CLINICIAN GUIDE

Diagnosing **Narcolepsy**

A Practical Reference Guide for an Underrecognized Disorder

Narcolepsy|Link®

This brochure can help you:

RECOGNIZE

possible manifestations of excessive daytime sleepiness, **the cardinal symptom of narcolepsy**[1-3]

SCREEN

all patients with manifestations of excessive daytime sleepiness for narcolepsy using validated screening tools[4-7]

DIAGNOSE

narcolepsy through a complete clinical interview and sleep laboratory testing[1]

Narcolepsy|Link®

Narcolepsy Link is an innovative, evidence-based education and resource support program. Its mission is to increase narcolepsy awareness and help improve recognition, screening, and diagnosis of narcolepsy.

Table of Contents

Narcolepsy Overview

Narcolepsy is a chronic neurologic disorder that affects the brain's ability to regulate sleep-wake cycles,[8-10] causing potentially disabling symptoms such as excessive daytime sleepiness and cataplexy.[1,11,12] When undiagnosed or left untreated, narcolepsy can be socially isolating and interfere with daily functioning.[1,8,13]

The prevalence of narcolepsy in the United States is approximately 1 in 2000, and it is estimated that approximately 50% or more of patients with narcolepsy have not yet received a diagnosis.[2] In a sample of US sleep clinics, narcolepsy was the second most common primary sleep diagnosis, affecting about 1 in 20 patients, with substantial variance in prevalence among clinics.[14] These findings suggest that narcolepsy may be more prevalent in sleep clinics compared with the general population.

Approximately **50%** of people with narcolepsy remain undiagnosed[2]

Several factors may contribute to underdiagnosis, including:

- Low comfort and limited experience among healthcare professionals with recognizing and diagnosing narcolepsy[10]
- Symptoms overlapping with other medical conditions (eg, depression, insomnia, obstructive sleep apnea, and attention deficit hyperactivity disorder), leading to misdiagnosis[2,15-17]
- Comorbid psychiatric and sleep disorders with similar symptoms[17-19]

Despite evidence for the potentially debilitating impact of narcolepsy, patients often suffer with these symptoms for many years and see multiple healthcare professionals before receiving an accurate diagnosis.[15] **A narcolepsy diagnosis must be made by a sleep specialist, whose ability to recognize, screen for, and accurately diagnose narcolepsy is essential to helping many patients get the treatment they require.[7,15]**

Narcolepsy Symptoms

There are 5 primary symptoms of narcolepsy, referred to by the acronym **CHESS**.[20] All patients with narcolepsy experience excessive daytime sleepiness; however, not all narcolepsy patients will experience all of the other 4 symptoms.[1,2]

Cataplexy: The sudden, generally brief (<2 minutes) loss of muscle tone, with retained consciousness, usually triggered by strong emotions[1,2,21]

Hypnagogic hallucinations: Vivid dreamlike experiences occurring during wake-sleep transitions[1,2]

Excessive daytime sleepiness: The inability to stay awake and alert during the day, with periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep[1,2]

Sleep paralysis: The disturbing, temporary inability to move voluntary muscles or speak during sleep-wake transitions[1,2,20,22]

Sleep disruption: The interruption of sleep due to poor sleep quality and frequent awakenings[1,2,23]

For additional information about all of the symptoms of narcolepsy, visit NarcolepsyLink.com

Narcolepsy|Link®

Pathophysiology of Narcolepsy

Neurobiology of Normal Wakefulness

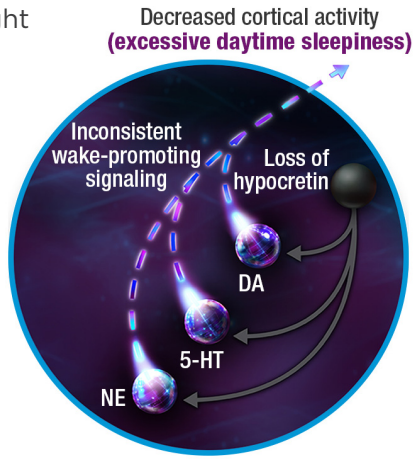
Interconnected wake-promoting neurons (ie, acetylcholinergic, dopaminergic, histaminergic, noradrenergic, and serotonergic neurons) activate cortical and subcortical arousal regions and inhibit neurons primarily responsible for promoting sleep (ie, GABAergic neurons) and REM sleep.[9,24] Hypocretin, or orexin, is a neuropeptide that activates these wake-promoting neurons to help maintain wakefulness and muscle tone and inhibit REM sleep during the day.[24,25]

Pathophysiology of Narcolepsy*

Narcolepsy Type 1 (narcolepsy with cataplexy)

