Narcolepsy, brain imaging, and cognition

Understanding the connections

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Neurology® 2018;90:e1544-e1547. doi:10.1212/WNL.0000000000005371

In “Neurocognition, sleep, and PET findings in type 2 vs type 1 narcolepsy,” Huang et al.¹ at the Chang Gung University College of Medicine, Taiwan, studied brain imaging, cognitive testing, and sleep study abnormalities in people with narcolepsy type 1 and type 2. They compared the test results against a group of similar people who had normal sleep. Their idea was straightforward: to better understand the differences between the 2 types of narcolepsy as compared to healthy people.

How was the study done?

Dr. Huang identified 104 people with type 1 narcolepsy, 29 people with type 2 narcolepsy, and 26 age-matched people without narcolepsy. All participants were studied at Chang Gung University College of Medicine. Narcolepsy starts when a person is young (see “What is narcolepsy?”). It is not surprising that average age of the type 1 group was 20 years and of the type 2 group was 19.5 years. The average age of the age-matched controls was 19.1 years. A total of 34.5% of the type 1 patients were female, 35.6% of type 2 patients were female, and 38.5% of the controls were female.

The people with type 1 narcolepsy had cataplexy—this is partly how the diagnosis is made (see “What is narcolepsy?”)—while those with type 2 narcolepsy did not. All patients had sleep studies, neuropsychological testing (Conners Continuous Performance Test and a Wisconsin Card Sorting Test), and a PET. To be sure that medication would not affect the test results, all people had to have either never taken medication or be off their medications for 7 days prior to taking any of the tests.

Both groups had already had extensive blood and CSF tests. CSF testing is done with a spinal tap: a sample of the fluid that surrounds the brain is examined in a laboratory. In the type 1 group, 38 people (36.5%) had been checked for orexin levels: all of the people with type 1 narcolepsy had low orexin levels in their CSF. In the type 2 group, 6 had undergone CSF testing. Five had normal orexin levels. This is in keeping with what is known about the 2 types of narcolepsy. Those with type 1 narcolepsy most often have low orexin. Those with type 2 narcolepsy usually have normal orexin levels.

What did the study show?

The first tests that were performed were the sleep study (polysomnography [PSG]) and the Multiple Sleep Latency Test (MSLT). As anticipated, all of the people with narcolepsy were significantly more sleepy than those without narcolepsy. However, overall, the people with type 1 narcolepsy had more abnormalities on their tests than those with type 2 narcolepsy. Next, Huang et al. looked at neuropsychological test results. Compared to the people without narcolepsy, people with type 1 narcolepsy performed less well than those with type 2 narcolepsy. Third, PET scans were compared. PET measures how the brain uses its main fuel source: sugar. In other words, PET measures sugar metabolism in the brain. In people with narcolepsy, compared with the normal controls, there were certain areas of the brain in which there was more sugar breakdown. In other areas, there was less sugar breakdown. In addition, the authors noticed differences in these patterns when comparing narcolepsy types 1 and 2.

What do the results mean?

Compared to controls, Huang et al. found that people with narcolepsy have abnormal brain metabolism (PET) and abnormal brain function (neuropsychological testing). The people with

type 1 narcolepsy had more significant abnormalities on both tests than did those with type 2 narcolepsy. These findings are new: previous studies had not separated the 2 types of narcolepsy. In fact, one large previous study had shown no difference between the 2 groups.

Although these findings are interesting, many questions remain. How is the neurotransmitter orexin (also called

hypocretin) connected to these findings? Did the injury that caused injury to the orexin-producing cells cause the problems on cognitive testing? There may be inflammation within the brain: this may be the cause of the abnormal testing. Much remains to be studied. However, as we learn more about this sleep disorder, we may get much closer to better treatments and perhaps a cure.

About narcolepsy

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What is narcolepsy?

Narcolepsy is a condition that causes sleepiness. It is one of the more common sleep disorders, affecting 1 in 2,000 (0.05%) people.² It begins when a person is young. Narcolepsy starts to cause problems when a person is between 5 and 15 years old. As a medical illness, it is most often diagnosed between the ages of 10 and 20 years. However, narcolepsy is an underrecognized illness. It is estimated that narcolepsy is only diagnosed about half (50%) of the time. In other words, there are many people who are never diagnosed. As a result, they never benefit from treatment.

