Abnormal brain circuits may prevent movement disorder

August 4 2009

Specific changes in brain pathways may counteract genetic mutations for the movement disorder dystonia, according to new research in the August 5 issue of *The Journal of Neuroscience*. Few people who inherit dystonia genes display symptoms -- namely sustained muscle contractions and involuntary gestures -- and the study provides a possible explanation. This result could lead to new treatments for the estimated 500,000 North Americans diagnosed with dystonia.

In this study, researchers looked for the first time at how brain connections might explain the disorder. "Our findings begin to show why someone can live with a genetic mutation without ever developing the disease," said David Eidelberg, MD, at The Feinstein Institute for Medical Research, the study's senior author.

Scientists at The Feinstein Institute used an MRI-based approach called diffusion tensor imaging, a technique that maps the connections between structures in the human brain. Twenty patients with mutated genes associated with dystonia were assessed (12 with symptoms, eight without), along with eight healthy patients without these mutations.

The authors identified two different brain pathways that determine the severity of symptoms. One pathway connecting the cerebellum with the thalamus is abnormal in all people carrying the mutant gene, and predisposes carriers to dystonia. In the patients with mutated genes but no symptoms, a second pathway between the thalamus and the cortex is also abnormal. Surprisingly, this second pathway is normal in patients

with symptoms. The researchers suggest that in people who have the mutations but no symptoms, the second abnormality may offset the effect of the first, preventing the disease's outward signs.

David Standaert, MD, PhD, at University of Alabama at Birmingham, is an expert in Parkinson's disease and other movement disorders and was not affiliated with the study. Standaert says that although dystonia is a relatively rare disorder, the study has implications for other neurological illnesses, such as Parkinson's, Alzheimer's, and Huntington's diseases; ataxia and muscular dystrophies; and even forms of migraine.

"The core idea here is that many diseases can be triggered by a single gene, but the expression of this gene can differ greatly, even in individuals from the same family," Standaert said. "Dystonia provides dramatic examples of this. Two siblings may have the same abnormal gene, but one will be severely disabled by twisting and cramping of the muscles, while the other will be essentially normal."

The pathway abnormalities identified in the study could likely have formed in an early stage of brain development, Standaert suggested. Symptoms in adult life, therefore, may be determined by subtle shifts in early brain growth. Detailed study of these newly implicated pathways in both humans and animals could lead to ways to prevent symptoms, if balance to the affected pathways is restored.

Source: Society for Neuroscience (news : web)