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Overview of Narcolepsy: How Can a Sleep Disorder Be Life-Threatening?

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ABSTRACT

Narcolepsy is a sleep disorder characterized by periods of sudden sleep attacks and drowsiness in the daytime. Those with type 1 narcolepsy may experience cataplexy, or weakness in muscle tone, drowsiness, and involuntary movements while they are awake. Many patients suffer from hypnagogic hallucinations, sleep paralysis, and disturbed sleep. Studies have emerged linking narcolepsy with various other conditions, ranging from neurodegenerative disease to cardiovascular health. However, the dangers of narcolepsy go beyond the presence of physical hindrances in an individual's life, they can go as far as threatening an individual's emotional and mental well-being.

Pathophysiology and Types

During periods of wakefulness, an unaffected individual's orexin, or hypocretin levels, stimulate the activity of the reticular activating system. Specifically, the reticular activating system, otherwise known as the RAS, helps generate certain neurotransmitters that maintain wakefulness and energy levels, including dopamine, serotonin, norepinephrine, and histamine (Collen et al., 2023). Those with type 1 narcolepsy lack the neurons to produce orexin or hypocretin. These chemicals normally help the brain maintain a balance between periods of wakefulness and sleep.

There are two types of narcolepsy as mentioned above; in individuals with type 1, almost all the neurons that produce hypocretin or orexin are destroyed, which causes cataplexy (DeBanto & Suni, 2023). Cataplexy is defined as episodes of weakness in muscles, often triggered by strong, intense emotions, such as happiness, anger, and grief. Individuals with type 2 have normal levels of orexin.

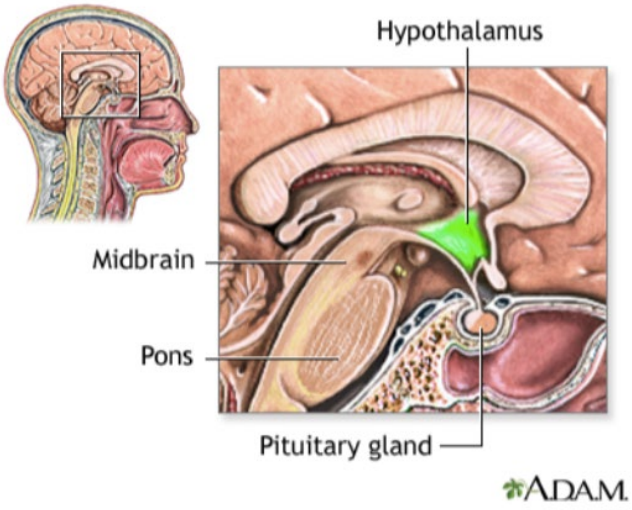

Figure 1. An image of the hypothalamus' location in the brain in relation to other structures.

The hypothalamus is responsible for regulating human body conditions: body temperature, blood pressure, hunger, and other functions. Neurons in the hypothalamus are responsible for producing orexin, which people with type 1 narcolepsy lack. Therefore, narcoleptic patients are not able to control periods of wakefulness and rapid eye movement (REM) sleep properly, leading to unwanted sleep attacks and a lack of control over their daily lives.

Signs and Symptoms

Among the many symptoms of narcolepsy, a major indicator is sudden sleep attacks and excessive daytime sleepiness. These indicators can be diagnosed through the use of sleep studies and related tests, as imaging tests prove unhelpful to diagnose this specific disorder. Some individuals may experience sleep paralysis when initially waking up and falling asleep (*Narcolepsy*, n.d.). Beyond the physical limitations sleep paralysis brings, it also impacts an individual's sense of control over their own life, which makes it very dangerous in all aspects. As many patients experience auditory, visual, and tactile hallucinations, this can make it difficult for them to separate reality from their perceived surroundings. Common themes of narcoleptic hallucinations include threatening strangers and animals.

