



Scientia Psychiatrica

Journal Homepage: www.scientiapsychiatrica.com

eISSN (Online): 2715-9736

Neurotransmitter Related Idiopathic Hypersomnia

Wahyudo Imami Muhammad¹, Patricia Wulandari^{2*}

¹Department of Neurology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

²Psychiatrist, Cattleya Consultation Center, Palembang, Indonesia

ARTICLE INFO

Keywords:

Idiopathic hypersomnia
Neurotransmitter
Sleep disorder
Sleep disturbance

*Corresponding author:

Patricia Wulandari

E-mail address:

dr.patricia.wulandari@gmail.com

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/scipsy.v4i3.123>

ABSTRACT

Idiopathic hypersomnia affects 5% of the adult population, and both men and women are equally susceptible. Excessive sleep, sleep attacks, or wake-time delays are all examples of primary hypersomnia. Hypersomnia can be caused by a mental disorder, an organic condition (such as medications), or it might be idiopathic. This condition is the polar opposite of insomnia. Patients are frequently misdiagnosed as having mental illnesses or being sluggish. Hypersomnia patients require more sleep than the average person. The patient will generally sleep 1-2 times each day, with each nap lasting more than an hour. Despite the fact that they sleep a lot, they are usually weary and sluggish during the day. The causes of hypersomnia can be diverse, including neurological, medical, or psychological disorders. Neurotransmitters can also play a role in regulating a person's sleep patterns and alertness. This review aimed to describe neurotransmitters related to idiopathic hypersomnia.

1. Introduction

Idiopathic hypersomnia is a type of sleep disorder with symptoms where a person experiences excessive sleep or excessive sleepiness during the day, even though they have slept enough at night.^{1,2} People with idiopathic hypersomnia tend to feel very sleepy and have difficulty staying awake and active during the hours they should be awake. Hypersomnia can have various causes, including medical disorders such as obstructive sleep apnea (OSA), restless leg syndrome, or circadian rhythm disorders.^{3,4} The psychiatric disorders that generally underlie hypersomnia are generally depression or anxiety. This review was aimed at describing clinical aspects and neurotransmitters related to idiopathic hypersomnia.

Etiologies of hypersomnia

Circadian rhythm disorders

Hypersomnia can be a symptom of circadian rhythm disorders, especially when a person's sleep and wake patterns are disturbed.⁵ Circadian rhythm disorders are disorders that affect a person's body's natural rhythm, which regulates sleeping, waking, and other activities in a cycle of approximately 24 hours. This disorder can cause a person to sleep at unusual times or have difficulty maintaining normal sleep patterns.

One example of a circadian rhythm disorder that can cause hypersomnia is sleep clock shift syndrome. This occurs when a person constantly changes their sleep schedule, such as night workers or rotational shift workers, which can disrupt the body's natural

sleep rhythm. As a result, they may experience excessive sleepiness and hypersomnia when they want to be awake and active.^{4,5}

Restless leg syndrome

Restless legs syndrome (RLS) is a neurological disorder that causes feelings of discomfort or a sensation such as burning, itching, or goosebumps in the feet or lower legs, especially when resting or sleeping at night.^{6,7} This sensation often triggers the urge to move the foot or leg to relieve the discomfort. Although RLS can cause sleep disturbances due to uncomfortable sensations and the urge to move, it is generally not associated with hypersomnia, which is the condition of excessive sleeping during the day. In contrast, RLS is more often associated with insomnia or difficulty sleeping because sufferers often feel the need to move their legs to relieve discomfort while resting or sleeping. However, there are several factors that can cause sleep disorders, such as hypersomnia in someone who also suffers from RLS. For example, if RLS disrupts sleep at night and disrupts a person's natural sleep patterns, then there can be an accumulation of sleep deprivation during the night, which can lead to excessive sleepiness and hypersomnia during the day.

Obstructive sleep apnea

Hypersomnia can be caused by obstructive sleep apnea (OSA). OSA is a sleep disorder characterized by the repeated stopping or narrowing of the throat cavity during sleep, which disrupts airflow and causes a person to stop breathing for several seconds during sleep.⁴ This disrupts natural sleep patterns and can result in severe sleep disturbances. One common symptom of OSA is waking frequently during the night to breathe again, which can disrupt deep sleep and leave a person feeling unrefreshed when they wake up. As a result, people with OSA often experience excessive sleepiness and hypersomnia during the day because they do not get quality sleep during the night.

