Medical Xpress

Researchers find genetic cause for body tremors

August 2 2012

Researchers at the University of Montreal and its affiliated CHU Sainte-Justine and CHUM hospitals have linked some cases of Essential Tremor (ET) to a specific genetic problem. ET is the most common movement disorder, becoming increasingly frequent with increasing age, which is characterized by an involuntary shaking movement (tremor) that occurs with motion, particularly when doing precise fine movement. The researchers will be publishing their findings tomorrow in The *American Journal of Human Genetics*.

Exactly why this shaking occurs has remained unknown, despite the work of many clinicians and researchers for decades. While it is known that there is a problem with the parts of the brain that control certain muscles, it has been a challenging endeavor to identify what exactly is malfunctioning in the nervous system of affected individuals. Despite strong evidence that the disease has a genetic basis and years of research effort, no actual genetic link had been identified until today.

Scientists already knew that mutations in a gene called FUS (Fused in Sarcoma) cause amyotrophic lateral sclerosis (ALS), a disease of the nerve cells in the brain and spinal cord that control voluntary muscle movement. The ET research team was successful in identifying mutations that cause ET in this gene, and they also proved that the disease mechanisms for ET and ALS FUS mutations are different. "When I started my post-doctoral work in the Rouleau laboratory, I felt compelled to study essential tremor. I saw a great opportunity to identify the first ET gene considering the plethora of families collected for study

in the laboratory, and the availability of new sequencing technologies that has revolutionized gene discovery efforts," said lead author Dr. Nancy Merner. "As a proof of principle study, we chose one family to sequence and took a simple approach to overcome particular clinical barriers that have hindered previous gene discovery attempts."

The other members of the research team share her clinical focus. "This discovery has provided the world with the first insight toward the disease mechanism of essential tremor, which is crucial for disease management, particularly for future drug developments. It also presents a logical approach that can be used for additional ET gene discoveries, which we are currently pursuing" said Dr. Guy Rouleau. "There is currently a lack of consensus on the diagnostic criteria of ET thus a genetic diagnosis can be beneficial, especially for familial cases. Transitioning to a genetic diagnosis would cut down on ET misdiagnosis," added Dr. Patrick Dion who is another key researcher on this project. Misdiagnosis occurs in 37-50% of individual cases.

To affected individuals, the tremors are generally annoying and embarrassing, and can interfere with everyday tasks such as working, writing, eating, or drinking, since tremors affecting the hands are the most common and affected individuals can have trouble holding or using small objects. "Our overall goal in this endeavor is to improve the quality of life of affected individuals," said Dr. Merner. "The road is now paved for improvement."

The identification of FUS was performed in the Rouleau laboratory and supported by the Chaire Jeanne-et-J.-Louis-Lévesque en Génétique des Maladies du Cerveau de l'Université de Montréal. The Canadian Institutes of Health Research has also funded the pursuit for additional ET genes.

More information: "Exome sequencing identifies FUS mutations as a

cause of essential tremor." *American Journal of Human Genetics*, 2012.

Provided by University of Montreal