People with narcolepsy may also experience hypnagogic hallucinations, which are hallucinations that take place when one is falling asleep (Brandt & Slon, 2020). They don't just experience symptoms of narcolepsy in the daytime. Due to the excessive daytime sleepiness that comes with the disorder, individuals with narcolepsy may experience difficulty falling asleep at night, leading to insomnia and other health concerns that extend to their personal lives. Patients suffering from narcolepsy often take periodic naps for as little as 15 minutes, but those short rest stretches can significantly improve their alertness for several hours. Another defining symptom is the presence of cataplexy. At moments of high emotion, cataplexy will cause momentary episodes of muscle weakness, typically within the face and neck. This can cause severe anxiety for patients who fear experiencing cataplexy in public.

Diagnosis

It is extremely difficult to diagnose narcolepsy based off of symptoms as many sleep disorders share many of the same signs. For this reason, narcolepsy can only be diagnosed by thorough evaluations of multiple medical exams.

Polysomnograms, otherwise known as PSG exams, are used to study an individual's brain and muscle activity, respiration, and eye movement overnight. They record bodily position, electroencephalogram (EEG) waves, air flow, and eye movements, among other factors. A narcoleptic patient can be identified by the rapid progression through sleep cycles. They tend to fall asleep and enter REM sleep very quickly (Rehman & Suni, 2023). These tests are generally reliable and produce accurate results to diagnose narcolepsy accordingly. This test can also reveal the presence of other sleep related disorders such as sleep apnea.

Multiple Sleep Latency Tests (MSLT) involve an individual taking five scheduled naps throughout the day in two-hour intervals. This exam would typically follow the polysomnogram test using the same sensors. The examiner takes note of sleep latency and how quickly REM sleep begins. Individuals with narcolepsy often have at least 2 naps where REM sleep is reached (Mayo Clinic Staff, 2023).

The lumbar puncture is a procedure in which cerebrospinal fluid is often extracted from the area surrounding the spinal column. As individuals with narcolepsy type 1 contain low hypocretin levels, this procedure proves to be beneficial to them, as healthcare professionals can use the results to further indicate a positive narcolepsy diagnosis.

Blood tests are a useful indicator to determine whether an individual has narcolepsy. Those with type 1 narcolepsy often have a genetic marker called HLA DQB1*0602 (Andres & Brogan, 2022). This is characterized as a hypocretin deficiency. However, a quarter of the entire United States population is positive for DQB1*0602, so this information is used to rule out hypocretin deficiency rather than be a definitive test for narcolepsy (*Narcolepsy*, n.d.). Diagnosing narcolepsy Type 1 and 2 have disparate criteria. They both have in common the requirement of three months of persistent excessive daytime sleepiness (EDS) and PSG/MSLT tests that show rapid onset of REM sleep.

In order to be diagnosed with narcolepsy type 1, the patient must have cataplexy, whereas type 2 patients must not display cataplexy symptoms, have normal levels of hypocretin, and have no other explanation for experienced symptoms (Rehman & Suni, 2023).

Misdiagnosis of the disorder, unfortunately, is another variable that individuals with the disorder and medical professionals have to worry about. Narcolepsy is often misdiagnosed as several psychiatric disorders, including anxiety and depression, as they share several symptoms. Due to the nature and side effects of treatments individuals may take to combat the disorder, including sodium oxybate and SSRI medications, a misdiagnosis may impact them both financially and physically. On the other hand, a delayed diagnosis may result in symptoms worsening, along with confusion related to experiencing symptoms. It is important to correctly assess a patient's symptoms and ensure accurate positive results before diagnosis and treatment takes place.