Comorbid psychiatric diseases

Depression can cause hypersomnia, which is one of the common symptoms of major depressive disorder. Hypersomnia in the context of depression is a condition where a person experiences excessive sleep or excessive sleepiness during the day, even after getting enough sleep at night or even sleeping excessively.⁸ Depression is a mood disorder that can affect a person's sleep in a variety of ways. Some people with depression may experience insomnia, which is difficulty falling asleep or intermittent sleep at night. However, others may experience hypersomnia, where they feel very sleepy and have difficulty staying awake during the hours they should be awake.

Hypersomnia in depression can have a negative impact on a person's quality of life and ability to carry out daily activities. This can also be an indicator that someone is suffering from depression. It is important to remember that hypersomnia associated with depression may not only be caused by physical changes in sleep but also by chemical changes in the brain and emotional feelings associated with depression.

In general, hypersomnia or excessive sleeping during the day is more common in individuals who experience depression compared to those who experience anxiety disorders.^{5,8} This is one of the typical symptoms of major depressive disorder. In individuals with depression, excessive daytime sleepiness and feelings of fatigue are often significant problems. They may feel very sleepy and have difficulty staying awake during the hours they should be awake. This can interfere with their ability to carry out daily activities and contribute to feelings of weakness and hopelessness often associated with depression. Meanwhile, in individuals with anxiety disorders, the more common sleep symptom is insomnia, namely difficulty falling asleep or intermittent sleep. Excessive anxiety and mental tension can make sleeping difficult, and individuals with anxiety disorders often feel restless or awake at night due to persistent thoughts.

Hypersomnia-related neurotransmitters

Hypersomnia is a condition of excessive sleeping or sleeping very deeply for long periods during the day or night, even though a person has had enough sleep the previous night. The causes of hypersomnia can be varied, including neurological, medical, or psychological disorders. Neurotransmitters can also play a role in regulating a person's sleep patterns and alertness. Neurotransmitters that play a role in the pathophysiology of hypersomnia are adenosine, serotonin, norepinephrine and hypocretin or orexin.⁹

Adenosine

One of the neurotransmitters that can play a role in hypersomnia is adenosine. Adenosine is a chemical compound that is formed in the brain during daily activities and increases in concentration during waking periods. When adenosine concentration increases, it affects adenosine receptors in the brain which play a role in stimulating drowsiness and reducing alertness. Caffeine is an example of a substance that can interfere with the effects of adenosine by binding to adenosine receptors without inducing drowsiness.

Serotonin and norepinephrine balance

Apart from adenosine, other neurotransmitters that can play a role in hypersomnia are serotonin and norepinephrine. The balance of serotonin and norepinephrine in the brain can affect mood and level of alertness. An imbalance of these neurotransmitters can contribute to sleep disorders such as depression, which can lead to hypersomnia. The balance of norepinephrine (also known as noradrenaline) and serotonin is an important factor in regulating a person's sleep patterns and alertness. An imbalance between these two neurotransmitters can influence the occurrence of hypersomnia and other sleep disorders.

Norepinephrine is a neurotransmitter that plays a role in stimulating alertness and increasing energy levels. When norepinephrine concentrations increase, a person becomes more alert and alert. Disorders that

result in a decrease in norepinephrine in the brain can cause symptoms such as excessive fatigue and lack of alertness, which can contribute to hypersomnia. Serotonin is a neurotransmitter that plays a role in regulating mood, mood, and also has a role in regulating sleep patterns. Serotonin imbalance can contribute to sleep problems such as insomnia or other sleep disorders. If serotonin concentrations are out of balance, this can affect sleep patterns and cause symptoms of hypersomnia.^{2,9}

When the balance between norepinephrine and serotonin is disturbed, it can result in a variety of sleep problems. For example, sleep disorders associated with depression often involve changes in the balance of serotonin and norepinephrine, which can lead to hypersomnia in some individuals suffering from depression. Additionally, certain sleep disorders, such as idiopathic hypersomnia, may be related to changes in certain neurotransmitters in the brain.