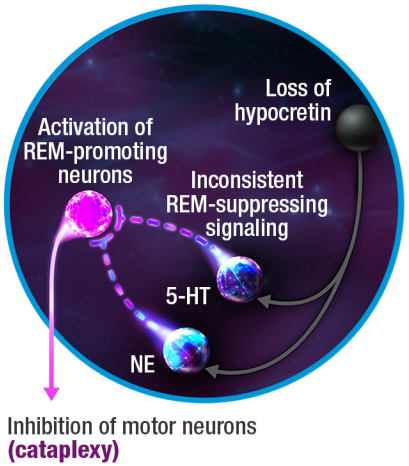
Narcolepsy type 1 (narcolepsy with cataplexy) is thought to be due to the permanent loss of hypocretin (or orexin) neurons.[1,24,25] Patients with narcolepsy type 1 have low or absent CSF hypocretin levels.[1,26]

Loss of hypocretin neurons is thought to lead to inconsistent signaling of wake-promoting neurons (eg, dopaminergic [DA], noradrenergic [NE], and serotonergic [5-HT] neurons) responsible for maintaining wakefulness and muscle tone and inhibiting sleep and REM sleep.[24,25] As a result, wake-promoting neurons fail to activate cortical and subcortical arousal regions and fail to inhibit sleep-promoting neurons (ie, GABAergic neurons), resulting in **excessive daytime sleepiness.**[25,†]



Certain wake-promoting neurons (eg, noradrenergic [NE] and serotonergic [5-HT] neurons) that also suppress REM signaling fail to inhibit REM-promoting neurons, resulting in[24,25,†]:

- Brief loss of muscle tone during strong emotions (**cataplexy**)[9,25]
- Abnormal manifestations of REM sleep at wake-sleep transitions (eg, hypnagogic hallucinations and sleep paralysis)[9,25]



Disruption of mutually inhibitory sleep-wake circuits may also lead to unwanted transitions from sleep to wakefulness and associated sleep disruption.[9,27]

Narcolepsy Type 2 (narcolepsy without cataplexy)

The exact cause of narcolepsy type 2 (narcolepsy without cataplexy) is unknown; however, it is likely a heterogeneous disorder.[1] In narcolepsy type 2, cataplexy is not present and CSF hypocretin-1 levels are usually normal or unknown.[1] One-quarter to one-third of patients with narcolepsy without cataplexy may have hypocretin deficiency, classifying them as narcolepsy type 1, and about 8% may have intermediate levels of CSF hypocretin-1.[1,26] These patients are more likely to develop cataplexy over time than those with normal levels.[1,26]

*Based on animal models.
†Other neuronal systems are also thought to be involved.

Recognizing Potential Narcolepsy Patients

Narcolepsy should be considered in all patients reporting excessive daytime sleepiness.[1] The only symptoms of narcolepsy that are considered diagnostic are excessive daytime sleepiness, the cardinal symptom, and cataplexy, the most specific.[1,28] If you recognize excessive daytime sleepiness or cataplexy in your patients, there are screening tools you can then use to help assess for their presence (see page 10).

Although they are not specific for narcolepsy, the presence of other symptoms such as hypnagogic hallucinations, sleep paralysis, and sleep disruption may help support the clinical diagnosis and the need for sleep laboratory testing.[1,7] More information about these symptoms, including questions to ask during the clinical interview, is included in the *Diagnosing Narcolepsy* section beginning on page 12.

Recognizing Excessive Daytime Sleepiness

Rather than report excessive daytime sleepiness specifically, patients may complain of other manifestations, such as tiredness, fatigue, drowsiness, difficulty concentrating, poor memory, irritability, and/or mood changes, making recognition difficult.[3,29,30] In patients reporting these manifestations, look deeper for excessive daytime sleepiness.

Recognize tiredness, fatigue, drowsiness, difficulty concentrating, and mood changes as possible manifestations of excessive daytime sleepiness[3,29,30]

Ask About Excessive Daytime Sleepiness

- How often do you experience "sleep attacks" in which you fall asleep without warning?
- How often do you take scheduled or unscheduled daytime naps, and how long do they usually last?
- Do you feel more alert, refreshed, or energized after a daytime nap? How long do these effects last?
- Do you dream during these naps? If yes, describe the dreams.

Recognizing Cataplexy

Cataplexy occurs in about 70% of narcolepsy patients.[21] Cataplexy is usually triggered by strong emotions and more commonly presents as partial loss of muscle tone limited to a few muscle groups, although complete collapse to the ground can occur.[1,2]

Cataplexy can be difficult to recognize because patients may describe their cataplexy differently and may associate the muscle weakness with certain situations rather than specific emotions.[12] In addition, patients may not volunteer information about their cataplexy.[17] Careful interviewing is important when looking for cataplexy in patients with excessive daytime sleepiness.[21] In patients reporting excessive daytime sleepiness, look deeper for cataplexy.