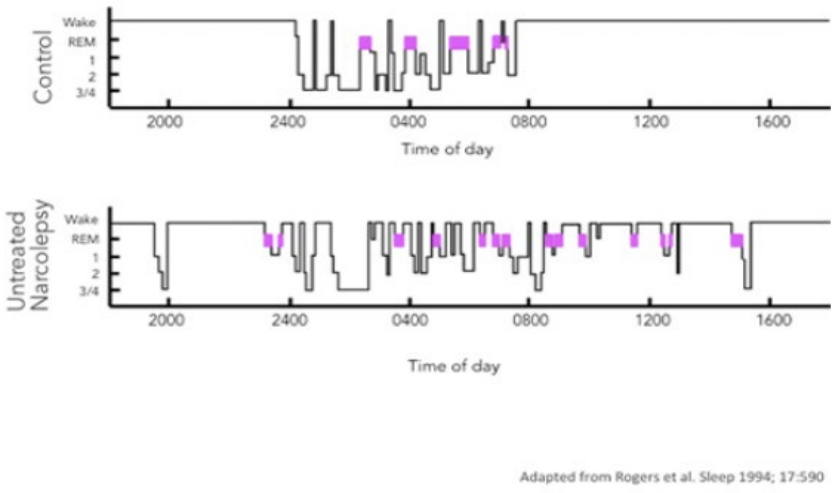

Figure 2. The sleep recordings of individuals with versus without narcolepsy. The patient with narcolepsy displays fragmented sleep/wake patterns throughout a 24-hour cycle and far more periods of REM sleep.

Causes

Narcolepsy is proven to have both genetic and environmental causes. Following the previous discussion and evidence of the involvement of the HLA genetic marker, the related gene family is responsible for constructing proteins called the human leukocyte antigen complex, which is then responsible for protecting the human body against unknown viruses and bacteria. Alterations to the HLA DQB1*0602 genetic marker is linked to individuals who have type 1 narcolepsy, which also increases the risk for cataplexy. Additionally, narcolepsy is thought to have a connection with an individual's weakened immune system, which can be caused by several factors, both environmental and genetic. Head injuries, strokes, and upper airway infections may cause narcolepsy, too. Minor infections can deceive the immune system into destroying the cells that produce hypocretin (Narcolepsy UK, n.d.).

With regards to family history, inheriting the disease is said to be random in most cases. That is, cases can occur in individuals with no family history of the disorder. However, a family history of narcolepsy can increase an individual's chances of developing the disease.

One special instance of a "narcolepsy epidemic" occurred in the United Kingdom during the Swine Flu epidemic. A vaccine called Panderemix was administered to the public despite the lack of clinical trials, but it was later found that one in every 55,000 patients who received the vaccine developed narcolepsy (Narcolepsy UK, n.d.).

