# Narcolepsy

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**Author: Ron Cridland, MD**

Narcolepsy is generally considered a genetic condition of excessive daytime sleepiness. The most recent classification system divides this condition into Type 1 and Type 2. Narcolepsy Type 1 consists of the classic symptoms of excessive daytime sleepiness associated with cataplexy. Type 2 is not associated with cataplexy.

Cataplexy consists of weakness triggered by a strong emotional response such as laughter or surprise. The weakness may be mild such as head drooping, difficulty speaking or having to sit down. In more severe cases complete collapse may occur and the person falls to the floor unable to move from a few seconds up to a couple of minutes. Observers may confuse this with fainting and unconsciousness. However the person with cataplexy is awake and aware of what is going on around them but may be unable to move, speak or respond in any way for a few moments. The person may have a few moments warning that the weakness is coming on and time to sit down, but there is significant potential for injury. The frequency of cataplexy may be as little as a few times per year in some people to as many as 20 times per day in others.

Narcoleptics usually do not have any trouble falling asleep although they may not have the best quality sleep. They may not feel sleepy when they wake up in the morning but they may start to feel sleepy fairly soon into their day. They may find naps irresistible and temporarily restorative. They are at significantly increased for accidents due to sleepiness and inattention. They may report driving somewhere and not remember parts of the drive or how they got there.

Onset of Narcolepsy symptoms typically begin between the ages of 10 and 25 although there is a smaller group in whom the onset occurs after the age of 35. It can occur in younger children but can be more difficult to diagnose in this age group. Between 33 and 80% of narcoleptics will have hypnagogic hallucinations, hypnopompic hallucinations and/or *sleep paralysis*. Hypnagogic hallucinations are dream-like states that occur as you fall asleep. Hypnopompic hallucinations are dream-like states that continue into your waking state. Quite often these hallucinations are associated with paralysis of the voluntary muscles. It can be quite scary the first few times that this occurs because you may hallucinate that there

is something or someone in the room and you cannot speak, move or do anything about it for a few moments. Then the next thing you know, the hallucination is gone, everything is back to normal and you can move and speak again. About half the population will experience this once or twice in their lifetime usually associated with disturbed sleep. In Narcolepsy this may occur anywhere from a few times per year to a number of times per week.

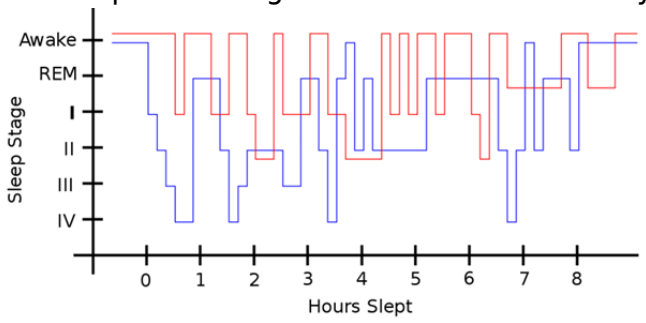
In 95% of cases, Narcolepsy Type 1 is associated with a deficiency of a neurotransmitter in the brain called Hypocretin-1 which normally helps the brain stay awake. Only about 24% of people with Narcolepsy Type 2 have a deficiency of Hypocretin-1.

Although Narcolepsy is considered a genetic condition, only about 1 – 2% of first degree relatives of narcoleptic patients may have it. The overall incidence is about 0.02 – 0.18% of the general population. It is associated with a genetic marker on the white blood cells called HLA (Human Leukocyte Antigen) subtypes DR2/DRB1*1501 and more commonly DQB1*0602. Almost everyone with cataplexy has HLA subtype DQB1*0602 antigen on their leukocytes (white blood cells). However, about 25% of the normal population also have this antigen so unfortunately it cannot be used by itself to make a diagnosis of Narcolepsy Type 1. Only 45% of those with Narcolepsy Type 2 patients have this antigen. So if a narcoleptic does not have this antigen, then they are more likely Type 2.

Although the condition appears to have a genetic component, it also seems to require a trigger. It is thought that an infectious illness or head trauma may trigger the onset of narcolepsy in some patients. Infection may trigger an autoimmune process that damages the hypocretin producing cells in the brain.

**Diagnosis**

Diagnosis of *Narcolepsy* requires a history of daily excessive sleepiness not explained by other medical or psychiatric illness, medication, recreational drug use or lack of sleep. A *Nocturnal Polysomnogram* is required to rule out other sleep disorders. The next day a *Multiple Sleep Latency Test* (MSLT) is conducted to objectively evaluate daytime sleepiness. This is a series of 4 or 5 twenty minute nap opportunities spaced out every 2 hours throughout the day. You lie down in a quiet, dark room and we determine how quickly you fall asleep on average. We also look to see if you go into REM sleep on two or more naps.