Ask About Cataplexy

- How often have you experienced a sudden loss of muscle strength or control, muscle weakness, or limp muscles when feeling very happy, laughing, being surprised, becoming angry, or hearing or telling a joke?
- Have you experienced any of the following during these attacks?
  - Head dropping
  - Neck weakness
  - Eyelid drooping
  - Drooping of the face or jaw
  - Slurred speech
  - Buckling of the knees
  - Leg or arm weakness
  - Complete collapse to the ground
- Have you ever avoided emotional situations or limited participation in certain activities (eg, sporting events, movies) to avoid an attack? If yes, describe one of these situations.

Narcolepsy|Link®

Screening Your Patients

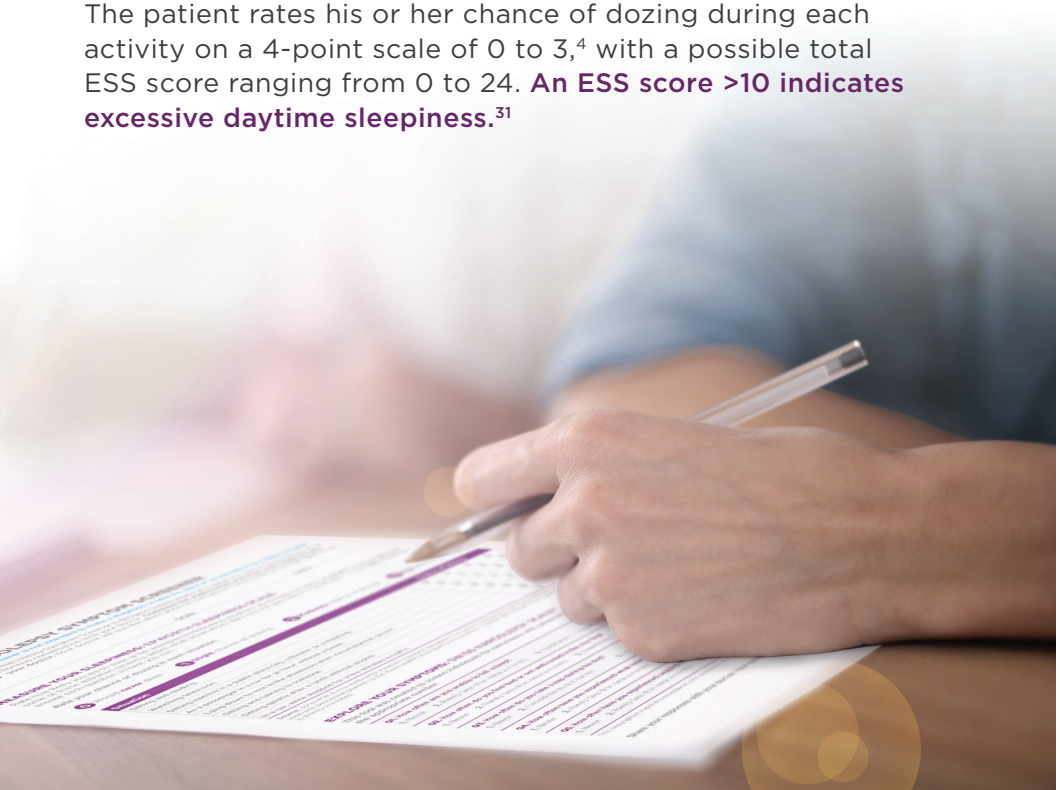
Simple, validated tools, such as the Epworth Sleepiness Scale (ESS) and the Swiss Narcolepsy Scale (SNS), are available to help screen patients who report manifestations of excessive daytime sleepiness or other possible narcolepsy symptoms.[4-6]

Screen all patients who present with manifestations of excessive daytime sleepiness using validated screening tools[4-7]

Epworth Sleepiness Scale

Many patients are not able to accurately describe the severity of their daytime sleepiness. The ESS is a validated screening tool that can help determine the level of daytime sleepiness by measuring the patient's tendency to doze or fall asleep during 8 common daily activities.[3,4]

The patient rates his or her chance of dozing during each activity on a 4-point scale of 0 to 3,[4] with a possible total ESS score ranging from 0 to 24. **An ESS score >10 indicates excessive daytime sleepiness.**[31]



Swiss Narcolepsy Scale

Cataplexy can be difficult to recognize because it can present in many, often subtle ways, and patients typically are unable to give a clear history of their cataplexy.[12,21] The SNS is a brief, self-reported, validated screening tool that can help you recognize narcolepsy with cataplexy.[5,6]