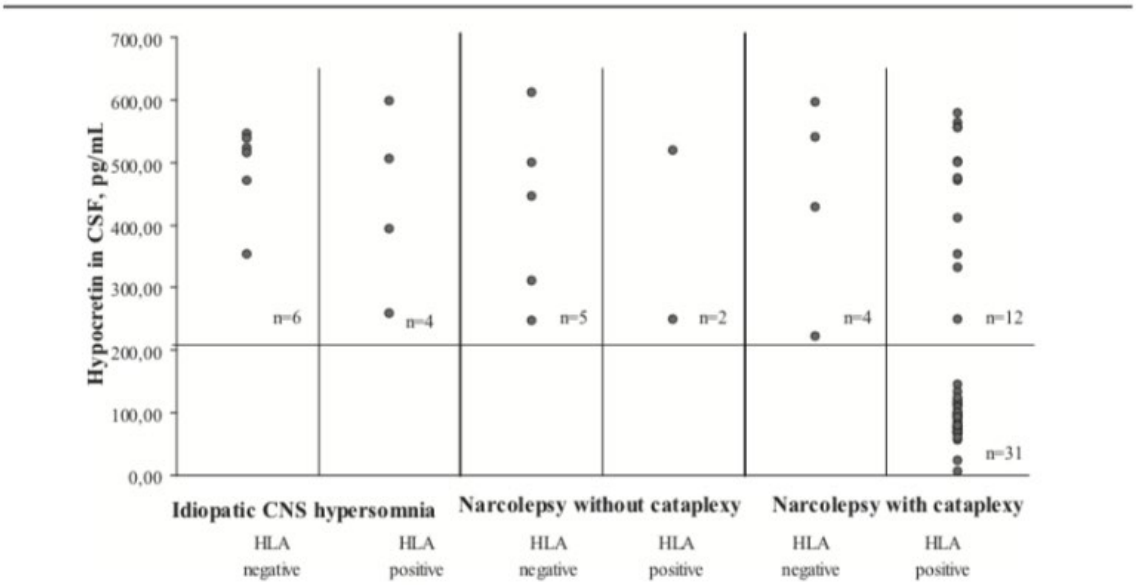

Figure 3. The assessment of CSF (cerebrospinal fluid) hypocretin levels in HLA DQB1*0602 positive and negative patients with narcolepsy with and without cataplexy, along with idiopathic CNS (central nervous system) hypersomnia.

In particular, we focus on the overall correlation between low levels of hypocretin in cerebrospinal fluid in accordance with the presence of cataplexy in people with narcolepsy. The data reflects that out of the 62 individuals assessed, 47 of them had narcolepsy with cataplexy, and 43 of those had the HLA DQB1*0602 gene (Heier et al., 2007).

Treatments

Currently, there is no definitive cure for narcolepsy. Fortunately, there are certain treatments and medications that help keep individuals awake during the daytime and manage their symptoms, leading to an overall increase in the quality of life. Some of these may include stimulants, which naturally keep individuals alert throughout the day, such as Provigil and Nuvigil (Mayo Clinic Staff, 2023). Individuals with type 1 narcolepsy, which includes symptoms of cataplexy, can benefit from taking sodium oxybate and oxybate salts, which help reduce this muscle weakness. These treatments may help promote sleep at night, while also keeping individuals awake in the daytime. However, common side effects of these treatments include potential bed-wetting and sleepwalking, which further demonstrates the extent of struggle individuals with narcolepsy go through daily. Some more uncommon side effects include headaches and an overall lack of appetite. Treatments that are targeted toward reducing REM sleep include SSRIs, or selective serotonin reuptake inhibitors. These medications work by stopping reuptake mechanisms, allowing for more serotonin to pass between neurons and relay messages (NHS 24, 2023). The side effects of utilizing SSRIs may include insomnia and digestive issues (NHS 24, 2023). Nonpharmacologic treatments include establishing a rigid sleep schedule and maintaining it every day. Scheduled naps can also improve alertness throughout the day. As a society, we hope that scientists can develop more effective treatments for those with narcolepsy with minimal side effects. Universal acknowledgment of narcolepsy as a disability is crucial to better serve patients suffering from this condition. It is important for places to be inclusive and sensitive to narcoleptics.

Implications

Besides impacting an individual's daily routine, narcolepsy is said to have a connection with mental health issues in people affected by the disorder. For instance, depression and anxiety are often found in people with narcolepsy, and ADHD (attention deficit hyperactivity disorder) symptoms are often found in children with narcolepsy. However, in relation to a person's daily life, narcolepsy can affect an individual's career, relationships, memory and more. For instance, an individual with narcolepsy has to manage their sleep throughout the day, often taking short naps to manage their sleepiness, which can lead to feelings of fatigue and instability in one's daily routine. Studies also show that the socioeconomic status of narcolepsy patients is far worse than that of the average individual. Unemployment rates among people with narcolepsy are also much higher than the control group (Jennum et al., 2009). Narcolepsy continues to be dangerous to a person's overall well-being, as it increases an individual's chances of developing more life-threatening health issues, which are discussed further in the article.

Narcolepsy in Relation to Alzheimer's

The Honolulu-Asia Aging Study found that there is up to a 44% increase in the risk of cognitive decline of elderly patients with EDS (Dauvilliers, 2021). Many caregivers note that patients with Alzheimer's Disease (AD) take naps more frequently, often starting before their diagnosis. Recent studies in Alzheimer's research show that AD attacks the same regions of the brain that are influenced by narcolepsy. These regions are the first to be affected by the neurodegeneration process as well. There is strong evidence showing that the presence of tau tangles is the underlying cause of degeneration in the hypothalamus (Sleep Review, 2019). There has also been a strong correlation discovered between excessive daytime sleepiness and cognitive decline in older patients. Other studies propose a link between orexin deficiency and the amyloid pathways involved in Alzheimer's. This led researchers to hypothesize that chronic loss of orexin early on in life could prevent the accumulation of amyloid-beta (Aβ). However, when a study tested this proposition by examining AD related neuropathic lesions, they found 33% of the autopsies conducted on narcoleptic patients has these lesions, which suggests that there might not be a significantly increased risk of AD lesions in narcolepsy patients compared to the general population (Dauvilliers, 2021). There is still much unknown information in regard to both Alzheimer's and narcolepsy research. While the two conditions do seem to be intertwined, emerging studies will have to uncover the extent of their correlation.

