberrant brain lateralization compared to a healthy control (HC) group in an attention-modulation version of a verbal dichotic listening task using consonant-vowel syllables. The modulation of attention to focus on the right ear stimulus in the dichotic listening situation is thought to involve the same prefrontal attentional and executive functions that are involved in the suppression of tics, whereas, performance when focusing attention on the left ear stimulus additionally involves a callosal transfer of information. In light of presumed disturbances in transfer of information across the corpus callosum, we hypothesized that children with TS would, however, have difficulty modulating the functional lateralization that ensues through a shift of attention to the left side. This hypothesis was tested by exploring the correlations between CC size and left ear score in the forced-left condition.

Twenty boys with TS were compared with 20 age- and handedness-matched healthy boys. Results indicated similar performance in the TS and HC groups for lateralization of hemispheric function. TS subjects were also able to shift attention normally when instructed to focus on the right ear stimulus. When instructed to focus attention on the left ear stimulus, however, performance deteriorated in the TS group. Correlations with CC area further supported the hypothesized presence of deviant callosal functioning in the TS group.

Keywords: Tourette syndrome; Dichotic listening; Corpus callosum; Executive functions

1. Introduction

Tourette syndrome (TS) is characterized by motor and phonic tics that fluctuate in severity (American Psychiatric Association, 1994). Cortico-Striato-Thalamo-Cortical (CSTC) circuits are thought to contribute both to the generation and the suppression of tics (Leckman, 2002). Early reports of altered basal ganglia asymmetries in subjects with TS (Peterson et al., 1993; Singer et al., 1993) suggested that anatomical and functional hemispheric asymmetries may be disrupted in persons with TS. In addition, the size the corpus callosum has been shown repeatedly to be altered in TS compared with control subjects (Baumgardner et al., 1996; Moriarty et al., 1997; Mostofsky, Wendlandt, Cutting, Denckla, & Singer, 1999; Peterson et al., 1994). A recent study from our laboratory (Plessen et al., 2004) found that children with TS have smaller areas of the midsagittal CC compared with control children and that a smaller CC area is associated with less severe tics. In addition, inverse correlations between prefrontal cortex and callosal area were significantly more prominent in the TS group. This study stimulated further interest in studies of hemispheric laterality in children TS, as the callosum is thought to be the brain structure that supports functional brain lateralization (Banich, 2003). Dichotic listening (DL) is an experimental paradigm that permits the non-invasive study of how lateralized information is processed in the two hemispheres of the brain (Bryden, 1988; Hugdahl, 2003; Kimura, 1961). Dichotic listening has to our knowledge not been studied previously in children with TS.

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Numerous studies have shown a consistent right ear advantage (REA) during performance of the DL task in healthy individuals (Hugdahl, 2003). The classic structural model (Kimura, 1967) posits that the phenomenon of REA arises as follows: first, auditory input is more strongly represented in the contralateral hemisphere than in the ipsilateral one. Second, the left hemisphere is specialized for language in most individuals. Third, auditory information sent along the ipsilateral pathways seems to be suppressed or blocked by information from contralateral pathways. Finally, the right ear advantage results from the fact that information reaches the right cerebral hemisphere via transfer across the corpus callosum to the contralateral (left) cerebral hemisphere language area for processing.

REA can be modified by instructing the individual to attend to the stimulus in either the right or left ear (Bryden, Munhall, & Allard, 1983; Hugdahl & Andersson, 1986), thus adding a "top-down" component to an originally "bottom-up" processing of lateralized auditory stimuli. Therefore, when focusing on the right ear stimulus ("forced-right" condition), REA actually increases, whereas, it decreases or even disappears during attentional focus on the left ear ("forced-left" condition), thus creating a left ear advantage (LEA). Thus, DL is regarded as a measure of auditory processing in the temporal lobe (Spreen & Strauss, 1991), and as a measure for frontal lobe functioning when combined with instructions of attentional shift (Hugdahl et al., 2003).

This study thus aimed to assess functional brain asymmetry in children with TS using a variant of the DL paradigm that also allows study of the effects of attention and executive functions to modulate lateralization (Hugdahl et al., 2003). The attention-modulated DL paradigm instructs the subject explicitly to focus attention on a stimulus in the right or left ear and to report the perceived syllable (Hugdahl & Andersson, 1986). The task assesses experimentally the "top-down" modulation of a stimulus-driven, or "bottom-up", laterality effect.