Using the SNS, the patient rates the frequency of symptomatic manifestations on a 5-point scale, from 1 (indicating never) to 5 (indicating almost always or almost daily).[5,6] The total score is calculated based on a weighted equation.[5] A calculated SNS score <0 is suggestive of narcolepsy with cataplexy.[5,6]

In one study of patients with narcolepsy with cataplexy, an SNS score <0 was shown to have a sensitivity of 96% and a specificity of 98%, but it is not diagnostic and does not screen for or rule out narcolepsy without cataplexy.[5,6] It is therefore important to **consider narcolepsy in the differential diagnosis for all patients with excessive daytime sleepiness,** even if their SNS score is >0.[7]

Two Convenient Ways to Screen Your Patients

Narcolepsy Symptom Screener

Narcolepsy Screener App

Access these screening tools at NarcolepsyLink.com

Narcolepsy|Link®

Diagnosing Narcolepsy

Establishing an accurate narcolepsy diagnosis requires a thorough clinical interview as well as sleep laboratory testing.[1] For full diagnostic criteria, see page 22.

Clinical Interview

A complete clinical interview including evaluation of all 5 narcolepsy symptoms (CHESS) is important to the differential diagnosis and provides clinical context when evaluating the results of sleep laboratory testing.[1,17,32]

Although not all patients experience all 5 symptoms,[1] evaluate for the presence of each narcolepsy symptom in all patients reporting excessive daytime sleepiness.

Assessing for Excessive Daytime Sleepiness

Comprehensive assessment of excessive daytime sleepiness begins with a clinical interview, including observation of the patient and asking questions about the nature, frequency, and impact of sleepiness.[3] If not completed during screening, use the ESS to obtain a subjective measure of a patient's level of daytime sleepiness. An ESS score >10 suggests excessive daytime sleepiness.[31]

Include the patient's spouse, bed partner, or family member in the clinical interview to help corroborate or refute the patient's report of sleepiness[3,29]

The questions on page 8 can help you to probe for excessive daytime sleepiness. Keep the following information in mind when interviewing your patients:

LOOK DEEPER

- Patients with excessive daytime sleepiness may be unable to carry out daily activities without substantial effort.[3]
- "Sleep attacks" or sudden and irresistible urges to sleep, even in inappropriate situations, can occur.[1,2,6]
- Patients may describe automatic behavior, continuing an activity as if on autopilot without memory or awareness.[1,2,6]

Differentiating Excessive Daytime Sleepiness in Narcolepsy

Evaluate the patient's sleepiness carefully to distinguish excessive daytime sleepiness in narcolepsy from that associated with mood disorders or idiopathic hypersomnia.[1,2]

- Other disorders with excessive daytime sleepiness are not associated with cataplexy.[1,2,17]
- Generally, daytime naps are refreshing for a short period of time in patients with narcolepsy, whereas they are not for patients with idiopathic hypersomnia.[1,2]
- In patients with mood disorders, differentiate a true increased propensity to sleep from decreased energy, lack of interest, or psychomotor retardation.[3]

Assessing for Cataplexy

Cataplexy is the most specific symptom of narcolepsy and should be assessed for in all patients with excessive daytime sleepiness.[1,17,28] Based on *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* criteria (see page 24), the presence of cataplexy in patients with chronic excessive daytime sleepiness is considered diagnostic for narcolepsy.[28]

In some patients with narcolepsy type 1, the onset of cataplexy can be delayed, occurring years or even decades after the onset of excessive daytime sleepiness.[1,6,16,28] Therefore, ongoing assessment for this symptom is important. If not completed during screening, use the SNS to help identify cataplexy. An SNS score <0 is suggestive of narcolepsy with cataplexy.[5,6]

Obtain information about potential cataplexy from others who know the patient well because patients may be unaware of subtle symptoms[1]

The questions on page 9 can help you to probe for cataplexy. Keep the following information in mind when interviewing your patients:

LOOK DEEPER

- Partial cataplexy, localized to certain muscle groups, is the most common.[1,2,12,21]
- Patients maintain consciousness during attacks.[1,20]
- Patients describe cataplexy in different ways (eg, “I’m clumsy and often drop things or fall”).[20]
- Patients may discuss situations rather than specific emotions that trigger cataplexy (eg, “When I hear a joke” rather than “When I laugh”).[12,21]
- Patients may avoid specific emotions or situations that trigger cataplexy and therefore may not be aware of or volunteer information about their attacks[21] or they may be embarrassed to report them.[17]

Differentiating Cataplexy

In other neuromuscular disorders, muscle weakness may be constant rather than episodic, or can be triggered by exercise.[1,33]