If you fall asleep on average in less than 8 minutes (Narcoleptics typically fall asleep in less than 5 minutes), you go into REM sleep on two or more naps, and there is no significant other sleep disorder seen on the Nocturnal Polysomnogram, then you meet the criteria for Narcolepsy. If you have cataplexy or your cerebral spinal fluid (CSF) shows low levels of Hypocretin-1 then you meet the criteria for Narcolepsy Type 1. Otherwise you have Narcolepsy Type 2.

Currently, testing for Hypocretin-1 is not available in Canada. CSF samples have to be sent to the United States for testing and this may not be covered by provincial health plans. Taking a sample of CSF requires a lumbar puncture which is a needle inserted into the spinal canal. This is an uncomfortable test associated with certain risks although these risks are relatively low in experienced hands. Although blood testing for HLA DQB1*0602 antigen is not diagnostic for Narcolepsy by itself, it can help differentiate between Type 1 and Type 2 when the MSLT is positive for Narcolepsy. The antigen is always positive if you have low Hypocretin levels which means Type 1. If the DQB1*0602 antigen is absent and you meet the other criteria for Narcolepsy, then most likely you have Type 2. If the antigen is positive then you would need to measure Hypocretin to differentiate between Type 1 and Type 2. Based on the effort, risk and expense to test for Hypocretin, it is debatable whether it is worth the trouble at this time since the treatment for Type 1 and Type 2 is the same.

**Management**

Since there is currently no way to replace hypocretin in narcoleptics like we can give insulin to diabetics, the treatment is symptomatic. Although patients are often not too keen on taking anything, if you truly have Narcolepsy, medication will change your life! Sleepiness is treated with stimulant medication. Cataplexy is suppressed with antidepressant medication. Scheduling naps into your day is an effective way of temporarily "taking the edge" off your sleepiness during the day and complimenting the stimulant medication you take. Following recommendations for good *sleep hygiene* will also help to improve sleep quality and daytime sleepiness. Narcoleptics need to protect their sleep. They need to make sure they schedule themselves with enough time to get adequate sleep. They should avoid jobs that require shift work or frequent time zone travel.

There are 3 stimulant medications plus their long acting variants.

Modafinil (Alertec) is the mildest and a good place to start because it generally has the least amount of side effects. Starting dosage is 100 mg twice per day taken morning and noon. After a week, the dose can be increased to two pills twice per day to control daytime sleepiness.

Methylphenidate (Ritalin) is 10 mg also twice per day. The dosage can be increased to a maximum of 60 mg per day to control daytime sleepiness. Sometimes the stimulation effect seems to fluctuate too much between dosages. You may alternate between feeling hyper and stimulated to feeling tired and let down before the next dose. Once the total daily dosage has been determined, you can either divide it into three dosages so you can take it more frequently, or you can convert to a longer acting version such as Concerta.

Dextroamphetamine (Dexedrine) is 5 mg twice per day increasing to a maximum of 60 mg per day to control daytime sleepiness. Once the total daily dosage has been determined, you can convert to the Dexedrine Spansules which are 10 mg or 15 mg and are longer lasting. If there are still too many ups and downs in the stimulation effect, you can consider a longer acting version such as Adderall.

Modafinil can interfere with the metabolism of birth control pills and so another form of contraception should be used in woman of child bearing potential. The most common side

effects of any of the stimulant medications include faster heart rate or palpitations, elevated blood pressure, dry mouth, reduced appetite, weight loss and insomnia. These are fairly uncommon for Modafinil but more common for Ritalin or Dexedrine which are stronger stimulants.

Some of my patients wonder why they would take a stimulant like Ritalin when people with ADHD take it apparently to calm them down. People with ADD or ADHD have trouble speeding up their brain wave frequency to a level that they can concentrate and think. Sometimes their hyperactivity is kind of a maladaptive way to help them stimulate their brains to function better. Stimulants help speed up the brain so it can focus and concentrate better which improves distractibility and hyperactivity. Even though these medications look like they are calming people with ADD and ADHD, they are actually stimulating their brains too.

Cataplexy is essentially the muscle paralysis of REM sleep intruding into the wakeful state in response to an emotional stimulus. Antidepressants are well known to suppress REM sleep and are also very effective at suppressing cataplexy too. We generally prefer to use the more stimulating antidepressants such as Fluoxetine (Prozac) so as not to add to the daytime sleepiness. The dosage is 10 – 60 mg each morning. Venlafaxine (Effexor) 75 – 300 mg each morning is also very effective.

A newer medication is now available called Sodium Oxybate (Xryem). Xryem is a sedative and is taken in two divided dosages; one dose at bedtime and another dose 4 hours later during the night. This medication not only improves daytime sleepiness, it also controls cataplexy. Although it improves sleep quality, it is not known how it works to improve daytime sleepiness because other sedating medications do not improve daytime sleepiness in Narcolepsy to the same degree. Similarly, the mechanism for how it controls cataplexy is also unknown. Xryem is carefully regulated and can only be prescribed by a sleep disorders physician registered with the manufacturer.