Functional MRI studies have shown that prefrontal cortices activate strongly during the voluntary suppression of tics (Peterson et al., 1998), and the frequent need to suppress tics is thought to induce a compensatory hypertrophy of frontal cortices in which the degree of hypertrophy corresponds with the degree of control over symptoms in persons with TS (Peterson et al., 2001). The forced attention condition in the DL paradigm is also considered a test of the attentional aspects of executive functioning mediated by the prefrontal cortex, in that the degree to which an individual is able to direct attention voluntarily to one ear or the other depends on the ability to overrule a bottom-up, stimulus-driven laterality effect, an ability that has been shown to be compromised in clinical populations with an impaired attentional focus (Hugdahl et al., 2003).

We therefore propose that shifting attention to the right ear stimulus could be regarded in children with TS as tapping the same regulatory circuits that subserve the top-down modulation or suppression of tic behaviors. Shifting attention to the left ear stimulus processed in the contralateral hemisphere, on the other hand, could be regarded as a test of callosal transfer of information, given that left ear performance in the forced-left attention condition depends on transfer of regulatory control across the CC (Milner, Taylor, & Sperry, 1968; Pollmann, Maertens, von Cramon, Lepsien, & Hugdahl, 2002). We predicted that callosal transfer would be impaired in children with TS as a consequence of their previously documented reduction in callosal size, similar to altered transfer in other conditions with abnormal morphologies of the CC (Reinvang, Bakke, Hugdahl, Karlsen, & Sundet, 1994).

We thus tested three specific hypotheses for the TS group compared with healthy control subjects. We predicted that the TS group would evidence reduced measures of a normal functional brain asymmetry, as well as an intact ability to shift attention actively towards the right ear stimulus, and finally an impaired callosal transfer during the forced-left attention condition. The first hypothesis was tested in the non-forced condition, the second in the forced-right, and the third in the forced-left condition, as well as by correlating the left ear scores with CC size.

2. Methods

2.1. Subjects

TS subjects were recruited from the Department of Child and Adolescent Psychiatry at the Haukeland University Hospital, University of Bergen, Norway, and from outpatient clinics in the greater Bergen area. All children met DSM-IV criteria for a diagnosis of TS (American Psychiatric Association, 1994). HC children were recruited by contacting local schools in the same geographic area. Controls were matched for age and gender with the children in the patient group. Written informed consent was obtained from all participants, and the study was clarified by the Regional Committee for Medical Research Ethics, West-Norway.

Exclusion criteria for the control group were a lifetime history of Tic Disorder, Obsessive Compulsive Disorder (OCD), Attention Deficit Hyperactivity Disorder (ADHD), or a current DSM-IV Axis I disorder. Additional exclusion criteria for both groups were epilepsy, head trauma with loss of consciousness, former or present substance abuse, or an IQ below 70, as measured with the WISC-III (Wechsler, 1996).

Parents and children were interviewed by a child and adolescent psychiatrist using the "Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version" (Kaufman et al., 1997). The psychiatric diagnoses were established through review of all available study materials in a best estimate consensus procedure (Leckman, Sholomskas, Thompson, Belanger, & Weissman, 1982). OCD symptoms were quantified using the Yale Brown Obsessive Compulsive Scale (Goodman et al., 1989; Scahill et al., 1997), and the severity of tics was rated with Yale Global Tic Severity Scale (YGTSS) (Leckman et al., 1989). Socioeconomic status (SES) was estimated from the level of parental education (JAACAP, 2005).

We enrolled 20 consecutively recruited subjects into the study who met diagnostic criteria for TS, without any criteria for exclusion. (Two girls with TS were recruited but had to be excluded prior to data analysis because of motion artifacts on their MR scans.) The final sample thus consisted of two male groups: 20 TS and 20 HC boys, 9–17 years of age. The groups were of comparable age (TS = 13.6 years, ±1.9; HC = 13.4 years, ±2.4; $t = -0.3$; $p = .77$) and SES. The groups, however, differed in full scale IQ (TS = 94.5 ± 10.2; HC = 105.7 ± 9.2; $t = 3.6$; $p < .001$), verbal IQ (TS = 94.4 ± 11.4; HC = 104.4 ± 10.5; $t = 2.9$; $p < .006$) and performance IQ (TS = 95.6 ± 10.8; HC = 106.1 ± 12.1; $t = 2.9$; $p < .006$).

Five of the subjects in the TS group had comorbid combined-type ADHD, and four others had comorbid OCD. In each group were two left-handed individuals (left-handed individuals differed between groups in their age by 1 and 12 months, respectively), all others being right-handed with a laterality index of 80% or above as measured by the Edinburgh handedness inventory (Oldfield, 1971). Nine subjects in the TS group were taking medication, either neuroleptics ($n = 4$), alpha agonists ($n = 2$), selective serotonin uptake inhibitors ($n = 1$), or stimulants ($n = 2$). HC subjects were not taking any psychotropic medication. Tic severity at the time of investigation in the TS group was 11.4 ± 2.9 for