Episodes of syncope or atonic seizures may be associated with loss of consciousness. Atonic seizures are usually not triggered by strong emotions and can be confirmed by electroencephalography (EEG).[2,20]

Assessing for Sleep Disruption

About half of patients with narcolepsy report nighttime sleep disruption,[1,23] which may even be the presenting symptom. Narcolepsy patients initiate sleep rather quickly, so sleep onset is rarely a problem; however, they may report fragmented sleep with frequent awakenings, as well as poor quality sleep.[1,2,6,23]

To identify sleep disruption, ask the patient to rate his or her sleep quality overall during the past month. In addition, ask:

- How long does it usually take you to fall asleep at night?
- How much total time do you spend in bed each night?
- How many hours of sleep do you usually get each night?
- How many times do you wake up during the night?
- Does poor sleep quality ever interfere with your activities the next day? If yes, please describe.

Differentiating Sleep Disruption

Sleep disruption in narcolepsy should be differentiated from the effects of alcohol, medications, poor sleep hygiene, and insomnia.[1,3,23] Unlike patients with insomnia, narcolepsy patients generally do not stay awake for prolonged periods and do not have difficulty falling back to sleep.[23]

Assessing for Hypnagogic Hallucinations

Hypnagogic hallucinations occur in up to 80% of patients with narcolepsy.[1] Patients may describe these experiences as vivid dreams or nightmares,[1,2,6] feeling someone's presence in the room, being chased, or flying.[6] Hypnagogic hallucinations can often occur with sleep paralysis[2] and can be so frightening and realistic that patients fear going to bed.[22]

Patients are often reluctant to discuss these experiences,[20,22] so ask specifically about these occurrences:

- How often have you had vivid dreamlike experiences when falling asleep or waking up?
- Do you ever avoid going to sleep to avoid these events? If yes, describe one of these situations.
- Do you avoid or limit participation in certain activities because of these events? If yes, describe one of these situations.

Differentiating Hypnagogic Hallucinations

Hypnagogic hallucinations can be differentiated from vivid dreams and nightmares because they occur at sleep-wake transitions rather than during ongoing sleep.[1,33] However, hypnagogic hallucinations are not specific to narcolepsy and may occur in any sleep-deprived person.[20,22]

To help differentiate hypnagogic hallucinations from those associated with schizophrenia, note that visual and kinetic hallucinations are more common in hypnagogic hallucinations, whereas auditory hallucinations are more common in patients with schizophrenia.[34] Unlike those in narcolepsy, hallucinations in patients with schizophrenia frequently occur with other characteristic symptoms, such as delusions and disorganized behavior.[34,35]

Assessing for Sleep Paralysis

The prevalence of sleep paralysis is similar to that of hypnagogic hallucinations.[1,2] Episodes can be accompanied by dyspnea[20,22,33] and typically end spontaneously within 1 to 10 minutes or when someone touches the patient.[2,22]

To clarify whether sleep paralysis is present and if it indicates narcolepsy, ask the patient:

- How often do you experience episodes of being unable to move or speak for a brief time when falling asleep or waking up?
- Do you ever avoid going to sleep to avoid these events? If yes, describe one of these situations.
- Do you avoid or limit participation in certain activities because of these events? If yes, describe one of these situations.

Differentiating Sleep Paralysis

It is important to distinguish sleep paralysis from fatigue and problems waking up.[33] Sleep paralysis may be reported *occasionally* by people who do not have narcolepsy, particularly in the middle of the night after a nightmare or dream, or by people who are sleep deprived.[20,22] In patients with narcolepsy, sleep paralysis occurs *regularly* at sleep onset or awakening.[22]

Sleep Laboratory Testing

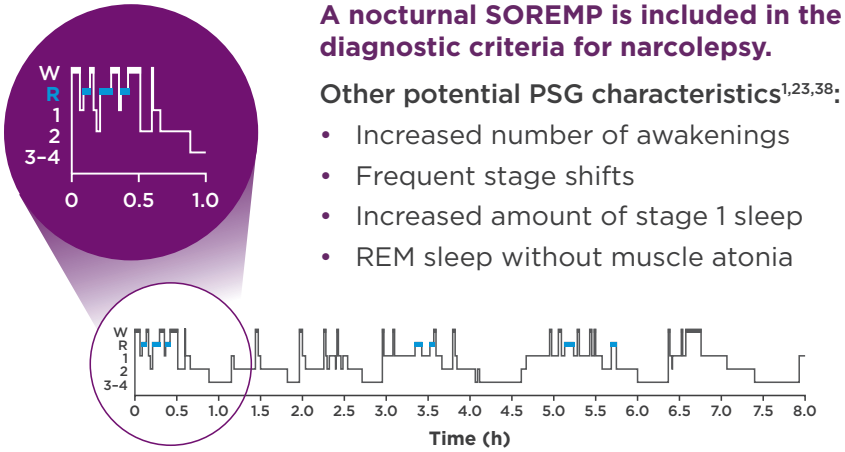
In addition to a clinical interview, sleep laboratory testing is required to confirm the narcolepsy diagnosis. Home sleep apnea testing (HSAT) cannot detect narcolepsy and should be avoided if narcolepsy is suspected clinically.[36,37] If narcolepsy is suspected clinically, overnight polysomnography (PSG) followed by a Multiple Sleep Latency Test (MSLT) should be performed.[1]

