

Study supports a causal role in narcolepsy for a common genetic variant

January 2 2014

A new study conducted across Europe found an extraordinary association between narcolepsy and a specific gene variant related to the immune system.

The modified genome-wide association study involved 1,261 people with narcolepsy, representing nearly 90 percent of European patients suffering from narcolepsy with cataplexy who have complete diagnostic work-up and DNA available. They were matched with 1,422 controls. High-resolution genotyping identified genetic variants including those in the [human leukocyte antigen](#) (HLA) system, which contains genes related to immune system function. Analysis was performed by logistic regression.

Results show that participants with the HLA allele DQB1*06:02 were 251 times more likely to have narcolepsy with cataplexy than participants without the [gene variant](#). DQB1*06:02 had a remarkably high negative predictive value of 99.32 percent, which means that nearly 100 percent of narcolepsy with cataplexy patients are DQB1*06:02 positive. Four other DQB1 alleles provided protection against narcolepsy, strongly supporting a causal role for DQB1 in narcolepsy.

"For the first time we have tested the HLA association all over Europe," said principal investigator and lead author Mehdi Tafti, professor in the Center for Integrative Genomics at the University of Lausanne and Lausanne Hospital in Switzerland. "This almost 100 percent association with HLA is somehow unique to narcolepsy and suggests a causal

implication."

Recent studies suggest that narcolepsy may be caused by an autoimmune response to an environmental trigger such as an infection. In people who are genetically susceptible to narcolepsy, the immune system may respond to the trigger by mistakenly attacking and destroying brain cells that make hypocretin, a hormone that helps promote alertness.

The authors noted that DQB1*06:02 is a common gene variant that is present in about 20 percent of the general European population. As a result, DQB1*06:02 had a low positive [predictive value](#) of only 65.68 percent. However, they suggested that high-resolution genotyping could play a valuable role in diagnosing patients suspected of having narcolepsy and evaluating at-risk populations.

"For clinicians these findings indicate they should reconsider the diagnosis of narcolepsy with cataplexy in HLA DQB1*06:02 negative patients," said American Academy of Sleep Medicine spokesperson Dr. Nathaniel Watson.

According to the American Academy of Sleep Medicine, narcolepsy is a rare but often disabling sleep illness characterized by excessive sleepiness. People with narcolepsy experience repeated daily episodes of an irrepressible need to sleep or lapses into sleep, which may occur as sudden, irresistible [sleep](#) "attacks." Another common symptom of [narcolepsy](#) is cataplexy, which involves sudden muscle weakness caused by strong emotions such as laughter.

Provided by American Academy of Sleep Medicine

Citation: Study supports a causal role in narcolepsy for a common genetic variant (2014, January 2) retrieved 6 April 2024 from

<https://medicalxpress.com/news/2014-01-causal-role-narcolepsy-common-genetic.html>

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