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Child's Brain May Adapt to Control Tourette Tics

BY JEFF EVANS

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Children with Tourette syndrome appear to undergo changes in brain structure and function that allow them to gain control over their symptoms, according to a prospective study.

These changes, manifested by faster manual response times to tasks presenting conflicting information, lend strength to the premise that children with Tourette syndrome have a "generalized increase in cognitive control over motor activity" because of their constant need to suppress tics, wrote Stephen R. Jackson, Ph.D., of the University of Nottingham and his associates (Curr. Biol. 2011;21:580-5).

The enhanced motor control that Dr. Jackson and his colleagues observed in children with Tourette syndrome was associated with changes in brain white matter microstructure within the prefrontal cortex and greater metabolic activity in the prefrontal cortex.

The investigators conducted a manual task-switching experiment on 13 children (including two females) at an average age of 14 years who had Tourette syndrome and 13 age- and gender-matched neurologically healthy children. None of the children had attention-deficit/hyperactivity disorder or obsessive-compulsive disorder.

In "pure block" trials, the children were presented with a green arrow pointing either right or left. They had to respond as quickly as possible by pushing a corresponding right or left key. When the arrow was red, the investigators asked the participants to push the key for the opposite direction. "Mixed block" trials included those in which green or red arrows could be randomly shown. These trials were repeated during functional MRI studies measuring blood oxygen level–dependent (BOLD) activation.

Both groups had similar response times in pure block trials and similar error rates in both types of trials. But Tourette children had significantly faster response times in mixed block trials. Tourette children also had significantly faster response times in mixed block trials when the type of key press that was required differed from that of the previous trial. This reduced response time to switching manual tasks was strongly and positively associated with tic severity as measured by the motor score on the Yale Global Tics Severity Scale, such that children with better cognitive control and faster response to switching manual tasks exhibited reduced levels of tic severity.

Diffusion-weighted imaging revealed widespread differences in white matter microstructure between 14 Tourette children and 14 controls, most notably in the corpus callosum and the forceps minor, which connects the lateral and medial areas of the prefrontal cortex. This is consistent with previous studies in individuals with Tourette syndrome, according to the authors.

In the corpus callosum and forceps minor, voxel-based measurements of fractional anisotropy and mean diffusivity, which reflect myelination and axonal fiber density, were positively associated with tic severity. Dr. Jackson and his colleagues said these changes in cortical white matter volume "most likely reflect a functional adaptation to Tourette syndrome rather than a core symptom of the disorder," which is supported by a previous study that indicated that the size of the corpus callosum is smaller in children with Tourette, is inversely associated with frontal cortex volumes and is positively associated with greater tic severity. Whether the differences in white matter between neurologically normal and Tourette children might reflect individual variation rather than a reorganization of the brain to suppress tics will require a longitudinal study, they noted.

The amount of white matter of the forceps minor predicted task response time only in the Tourette children. However, white matter in the corpus callosum was strongly associated with response time in healthy controls, but not in Tourette children. The results support the "hypothesis that for the Tourette syndrome group, the normal role performed by the corpus callosum in resolving the selection of motor outputs may be reduced in favor of an increased role for prefrontal cortex," the investigators wrote.

Functional MRI measurement of BOLD data taken during testing with the mixed blocks task in 10 Tourette children and 15 controls showed that BOLD activation in regions of interest within the left and right hemisphere motor cortex was similar between the groups across the various types of task trials, "suggesting that motor execution was equivalent across the groups." But in consecutive trials that involved switches of the red arrow's direction relative to consecutive trials in which the red arrow did not change direction, BOLD activation in regions of interest in the right prefrontal cortex adjacent to the forceps minor was significantly greater among Tourette children than in controls, which is consistent with evidence from monkey and human trials that suggest "the right prefrontal cortex is implicated in inhibitory processes underlying task switching." BOLD activation also was strongly and linearly associated with increased response time in consecutive trials that involved switches of the red arrow's direction in only Tourette children, confirming that "the prefrontal cortex is significantly involved in the cognitive control of motor outputs."

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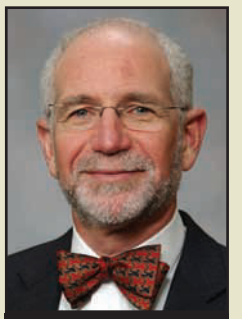
ADVISER'S VIEWPOINT

Study Finds Altered Activity

Tourette syndrome (TS) is an age-dependent movement disorder characterized by simple and/or complex motor and vocal tics that have occurred intermittently over a 1-year period. Motor tics usually begin at 3-5 years of age followed by onset of vocal tics several years later. In the mid- to late teen years, approximately one-third of children will stop and have complete resolution of their tics, with another third experiencing significant decrease in symptoms. Although TS occurs in approximately 1%-2% of the pediatric population, it is estimated that as many as 20% of children will have a motor or vocal tic. An important feature of tic phenomenology is the ability of the individual to temporarily suppress the tic and if the effort is sustained, the affected individual may report mental fatigue or exhaustion.



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Thus, tics appear to follow a neurodevelopmental sequence characterized by specific ranges of onset, peak, and resolution or amelioration. The latter has given rise to the concept that tics are a "normal" part of the developmental process. That process can be considered part of the adolescents' progressive command of motor, behavioral, and emotional experiences. Dysregulation of these complex control processes can result in the occurrence of the attentional disorders, impulsivity and hyperactivity, and the obsessive thoughts and compulsive actions that are the major comorbidities of TS.

One way to conceive of the active control processes that must take place during development is an alteration in neuronal function and perhaps anatomy, that is, neuroplasticity. As neurologists, we tend to think of neuroplasticity as the brain's response to acquired damage such as stroke or traumatic brain injury or recovery from resective surgery. However, the alteration of brain physiology and anatomy based upon activity in a pathway or network is a fundamental property that literally shapes the nervous system during development. Just as apoptosis eliminates neurons, activity in circuits increases synaptic strength and preservation of the involved neural elements.

MRI has allowed us to explore potential structural and functional alterations that accompany normal development as well as seemingly aberrant states such as TS. Several of the most interesting and reproducible findings from the recent imaging in TS literature include small caudate volumes in children and adults with TS, suggesting that this may be a trait characteristic of refractory tics; thinning of the sensorimotor cortex in children with TS; and enlargement of corpus callosum in adults, but reduction in children with TS.

Recently, the use of modern MRI technology, combined with rigorous behavioral study design and statistical analysis has provided evidence for an active process by which individuals with TS have an enhanced ability to suppress extraneous or conflicting information leading to motor task. In the experiments performed by Dr. Jackson and his colleagues, children with TS exhibited superior control over motor activity when compared with controls, suggesting that their previous cognitive "training" in tic suppression resulted in persistent functional changes. Furthermore, this group had anatomic differences in the white matter of the corpus callosum and forceps minor that correlated with tic severity. Of note, these structures are directly connected to the prefrontal cortex that provides the anatomic substrate for volitional tic suppression. Viewed from the perspective of normal development, the prefrontal cortex is known to be involved in the regulation of motor function. The authors also demonstrate that the right prefrontal cortex has a larger BOLD response during the motor task in which the TS cohort demonstrated better performance.

Taken together, the findings of Dr. Jackson and his associates suggest that the developmental processes by which children learn to control nonvolitional movements are the same that are used to compensate for the excessive motor overflow that characterizes TS. The implications for treatment of both developmental disorders and acquired injury to the nervous system may be profound if existing mechanisms that mediate normal development can be used as part of specific therapeutic regimens.

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