MedicalXpress

Mutation links inherited narcolepsy with multiple neuropsychiatric disorders

September 8 2011

Narcolepsy is a rare disorder characterized by an excessive urge to sleep at inappropriate times and places. Narcoleptics are also often subject to "cataplexy," a sudden muscle weakness that is triggered by strong emotions. Although most cases of narcolepsy are thought to be caused by complex mechanisms, a small percentage of cases are associated with unidentified inherited mutations. Now, a new study published by Cell Press on September 8th in the *American Journal of Human Genetics* uncovers a mutation that causes narcolepsy in a large family affected by the disorder. The research sheds new light on the genetics of inherited narcolepsy and provides intriguing insight into other complex neuropsychiatric disorders.

"The cause of this rare form of inherited narcolepsy has been very difficult to study and is not well understood," explains the senior study author, Dr. Rosa Peraita-Adrados from the Gregorio Marañón University Hospital in Madrid, Spain. "To identify a causative mutation in familial narcolepsy, we performed a genetic analysis in the largest-ever reported family with twelve affected members and then performed an even more sensitive analysis of three affected members with narcolepsy and cataplexy."

Dr. Peraita-Adrados, co-author Dr. Mehdi Tafti from the University of Lausanne in Switzerland, and their colleagues found that the myelin oligodendrocyte gene (MOG) in the affected family members harbored a mutation that was not present in unaffected family members or in hundreds of unrelated controls. Myelin is a protein produced by

oligodendrocytes, support cells in the central nervous system. It is essential for proper functioning of the nervous system. When the researchers put the abnormal form of MOG in mouse oligodendrocytes, they observed that the MOG protein was not properly distributed within the cells. This suggests that the mutant MOG must not function properly.

Although further studies are needed to identify the links between myelin, oligodendrocytes, and narcolepsy, the finding is particularly intriguing because MOG has recently been linked to various neuropsychiatric disorders. "Gene-expression studies in major depression, bipolar disorder, schizophrenia, and multiple sclerosis indicate that genes expressed in oligodendrocytes are downregulated, supporting the hypothesis that problems with oligodendrocytes might cause neurodevelopmental disorders," concludes Dr. Tafti. "The identification of a mutation in MOG, so far unique to our family, not only provides insight into the pathogenesis of narcolepsy but also highlights the role of myelin and oligodendrocytes in disease susceptibility in other complex neuropsychiatric disorders."

Provided by Cell Press