Polysomnography

PSG should be performed the night before MSLT testing to rule out other untreated significant sleep disorders that cause excessive daytime sleepiness or could mimic diagnostic features of narcolepsy, as well as assess for common comorbid conditions (eg, obstructive sleep apnea and periodic limb movement disorder).[1,37]

In addition, PSG can help to identify a sleep pattern characteristic of narcolepsy[38]:

- Latency to REM sleep ≤15 minutes on overnight PSG (nocturnal sleep-onset REM period [SOREMP]) is a highly specific marker for narcolepsy.[1,28,39]
- A nocturnal SOREMP should alert the clinician to the possibility of a narcolepsy diagnosis in patients being evaluated for another sleep disorder.[39]



A nocturnal SOREMP is included in the diagnostic criteria for narcolepsy.

Other potential PSG characteristics[1,23,38]:

- Increased number of awakenings
- Frequent stage shifts
- Increased amount of stage 1 sleep
- REM sleep without muscle atonia

This hypnogram from an actual patient with narcolepsy depicts a representative sleep-wake pattern but does not reflect variations between patients.

Narcolepsy|Link®

Multiple Sleep Latency Test

The MSLT is performed immediately following the overnight PSG to[1,32]:

- Quantify the severity of excessive daytime sleepiness
  - The MSLT measures the physiologic ability or tendency to fall asleep in standardized conditions.[1,32]
- Identify if a sleep profile that meets the diagnostic criteria for narcolepsy is present[1,28]
  - Mean sleep latency ≤8 minutes[1,28]
  - ≥2 SOREMPs within 15 minutes of sleep onset.[1,28] According to the ICSD-3 diagnostic criteria, the presence of a SOREMP on overnight PSG counts as one of the 2 SOREMPs required to diagnose narcolepsy.[1]

If narcolepsy is strongly suspected clinically but MSLT criteria are not met, the ICSD-3 diagnostic criteria suggest repeating the MSLT.[1]

Sleep laboratory test results should be interpreted within the clinical context of the patient's history and symptoms.[1,32] It is strongly recommended that adequate sleep be documented by a sleep log and, whenever possible, actigraphy be conducted for a period of 1 to 2 weeks before the MSLT.[1]

Diagnostic Criteria for Narcolepsy

Two standardized sets of criteria are used for the diagnosis of narcolepsy: the American Academy of Sleep Medicine (AASM) *International Classification of Sleep Disorders (ICSD-3)* criteria and the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* criteria.

ICSD-3 Criteria for Narcolepsy Diagnosis

For narcolepsy type 1, criteria A and B must be met[1]:

A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.*

B. The presence of one or both of the following:

1. Cataplexy (as defined below) *and* a mean sleep latency of ≤8 minutes and two or more sleep-onset REM periods (SOREMPs) on an MSLT performed according to standard techniques. A SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.†

2. CSF hypocretin-1 concentration, measured by immunoreactivity, is either ≤110 pg/mL or <1/3 of mean values obtained in normal subjects with the same standardized assay.

Notes:

*In young children, narcolepsy may sometimes present as excessively long night sleep or as resumption of previously discontinued daytime napping.

†If narcolepsy type 1 is strongly suspected clinically but the MSLT criteria of B1 are not met, a possible strategy is to repeat the MSLT.

For narcolepsy type 2, criteria A-E must be met[1]:

A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.

B. A mean sleep latency of ≤8 minutes and two or more sleep-onset REM periods (SOREMPs) are found on a MSLT performed according to standard techniques. A SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.

C. Cataplexy is absent.‡

D. Either CSF hypocretin-1 concentration has not been measured or CSF hypocretin-1 concentration measured by immunoreactivity is either >110 pg/mL or >1/3 of mean values obtained in normal subjects with the same standardized assay.§

E. The hypersomnolence and/or MSLT findings are not better explained by other causes such as insufficient sleep, obstructive sleep apnea, delayed sleep phase disorder, or the effect of medication or substances or their withdrawal.

Notes:

‡If cataplexy develops later, then the disorder should be reclassified as narcolepsy type 1.

