Researchers discover gene responsible for Restless Legs Syndrome

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An international team of researchers has identified the first gene associated with Restless Legs Syndrome (RLS), a common sleep disorder affecting tens of millions of people worldwide. The findings will be published July 18 in the online edition of the *New England Journal of Medicine* and will appear in an upcoming printed edition of the journal. The work was led by scientists at Emory University and deCODE Genetics, Inc., in Reykjavik, Iceland.

Restless legs syndrome is a condition that produces an intense, often irresistible urge to move the legs and is a major cause of insomnia and sleep disruption. RLS affects approximately 10 percent of the U.S. population and about one percent of school-aged children. The discovery provides strong new evidence that RLS is a genuine syndrome, a fact which has recently been the subject of some debate.

"We now have concrete evidence that RLS is an authentic disorder with recognizable features and underlying biological basis," says David Rye, MD, PhD, professor of neurology at Emory University School of Medicine, director of the Emory Healthcare Program in Sleep, and one of the study's lead authors. "This is the most definitive link between genetics and RLS that has been reported to date. We have known for quite some time that the majority of RLS patients have a close family member with the disorder, and now we have found a gene which is clearly linked to RLS," says Dr. Rye.

The researchers report a population-attributable risk for RLS of at least

50 percent, meaning that were the gene variant not present, more than half of all RLS cases would disappear.

The variant is very common--nearly 65 percent of the population carries at least one copy of the variant. Two copies of the variant more than doubles one's risk of experiencing RLS.

According to Dr. Rye, having two copies does not ensure that one will develop symptoms of RLS. "There remain yet-to-be-identified medical, environmental or genetic factors that appear necessary to translate genetic susceptibility into RLS symptoms," he says.

RLS researchers have known for some time that anemia and low iron levels contribute to more severe RLS symptoms. The current study revealed the gene variant to be more common in Icelandic subjects deficient in iron.

The medical breakthrough is the result of a four-year study led jointly by Dr. Rye and deCODE Genetics scientist Dr. Hreinn Stefansson. With the goal of identifying genes causing RLS, the research team conducted genome-wide scans of nearly 1,000 Icelanders and 188 Americans. A new chip technology was applied along with genome wide association methods.

This approach allowed Drs. Rye and Stefansson to probe more than 300,000 small regions (single nucleotides) distributed across the entire genome for differences more common to RLS sufferers as compared to population-based controls.

According to Dr. Rye, very little is known about the function of the gene variant discovered.

"Additional work will be required to translate this knowledge into a

plausible mechanism and, in turn, more rational and better treatments," notes Dr. Rye. "Future advances will depend upon additional monies which to this point have come solely from private foundations and industry."

Dr. Rye says RLS is exceedingly common but not taught as a part of standard medical education, in part leading many medical professionals, educators and academicians to challenge its commonality and authenticity.

Source: Emory University