

New study draws connection between narcolepsy, influenza

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The onset of narcolepsy appears to follow seasonal patterns of H1N1 and other upper airway infections, according to a new study of patients in China that was led by Stanford University School of Medicine narcolepsy expert Emmanuel Mignot, MD.

The findings, which will be published online Aug. 22 in *Annals of Neurology*, a journal of the American Neurological Association and Child Neurology Society, show that a peak in narcolepsy cases occurred five to seven months after a peak in flu/cold or H1N1 infections in the country.

"Together with recent findings, these results strongly suggest that winter airway infections such as influenza A (including H1N1), and/or *Streptococcus pyogenes* are triggers for narcolepsy," Mignot, a professor of [psychiatry](#) and behavioral sciences, and his colleagues wrote in the paper.

The study follows recent reports that a particular H1N1 vaccine, not one used in the United States or China, seemed to lead to narcolepsy. This new paper, however, found no correlation between vaccination and narcolepsy among the patients studied in China. "The new finding of an association with infection, and not vaccination, is important as it suggests that limiting vaccination because of a fear of narcolepsy could actually increase overall risk," the authors wrote.

Approximately 3 million people worldwide suffer from narcolepsy, a

neurological disease that is characterized by daytime drowsiness, irregular sleep at night and cataplexy — a sudden loss of muscle tone and strength. In 2009 Mignot and colleagues confirmed scientists' long-held suspicion that narcolepsy is an autoimmune disease, caused when patients' immune systems kill the neurons that produce the protein hypocretin.

Experts believe that a person has a genetic predisposition to the disease, and some environmental factor kicks his or her immune system into action leading to narcolepsy. As noted in the paper, past studies have shown that [Streptococcus pyogenes](#) infections, such as strep throat, have preceded the onset of narcolepsy in Caucasians, suggesting a role for upper airway infections in triggering the disease, Mignot said.

Last year, several European countries reported new cases of narcolepsy in children who had been vaccinated for the H1N1 strain of influenza; children who received the Pandemrix H1N1 vaccine in Finland, for example, faced a ninefold increased risk of narcolepsy. The World Health Organization led an investigation and determined that something about this particular vaccine acted in a "joint effort" with "some other, still unknown factor" to increase risk in those already genetically predisposed. (Pandemrix contains two adjuvants to invoke a stronger immune response; these additives are not included in the H1N1 vaccines used in the United States and China.)

For the new study, the researchers looked at the data of 906 patients who were diagnosed with narcolepsy in Beijing between September 1998 and February 2011, and determined the patients' month of onset of cataplexy and sleepiness. They conducted brief phone interviews with 154 patients whose narcolepsy appeared after October 2009, the date of the first H1N1 vaccination administered in China. The researchers also queried the patients about their history of seasonal flu, H1N1 vaccinations and other diseases.

Mignot's group found that the occurrence of narcolepsy onset was seasonal and significantly influenced by month. Onset was least frequent in November and most frequent in April; there was a five- to seven-month delay between the seasonal peak in flu/cold or H1N1 infections and the peak in narcolepsy onset occurrences.

The paper doesn't show cause and effect, but it does show a strong correlation between narcolepsy onset and this seasonal pattern.

The team also found a threefold increase in disease onset following the 2009-10 H1N1 winter flu pandemic compared with other years.

Only a small amount — 5.6 percent — of the patients interviewed recalled receiving an H1N1 vaccine. The onset, the researchers concluded, is unlikely to be explained by vaccinations. Instead, as they wrote in the paper, these winter infections appear to "initiate or reactivate an immune response that leads to hypocretin cell loss and narcolepsy in genetically susceptible individuals."

Mignot said the work is exciting because it provides insight on how the disease is triggered. "We're much closer to understanding what's happening in the autoimmune destruction of hypocretin cells," he explained.

From a public-health standpoint, Mignot said the work suggests that getting vaccinated and avoiding [influenza](#) may provide a protective benefit to patients. He said, "It's very possible that being vaccinated with a mild vaccine, one without the adjuvants in question, blocks you from getting a big infection that could increase your risk of narcolepsy."

As for the differences between the findings of the study and what has been observed in Europe, Mignot said it's possible that the strong immune response prompted by the Pandemrix [vaccine](#) increases the risk

of [narcolepsy](#). He emphasized, however, that more study is needed and that people shouldn't avoid getting vaccinated.

"Even with Pandemrix, it's still a very small risk — and there's a bigger risk from dying of an infection if you don't get vaccinated," he said.

More information: "Narcolepsy Onset is Seasonal and Increased Following the H1N1 Pandemic in China." Fang Han, Ling Lin, Simon C Warby, Juliette Faraco, Jing Li , Song X. Dong, Pei. An, Long Zhao, Ling H. Wang, Qian Y. Li, Han Yan, Zhan C. Gao, Yuan Yuan, Kingman P. Strohl and Emmanuel Mignot, *Annals of Neurology*; Published Online: August 22, 2011 (DOI:10.1002/ana.22587).
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