Study explains why H1N1 flu can cause narcolepsy

Some three million people worldwide suffer from the debilitating sleep disorder narcolepsy. These people have difficulty in controlling their sleep pattern and can only sleep or stay awake for a few hours at a time.

Now an international research team has identified the cause of narcolepsy, and at the same time they have also found an explanation why the many new cases of the disorder followed in the wake of the H1N1 flu epidemic in 2009. The discovery may lead to improved diagnoses and better treatment.

The new findings show that the disorder is caused by cells in our immune system mistakenly seeing cells in the brain as being infected with a flu virus. When the immune system attacks these cells, narcolepsy occurs, explains the Danish researcher in the study:

"It has long been suspected that narcolepsy is caused by the immune system attacking some specific nerve cells in the brain, thus destroying the brain’s ability to regulate the sleep pattern. Our study confirms this suspicion, as we have figured out which cells in the immune system are responsible for the attack,” says Birgitte Rahbek Kornum, a senior researcher at the Molecular Sleep Laboratory, Department of Diagnostics at Glostrup Hospital in Denmark.

The findings are published in the journal Science Translational Medicine.

In the long term, the new findings may have profound implications for the treatment of people with narcolepsy. In the short term, the findings will primarily be of importance to people who are at risk of developing the disorder.

Since the researchers have found that the disorder is caused by specific cells in the immune system, it is now clear that only those who have these specific cells in their bloodstream are at risk of developing the disorder, and it will be possible to test for this.

“Up to now, it has only been possible to diagnose narcolepsy either through sleep analysis or by extracting fluids from the spinal cord. Our new discovery will make it possible to develop a simple blood test for diagnostic use. Our discovery can hopefully also be used to develop treatments against the disorder now that we know why it occurs,” says Kornum, adding that autoimmune disorders like narcolepsy are notoriously difficult to treat (see Factbox).
Vaccine led to narcolepsy

A remarkable part of the new discovery is that certain cells in the immune system appear to attack nerve cells in the brain because they mistakenly see the nerve cells as being infected with a flu virus.

This happens because the nerve cells contain some molecules that are almost identical to molecules that sit on the surface of the H1N1 swine flu.

The new discovery may explain why there was an increase in the number of narcolepsy cases in 2009-2010, when many Scandinavians were vaccinated against H1N1.

“The immune system can become confused when two molecules are very similar. Our studies show that parts of H1N1 are similar to hypocretin, the neuropeptide in the brain that regulates sleep,” says the Danish researcher.

“If a person’s immune system contains the cells that we have identified as the culprits behind narcolepsy and comes into contact with either H1N1 or the vaccine against H1N1, the immune system’s response can become activated and the disorder can develop.”

The vaccine in question – Pandemrix – has now been discontinued.

Narcolepsy is caused by damaged nerve cells

More specifically, narcolepsy is caused by a deficiency of a molecule in the brain called hypocretin, which is produced by certain nerve cells.

Hypocretin helps regulate the sleep rhythm so that we can stay awake and sleep for extended periods.

If our immune system destroys the nerve cells, the production of hypocretin stops, and the sleep rhythm of 16 waking hours and eight hours of sleep is replaced by an irregular sleep pattern in which sleep and wakefulness only occur in short periods.

The immune system possibly attacks the nerve cells because it registers tiny fragments of hypocretin on the surface of the cells.

These fragments of hypocretin are similar to the flu virus, which is why the immune system reacts to them.

However, this only happens if the immune system possesses some specific cells that can recognise the hypocretin fragments.

“We have now identified these cells that are essential in narcolepsy,” says Kornum. “These cells are present in people who would be at risk of developing the disorder if for instance a flu virus activates the cells.”

"We hit the nail on the head"

The new study contained experiments with identical twins, where one of the twins suffered from narcolepsy and the other did not.

The experiments revealed that the twins with narcolepsy carried the special immune system cells, while the healthy ones did not carry the cells.

The researchers then examined whether these immune system cells also react to hypocretin.
Here, they found that the cells reacted to fragments of hypocretin and to the flu virus, and that the flu virus caused the immune system cells to react more strongly to hypocretin and vice versa.

"You could say that we hit the nail on the head. There is no doubt that this is essential in the development of narcolepsy," says Kornum, whose research will continue to look for answers to exactly how the immune system cells destroy the nerve cells.

--------------------------

Read the Danish version of this article at [videnskab.dk](http://sciencenordic.com/study-explains-why-h1n1-flu-can-cause-narcolepsy)

Fact box

Molecular mimicry is a term used for when a bacteria or a virus can cause the body’s immune system to turn against the body and create an autoimmune disease.

Autoimmune diseases can be very difficult to treat, as it is the body’s own immune system that the body needs to be protected against, and this is not something one would want to put out of function.

Sclerosis is another example of an autoimmune disease in which the immune system attacks nerve cells in the brain.

Scientists hope that their research into a variety of autoimmune diseases will eventually lead to the development of a method to cure these diseases.

Up to now, it has only been possible to diagnose narcolepsy either through sleep analysis or by extracting fluids from the spinal cord. Our new discovery will make it possible to develop a simple blood test for diagnostic use. Our discovery can hopefully also be used to develop treatments against the disorder now that we know why it occurs.

Birgitte Rahbek Kornum

---
