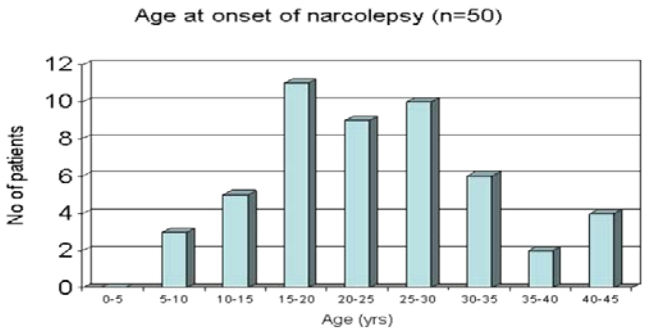
NARCOLEPSY

Narcolepsy was first identified as a medical condition in the early twentieth century. Its typical onset is in adolescence/early adulthood, but it can occur earlier or later in life (around a quarter of cases actually occur after age 40).



Narcolepsy affects about 0.5-1 in 1000 people *worldwide*, and so is very rare. There are four general symptoms associated with narcolepsy:

(1) **Excessive daytime sleepiness and sudden sleep attacks:** These can occur at any time (e.g. whilst eating or driving). An episode typically lasts 10-20 minutes, with the person waking up feeling refreshed, only to start feeling tired again soon afterwards

(2) **Sleep paralysis:** A consciously experienced inability to move just prior to falling asleep or waking up

(3) **Dreamlike experiences while still awake and just before falling asleep or just before being fully awake:** The former are called *hypnagogic hallucinations* and the latter are called **hypnopompic hallucinations**. These experiences are difficult to distinguish from reality.

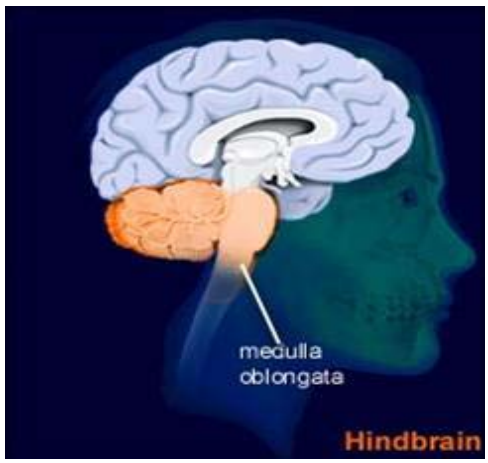
(4) **Cataplexy:** This is the most dramatic symptom, in which the skeletal muscles weaken or are paralysed, and the person collapses and enters 'REM sleep'. Cataplexy is often triggered by some strong *emotional event* (e.g. laughter or anger). The person may be able to see/hear during the episode, which typically lasts from a few seconds to a few minutes.

Cataplexy

Note that not all of the symptoms are shown by all narcoleptics. Cataplexy, for example, occurs in about 70% of all narcoleptics.

Explanations of narcolepsy

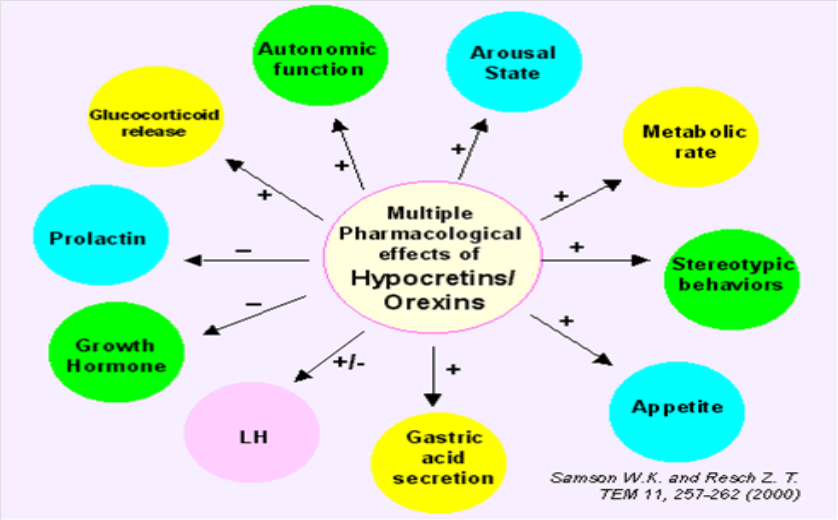
Narcolepsy is clearly a malfunction of the normal sleep-waking regulating system in the brain. In cataplexy, neurons in the **medulla**, which are active during REM sleep and suppress skeletal muscle movements, are activated when they shouldn't be. Essentially, then, narcolepsy is a kind of *REM sleep* occurring at an inappropriate time.



Narcolepsy seems to run in families, with a person being ten times more likely to suffer from it if there is a family history of it. This has led researchers to suggest that narcolepsy is **genetic**. Genes exert their influence through biochemical events, so researchers have looked for neurotransmitters that might be involved.

In the 1990s, an American research team found that mice who could not make a neurotransmitter called **hypocretin** (also known as orexin) displayed

sleep attacks and cataplexy. Another American team found that some strains of dogs (e.g. Dobermans and Labradors) also exhibited narcolepsy following bouts of excitement. The researchers identified a mutant gene on chromosome 12 in the dogs which affects neurons that secrete hypocretin.



Hypocretin-secreting neurons are ordinarily active during wakefulness, and keep the brain from shutting down unexpectedly. Therefore, narcolepsy is caused by a *deficiency* of hypocretin. This view is supported by the finding that *stimulant drugs* which are used to treat narcolepsy in both humans and dogs are believed to work by activating hypocretin-containing neurons.

Research also shows that hypocretin levels in the cerebrospinal fluid of narcoleptics are either very low or undetectable, and that narcoleptics have lost around 90% of their hypocretin-secreting neurons from the hypothalamus. Additionally, people with Parkinson's disease show a sleep disorder very similar to narcolepsy, and post-mortems show a loss of around 60% of brain cells containing hypocretin in Parkinson's sufferers.

In a case study of a sixteen-year-old girl, **Arii et al (2001)** reported that the girl had developed narcolepsy following surgery to remove a brain tumour. The tumour was located close to her hypothalamus, and it is possible that her narcolepsy arose because the surgery had affected the neurons that secrete hypocretin from the hypothalamus.

However, whilst there might be a single mutant gene associated with narcolepsy in dogs, this isn't the case with humans. This is because the *concordance rate* for identical twins is only 30%, so other factors must play some role in the development of the condition. *Hormonal changes*, *infection*, and *trauma* have all been suggested to be involved. Thus, there may be other causes of narcolepsy that we don't know about, and don't share with dogs.

It should also be noted that research into a condition that affects humans using dogs as the experimental subject raises important questions about generalizing results. There are also important ethical issues that arise when narcoleptic dogs are bred for research purposes.

A final evaluative point is that whilst narcolepsy may be a result of reduced hypocretin, it isn't known what causes this reduction. The most popular proposal is that the *immune system* identifies hypocretin-producing cells as foreign, and selectively destroys them. However, what might cause this to happen isn't known either.