Hypocretin (orexin)

Hypocretin, also known as orexin, is a neurotransmitter that plays an important role in regulating a person's alertness and sleep patterns. Hypocretin imbalance or deficiency can contribute to certain sleep disorders, such as narcolepsy, which often causes symptoms of hypersomnia. Narcolepsy is a chronic sleep disorder characterized by sudden and uncontrollable sleep attacks during periods of wakefulness. One of the main causes of narcolepsy is a lack of hypocretin in the brain. Hypocretin is a neurotransmitter that is produced in certain cells in the brain and plays a role in maintaining alertness and regulating sleep patterns. When a person has a deficiency or loss of hypocretin, this can interfere with the body's ability to maintain alertness during the day and regulate sleep at night, which can lead to symptoms of hypersomnia. However, it is important to remember that hypersomnia is not always caused by a hypocretin deficiency. There are many other factors that can influence a person's sleep patterns, including other sleep disorders, medical problems, and psychological factors.^{10,11}

Hypersomnia, on the other hand, is a condition in which a person experiences excessive or very deep sleep for extended periods during the day or night despite having had sufficient sleep the previous night. Orexin is supposed to play a role in maintaining alertness and preventing excessive sleep rather than triggering hypersomnia. An orexin imbalance or orexin deficiency can interfere with the body's ability to maintain alertness during the day, which can lead to symptoms such as sudden sleep attacks that are more commonly associated with narcolepsy than hypersomnia.

Supporting examinations for idiopathic hypersomnia

Epworth sleepiness scale

The Epworth sleepiness scale (ESS) is an assessment tool used to measure a person's level of excessive sleepiness or daytime fatigue and can help in detecting potential sleep disorders or other sleep problems. The ESS is a questionnaire that requires individuals to answer a series of short questions about how often they feel sleepy or fall asleep in various everyday situations. ESS is commonly used to assist in assessing the level of excessive sleepiness that may be associated with sleep disorders such as sleep apnea, narcolepsy, or restless legs syndrome during sleep. It can also provide initial clues about whether a person needs to undergo further sleep evaluation.¹¹

Polysomnography

Polysomnography is a sleep test that is used to monitor and record your body's activities during sleep, such as brain patterns, eye activity, heart activity, breathing, muscle movements, and others. Polysomnography can also be helpful in detecting some aspects of hypersomnia, especially if there is an underlying sleep disorder. Polysomnography is usually used to identify sleep causes that may be causing hypersomnia, such as sleep apnea or parasomnia. The results of polysomnography will provide an idea of the quality of sleep, whether there were periods of abnormal awakening during sleep, and whether there

were any breathing or body movement problems that could disrupt sleep.¹²

Electroencephalography

Electroencephalography (EEG) is a test used to measure electrical activity in a person's brain and can help in assessing the cause of sleep disorders or other neurological disorders. Although EEG is not directly used to diagnose sleep disorders, it can aid in the understanding of brain activity during sleep and during waking periods. EEG can help identify abnormal brain activity during sleep that could indicate certain sleep disorders, such as sleep epilepsy (seizures that occur during sleep), disorders of brain stomach activity (parasomnias), or other brain activity that can affect sleep patterns.^{3,13}

Multiple sleep latency test

Multiple sleep latency tests (MSLT) can help determine the cause of hypersomnia and identify the type of hypersomnia. The MSLT is a special sleep test used to measure the level of excessive sleepiness and identify how quickly a person falls asleep during the daytime period. The MSLT procedure involves a series of short sleep tests scheduled during the day after overnight polysomnography testing (a sleep test that records sleep and wake activity during the night). During MSLT, the patient will be asked to lie in bed in a quiet, dark condition for a specified period of time (usually 20 to 30 minutes) and try to sleep. Results from the MSLT include the time it takes to sleep (sleep latency) and whether the patient achieved REM (rapid eye movement) sleep during the nap test.^{14,15}

The MSLT sleep test is one of the important diagnostic tools in assessing hypersomnia and helps in determining its cause.¹⁶ MSLT results can be helpful in identifying the type of hypersomnia a patient may be experiencing: 1) Sleep-onset REM (SOREM) hypersomnia: If the patient falls asleep quickly during MSLT and achieves REM sleep in multiple sleep tests, this may indicate the presence of a sleep disorder such as narcolepsy, which often causes excessive sleepiness and rapid REM sleep during the day. 2) Hypersomnia

without Rapid REM sleep: If the patient falls asleep rapidly during the MSLT but does not achieve REM sleep in the nap test, this may indicate idiopathic hypersomnia or another sleep disorder that may be the cause of excessive sleepiness.