Recently, there has been extensive study of narcolepsy. Two types have been found. Both start at the same age and cause many of the same symptoms. The most common symptom is being tired during the day. A person with narcolepsy will fall asleep, and often awakens feeling refreshed. However, a few hours after waking up, they are tired again, especially when they sit down or rest for extended periods of time. Because of the sleepiness during the day, they may have poor school or work performance. They may fall asleep while driving.

A person with narcolepsy has sleep abnormalities. He or she may experience REM sleep within 15 minutes of falling asleep. Often, he or she will also have dreams when briefly taking a nap (most people do not dream when they take a nap). Because of this, their dreams may intrude into their wakeful state. When this happens, the person experiences hallucinations. These happen when the person is either falling asleep (called hypnagogic hallucinations) or waking up (called hypnopompic hallucinations). The hallucinations can seem so real that the person can be convinced, for instance, that there is an intruder in the house, and call the police.

Type 1 narcolepsy is diagnosed more often than type 2 narcolepsy. One reason is that people with type 1 narcolepsy often have something called cataplexy. This is a partial paralysis that occurs after a strong emotion. The paralysis often starts in the face, and then moves to the chest and arms. The paralysis spares the muscles of breathing. It often lasts 1–2 minutes. It occurs more often after a sudden happy emotion (like laughter, or encountering a friend unexpectedly) than with negative emotions (like anger or frustration).

Causes of narcolepsy

Scientists are beginning to understand the causes of narcolepsy. In type 1 narcolepsy, scientists have found that there is a loss of a specific group of brain cells. These cells live in a part of the brain called the hypothalamus. They make neurotransmitters called orexin A and orexin B (also called hypocretin A and hypocretin B). In people with type 1 narcolepsy, because they have a small number of these cells, their orexin A levels are very low. Orexin levels are measured by taking a sample of CSF. Thus a person has to have a spinal tap for this test to be performed. The test is still considered experimental: it is not yet a test that all doctors can perform.

In both narcolepsy types, there appears to be a link to genetics. Narcolepsy runs in families. One finding is that people with narcolepsy have a specific human leucocyte antigen (HLA) called HLA-DQB1. However, there also seems to be an association with the springtime: narcolepsy starts most often in the spring. Perhaps there is a link to viruses that a person would be most likely to encounter in the winter. In other words, narcolepsy may be connected, in part, to an immune system problem. Perhaps the virus causes injury to the orexin-producing brain cells. Further research is needed to understand this connection better.

How is narcolepsy diagnosed?

In most people, the first step towards a diagnosis is a careful history. This occurs in the doctor's office, where the doctor will need to ask many questions about the person's sleep and sleep problems. Often, the doctor will use the Epworth Sleepiness Scale. This is a series of 8 situations wherein the person will report how likely he or she is to fall asleep. The higher the score, the more likely the patient is to have a sleep problem. Doctors use this scale for diagnosis and to measure how well a treatment is going.

Next, the doctor will order a sleep study. There are 2 parts to the sleep study. The first part is a PSG, which measures the amount and type of sleep that occurs during the night. In the second part, called MSLT, the time to falling asleep is measured. In people with both types of narcolepsy, the MSLT is abnormal. In fact, this test is one of the most helpful tests in the diagnosis of narcolepsy.

Treatment of narcolepsy

Nowadays, there are many possible treatments for narcolepsy. Often, a combination of behavioral changes is made

along with medications. Behavioral changes include taking scheduled naps or obtaining the proper amount of sleep. Most narcolepsy medications are stimulants, and are taken during the day to promote wakefulness. For cataplexy, antidepressants are helpful. A discussion with a specialist may be needed to identify the right combination of treatments for an individual.

Additional resources

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Narcolepsy Network, Inc.

narcolepsynetwork.org

National Sleep Foundation

sleepfoundation.org

References

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DOI 10.1212/WNL.0000000000005371

This information is current as of April 23, 2018

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