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First potential pathogenic mutation for restless legs syndrome found

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An international team of researchers led by scientists at the Mayo Clinic campus in Florida have found what they believe is the first mutated gene linked to restless legs syndrome, a common neurologic disorder.

The researchers, who reported the findings in the July 21 issue of *Neurology,* doubt that a large proportion of the millions of people who suffer from the syndrome have this mutated MEIS1 gene. They point out, however, that understanding the function of both the normal and abnormal genes will shed some insights into this mysterious disorder.

Restless legs syndrome affects between 5 and 11 percent of the population in Europe and in North America. The condition is characterized by unpleasant sensations in the legs at rest, especially in the evening, that are temporarily relieved by movement. Because restless legs syndrome often interrupts sleep, people commonly are diagnosed after they consult a sleep specialist for assistance.

"We think restless legs syndrome may be due to a number of clinical factors, but we also believe that there is a strong genetic component to the disorder," says the study's lead investigator, Carles Vilariño-Güell, Ph.D., a neuroscientist at Mayo Clinic, Jacksonville.

"The mutation we found is in a portion of the protein that is identical in species as distinct to human as frogs and fish, which tells us that this portion is very important for the proper function of the protein and that the mutation has a very high chance of causing disease," he says.

While common variants (different versions) of MEIS1 and BTBD9, another associated gene, have been found in families with a high incidence of restless legs syndrome, it is not clear that those variants are capable of causing disease, Dr. Vilariño-Güell says.

"This mutation, on the other hand, is the first that we think can be a real candidate for causing or promoting restless legs syndrome," he says.

Researchers did not find mutations in the BTBD9 gene in study participants, but they found one in the MEIS1 gene that resulted in the production of an aberrant protein. The family that has the MEIS1 mutation consists of six members. Three who had restless legs syndrome had the mutation and the other three without the disease did not. "The presence of the mutation in all affected individuals supports a pathogenic role for the MEIS1 gene, and we now need to confirm this finding with other international research groups who study restless legs syndrome," Dr. Vilariño-Güell says.

Researchers from Canada, Ireland, and Norway also participated in the study. In total 378 restless legs syndrome patients and 853 healthy participants were evaluated for the presence of this newly discovered mutation in their DNA. This analysis only identified one additional individual from Ireland who did not present any symptoms of restless legs syndrome. This suggests that the gene defect may need additional triggers to develop the syndrome, Dr. Vilariño-Güell says. "This gene is probably not the most common cause of restless legs syndrome in the population we studied, but it may be more prevalent in other regions of the world," he says.

Source: Mayo Clinic (news : web)