It is preferable to ascertain the kind and length of sleep problem (duration of sleep disorder) before obtaining a diagnosis of the reason for the sleep disorder. Assessing the type and duration of the sleep disorder, in addition to assisting in identifying the cause, may also offer proper therapy. The patient complains of a morning headache, not feeling refreshed upon waking, issues with mental or emotional functioning, excessive daily drowsiness, and weariness throughout the examination. When a person has sleep apnea, their sleeping companion may complain of snoring. Individuals and their relatives with narcolepsy complain of falling asleep at inconvenient times, cataplexy, hypnagogic hallucinations, and a brief incapacity to move or talk when they wake up (sleep paralysis).

2. Conclusion

Idiopathic hypersomnia is a sleep disorder characterized by extreme daytime drowsiness for a month or longer. A proper history and diagnosis can help recognize the condition and give treatment according to the cause of hypersomnia.

3. References

1. Billiard M, Sonka K. Idiopathic hypersomnia: historical account, critical review of current tests and criteria, diagnostic evaluation in the absence of biological markers and robust electrophysiological diagnostic criteria. *Nat Sci Sleep*. 2022; 14: 311-22.
2. Sonka K, Susta M, Billiard M. Narcolepsy with and without cataplexy, idiopathic hypersomnia with and without long sleep time. A cluster analysis. *Sleep Med*. 2015; 16(2): 225-31.
3. Fronczek R, Arnulf I, Baumann CR, Maski K, Pizza F, Trotti LM. To split or to lump? Classifying the central disorders of hypersomnolence. *Sleep*. 2020; 43(8): 1-8.
4. Trotti LM, Ong JC, Plante DT, Friederich MC, King R, Bliwise DL. Disease symptomatology and response to treatment in people with idiopathic hypersomnia: initial data from Hypersomnia Foundation Registry. *Sleep Med*. 2020; 75: 343-9.
5. Thomas RJ, Naik S. The circadian variant of idiopathic hypersomnia. *Sleep*. 2017; 40(Suppl 1): A243.
6. Nevsimalova S, Susta M, Prihodova I, Maurovich Horvat E, Milata M, Sonka K. Idiopathic hypersomnia: A homogeneous or heterogeneous disease? *Sleep Med*. 2021; 80: 86-91.
7. Miglis MG, Schneider L, Kim P, Cheung J, Trotti LM. Frequency and severity of autonomic symptoms in idiopathic hypersomnia. *J Clin Sleep Med*. 2020; 16(5): 749-56.
8. Trotti LM. Are we there yet? Getting closer to certainty in idiopathic hypersomnia diagnosis. *J Clin Sleep Med*. 2019; 15(4): 539-40.
9. Bollu PC, Manjamalai S, Thakkar M, Sahota P. Hypersomnia. *Mo Med*. 2018; 115(1): 85-91.
10. Cairns A, Bogan R. Comparison of the macro and microstructure of sleep in a sample of sleep clinic hypersomnia cases. *Neurobiol Sleep Circadian Rhythms*. 2019; 6: 62-9.
11. Trotti LM, Saini P, Crosson B, Meltzer CC, Rye DB, Nye JA. Regional brain metabolism differs between narcolepsy type 1 and idiopathic hypersomnia. *Sleep*. 2021; 44(8): zsab050.
12. Pizza F, Moghadam KK, Vandi S. Daytime continuous polysomnography predicts multiple sleep latency results in hypersomnias of central origin. *J Sleep Res*. 2013; 22(1): 32-40.
13. Evangelista E, Lopez R, Barateau L. Alternative diagnostic criteria for idiopathic hypersomnia: a 32-hour protocol. *Ann Neurol*. 2018; 83(2): 235-47.
14. Lopez R, Doukkali A, Barateau L. Test-retest reliability of the multiple sleep latency test in central disorders of hypersomnolence. *Sleep*.

2017; 40: 12.

15. Cook JD, Eftekari SC, Leavitt LA, Prairie LM, Plante DT. Optimizing actigraphic estimation of sleep duration in suspected idiopathic hypersomnia. *J Clin Sleep Med*. 2019; 15(4): 597–602.
16. Drakatos P, Kosky CA, Higgins SE, Muza RT, Williams AJ, Leschziner GD. First rapid eye movement sleep periods and sleep-onset rapid eye movement periods in sleep-stage sequencing of hypersomnias. *Sleep Med*. 2013; 14(9): 897–901.