Narcolepsy and its Connection to Cardiovascular Health

Narcolepsy is suspected to be linked to cardiovascular disease as it impacts an individual's overall health, leading to a greater risk of cardiovascular issues. For example, narcolepsy can cause obesity, diabetes, and high blood pressure, which significantly impact cardiovascular health. Because of these risk factors, and the combined mental and physical impacts of narcolepsy, individuals are at higher risk for having a heart attack, heart failure, and stroke (American Heart Association, n.d.). In one study, scientists studied the presence of comorbidities in individuals with narcolepsy, for a presence of multiple health issues that exist independently of one another. Their results reflected a significant existence of multiple health disorders in patients with narcolepsy compared to their control group (Black, et al., 2017). According to their findings, the greatest comorbidities were for mental health issues, digestive system diseases, and nervous system issues (Black, et al., 2017).

Other Perspectives on Narcolepsy and Common Misinformation

Women with narcolepsy are more likely to have trouble functioning in their everyday lives, especially if they are caregivers. While caring for their children, they may experience sleep attacks and other symptoms, endangering both mother and child in the process. Young children with narcolepsy also go through similar difficulties, as they are still developing and may be confused about their symptoms, fearing that no one would be able to understand what they are going through. As a result, they may not be able to properly communicate their struggles and symptoms of the disorder to a medical professional, which could result in various treatment issues later on (Barker et al., 2020).

Studies have shown significant racial disparities in narcolepsy patients. African Americans have a much lower chance of having cataplexy despite having lower levels of hypocretin. Due to this, more patients have Type 1 narcolepsy without any cataplexy. (Kawai et al., 2015). Symptoms often onset earlier in African Americans as well. Extra care should be taken to ensure that members of this group are properly diagnosed.

Gender also plays a role in the timeliness for narcolepsy diagnosis. In a recent cross-sectional study, researchers found that 85% of men received a narcolepsy diagnosis 16 years after the onset of symptoms whereas on average, women received their diagnosis 28 years after (Won et al., 2014). At any point in time, women are more likely to have undiagnosed narcolepsy than men. This study contributes to the bigger picture of female patients often having their symptoms undermined as a whole.

Narcolepsy is often referred to as a disorder characterized by “randomly falling asleep,” without being considered as the dangerous and life-threatening disorder that it is. Many believe that people with narcolepsy can control when they fall asleep and stay awake and are lazy, when they must compromise certain aspects of their lives to function, while potentially experiencing judgment and misconceptions from the people around them. It is important to recognize narcolepsy for what it is and understand the extent to which it impacts one’s life and relationships by effect. To do this, we as a society should educate ourselves on narcolepsy as a whole and use our knowledge to help those who are impacted by the disorder.

Conclusion

Narcolepsy poses a significant risk to individuals who have it, as it can cause subsequent life-threatening diseases and comorbidities to develop in affected individuals throughout their lifetime. Many daily activities that unaffected individuals complete with ease can pose grave dangers for narcoleptic patients. Apart from the existing everyday dangers that exist in the lives of these individuals, they are continuously affected by the misconceptions and lack of knowledge of those around them, making their situations even more difficult. Misdiagnosis of the disorder continues to be common, due to an overall lack of understanding of its symptoms and implications. We hope that there can be further research conducted on narcolepsy to develop a sustainable solution and cure in the near future, and that treatment and support can become more widely accessible to those who need it.

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