§If the CSF hypocretin-1 concentration is tested at a later stage and found to be either ≤110 pg/mL or <1/3 of mean values obtained in normal subjects with the same assay, then the disorder should be reclassified as narcolepsy type 1.

DSM-5 Criteria for Narcolepsy Diagnosis

Criteria A and B must be met[28]:

A. Recurrent periods of an irrepressible need to sleep, lapsing into sleep, or napping occurring within the same day. These must have been occurring ≥3 times per week over the past 3 months.

B. The presence of at least one of the following:

1. Episodes of cataplexy, defined as either (**a**) or (**b**), occurring at least a few times per month:

a. In individuals with long-standing disease, brief (seconds to minutes) episodes of sudden bilateral loss of muscle tone with maintained consciousness that are precipitated by laughter or joking.

b. In children or in individuals within 6 months of onset, spontaneous grimaces or jaw-opening episodes with tongue thrusting or a global hypotonia, without any obvious emotional triggers.

2. Hypocretin deficiency, as measured using CSF hypocretin-1 immunoreactivity values (≤1/3 of values obtained in healthy subjects tested using the same assay, or ≤110 pg/mL). Low CSF levels of hypocretin-1 must not be observed in the context of acute brain injury, inflammation, or infection.

3. Nocturnal sleep polysomnography showing rapid eye movement (REM) sleep latency ≤15 minutes, or a multiple sleep latency test showing a mean sleep latency ≤8 minutes and 2 or more sleep-onset REM periods.

Important Role of the Sleep Specialist

Undiagnosed narcolepsy can have a significant effect on quality of life as well as a significant socioeconomic impact.[1,8,13] Diagnosis is often delayed due to a lack of awareness and understanding of this disorder, and patients may suffer with debilitating symptoms for years before receiving an accurate diagnosis.[10,15]

Sleep specialists have an important role in assessing and diagnosing narcolepsy in these patients. Looking deeper at all patients who present with excessive daytime sleepiness through the clinical interview and appropriate sleep laboratory testing is important to helping many patients get the treatment they require.[15,17]

References

1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
2. Ahmed I, Thorpy M. Clinical features, diagnosis and treatment of narcolepsy. *Clin Chest Med.* 2010;31(2):371-381.
3. Ahmed IM, Thorpy MJ. Clinical evaluation of the patient with excessive sleepiness. In: Thorpy MJ, Billiard M, eds. *Sleepiness: Causes, Consequences and Treatment.* Cambridge, United Kingdom: Cambridge University Press; 2011:36-49.
4. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep.* 1991;14(6):540-545.
5. Bassetti CL. Spectrum of narcolepsy. In: Baumann CR, Bassetti CL, Scammell TE, eds. *Narcolepsy: Pathophysiology, Diagnosis, and Treatment.* New York: Springer Science+Business Media, LLC; 2011:309-319.
6. Sturzenegger C, Bassetti CL. The clinical spectrum of narcolepsy with cataplexy: a reappraisal. *J Sleep Res.* 2004;13(4):395-406.
7. Thorpy M, Morse AM. Reducing the clinical and socioeconomic burden of narcolepsy by earlier diagnosis and effective treatment. *Sleep Med Clin.* 2017;12(1):61-71.
8. NINDS Narcolepsy Information Page. National Institute of Neurological Disorders and Stroke website. https://www.ninds.nih.gov/Disorders/All-Disorders/Narcolepsy-Information-Page. Accessed May 30, 2017.
9. Scammell TE. The neurobiology, diagnosis, and treatment of narcolepsy. *Ann Neurol.* 2003;53(2):154-166.
10. Rosenberg R, Kim AY. The AWAKEN survey: knowledge of narcolepsy among physicians and the general population. *Postgrad Med.* 2014;125(1):78-86.
11. Dauvilliers Y, Siegel JM, Lopez R, Torontali ZA, Peever JH. Cataplexy—clincial aspects, pathophysiology and management strategy. *Nat Rev Neurol.* 2014;10:386-395.
12. Overeem S, van Nues SJ, van der Zande WL, et al. The clinical features of cataplexy: a questionnaire study in narcolepsy patients with and without hypocretin-1 deficiency. *Sleep Med.* 2011;12(1):12-18.
13. Daniels E, King MA, Smith IE, Shneerson JM. Health-related quality of life in narcolepsy. *Sleep Res.* 2001;10(1):75-81.
14. Punjabi NM, Welch D, Strohl K; for the Coleman II Study Investigators. Sleep disorders in regional sleep centers: a national cooperative study. *Sleep.* 2000;23(4):471-480.
15. Carter LP, Acebo C, Kim A. Patients' journeys to a narcolepsy diagnosis: a physician survey and retrospective chart review. *Postgrad Med.* 2014;126(3):216-224.
16. Luca G, Haba-Rubio J, Dauvilliers Y, et al; European Narcolepsy Network. Clinical, polysomnographic and genome-wide association analyses of narcolepsy with cataplexy: a European Narcolepsy Network study. *J Sleep Res.* 2013;22(5):482-495.
17. Thorpy MJ, Krieger AC. Delayed diagnosis of narcolepsy: characterization and impact. *Sleep Med.* 2014;15(5):502-507.
18. Ohayon MM. Narcolepsy is complicated with high medical and psychiatric comorbidities: a comparison with the general population. *Sleep Med.* 2013;14(6):488-492.
19. Peacock J, Benca RM. Narcolepsy: clinical features, co-morbidities & treatment. *Indian J Med Res.* 2010;131:338-349.
20. Pelayo R, Lopes MC. Narcolepsy. In: Lee-Chiong TL. *Sleep.* Hoboken: Wiley and Sons, Inc.; 2006:145-149.
21. Overeem S. The clinical features of cataplexy. In: Baumann CR, Bassetti CL, Scammell TE, eds. *Narcolepsy: Pathophysiology, Diagnosis and Treatment.* New York: Springer Science+Business Media; 2011:283-299.
22. Dauvilliers Y, Lopez R. Parasomnias in narcolepsy with cataplexy. In: Baumann CR, Bassetti CL, Scammell TE, eds. *Narcolepsy: Pathophysiology, Diagnosis and Treatment.* New York: Springer Science+Business Media; 2011:291-299.
23. Roth T, Dauvilliers Y, Mignot E, et al. Disrupted nighttime sleep in narcolepsy. *J Clin Sleep Med.* 2013;9(9):955-965.
24. España RA, Scammell TE. Sleep neurobiology from a clinical perspective. *Sleep.* 2011;34(7):845-858.
25. Scammell TE. Narcolepsy. *New Engl J Med.* 2015;373(27):2654-2662.
26. Andlauer O, Moore H 4th, Hong SC, et al. Predictors of hypocretin (orexin) deficiency in narcolepsy without cataplexy. *Sleep.* 2012;35(9):1247-1255F.
27. Alakuijala A, Sarkanen T, Partinen M. Hypocretin-1 levels associate with fragmented sleep in patients with narcolepsy type 1. *Sleep.* 2016;39(5):1047-1050.
28. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Washington, DC: American Psychiatric Association; 2013.
29. Guilleminault C, Brooks SN. Excessive daytime sleepiness: a challenge for the practising neurologist. *Brain.* 2001;124(Pt 8):1482-1491.
30. Miglis MG, Kushida CA. Daytime sleepiness. *Sleep Med Clin.* 2014;9(4):491-498.
31. Johns M, Hocking B. Daytime sleepiness and sleep habits of Australian workers. *Sleep.* 1997;20(10):844-849.
32. Littner MR, Kushida C, Wise M, et al. Practice parameters for clinical use of the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test. *Sleep.* 2005;28(1):113-121.
33. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 2nd ed. Darien, IL: American Academy of Sleep Medicine; 2005.
34. Dahmen N, Kasten M, Mittag K, Müller MJ. Narcoleptic and schizophrenic hallucinations. Implications for differential diagnosis and pathophysiology. *Eur J Health Econ.* 2002;3(Suppl 2):S94-S98.
35. Fortuyn HAD, Lappenschaar GA, Nienhuis FJ, et al. Psychotic symptoms in narcolepsy: pharmacology and a comparison with schizophrenia. *Gen Hosp Psychiatry.* 2009;31(2):146-154.
36. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnositc testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2017;13(3):479-504.
37. Kushida CA, Littner MR, Morgenthaler T, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep.* 2005;28(4):499-521.
38. Plazzi G, Serra L, Ferri R. Nocturnal aspects of narcolepsy with cataplexy. *Sleep Med Review.* 2008;12(2):109-128.
39. Andlauer O, Moore H, Jouhier L, et al. Nocturnal rapid eye movement sleep latency for identifying patients with narcolepsy/hypocretin deficiency. *JAMA Neurol.* 2013;70(7):891-902.

Patients with excessive daytime sleepiness may report being tired all the time, fatigue, drowsiness, difficulty concentrating, or mood changes.

For patients who report these symptoms...

RECOGNIZE **SCREEN** **DIAGNOSE**

Narcolepsy|Link®

Visit NarcolepsyLink.com

Learn how to recognize manifestations of excessive daytime sleepiness and other narcolepsy symptoms

Access validated screening tools to help identify potential narcolepsy patients

Gain helpful insight for making the narcolepsy diagnosis

Jazz Pharmaceuticals®

Printed in the USA NDS-0297 REV0917