Published in final edited form as:

Am J Med. 2015 January ; 128(1): 10–13. doi:10.1016/j.amjmed.2014.05.037.

Narcolepsy: Let the Patient's Voice Awaken Us!

Julie Flygare, J.D.¹ and Sairam Parthasarathy, MD^{2,3}

¹Narcolepsy Spokesperson and Author, University of Arizona, Tucson, AZ

²Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, Department of Medicine, University of Arizona, Tucson, AZ

³Arizona Respiratory Center of University of Arizona, Tucson, AZ

Abstract

This is a “patient-centered” review about narcolepsy that aims to awaken the reader to the narcolepsy condition and to the trials and tribulations of patients with sleep problems in general. Narcolepsy is a neurological disorder with a classic tetrad of symptoms consisting of excessive daytime sleepiness, cataplexy, sleep onset hallucinations, and sleep paralysis. The diagnosis of narcolepsy and other sleep disorders are often overlooked and could be attributed to other medical or even psychiatric conditions with years of missed diagnosis. Implementation of “two sleep-related questions” to the review of systems in the primary care physicians’ office visit may help address the issue of missed diagnosis and allow patients to seek prompt medical attention. Definitive diagnosis can be made by overnight sleep study followed by a nap test, “multiple sleep latency test” (MSLT). There is currently no cure for narcolepsy with the treatments addressing symptoms of excessive daytime sleepiness, cataplexy, and nighttime sleep disruption with stimulants (modafinil, methylphenidate, and amphetamines), anti-cataplexy medications (Serotonin-specific reuptake inhibitors and tricyclic antidepressants) and sedative-hypnotics including sodium oxybate. Narcolepsy, like other sleep disorders, can lead to marked reductions of health-related quality of life and affect patients’ social and work lives deleteriously. While traditional healthcare approaches are focused more on hard biomedical outcomes, a patient-centered approach with novel methods for better sleep assessment of patients, that can bypass the “impossibly crammed” physician office visit, would allow healthcare providers to better detect, diagnose and treat narcolepsy and other such sleep problems.

Keywords

narcolepsy; patient-centered care; patient satisfaction; sleep; patient outcome assessments

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Corresponding Author: Sairam Parthasarathy, MD, Associate Professor of Medicine, University of Arizona, 1501 N Campbell Ave, Rm 2342D, Tucson, AZ 85724, Ph: 520-626-6109; Fax: 520-626-1876, spartha@arc.arizona.edu.

All authors had access to the data and a role in writing the manuscript

None of the authors have any conflict of interest with the material submitted.

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Introduction

Patient experiences bring us closer to comprehending the humanity of caring for the sick – an experience that can only be better learned by practicing a lifetime of empathy and artful listening. This is a “patient-centered” review written by both a patient-advocate and a sleep expert that is followed by a conversation that intends to awaken the reader to the narcolepsy condition and give a key-hole view of the trials and tribulations of patients with such sleep problems.

Personal Story by Julie Flygare

In May of 2007, I woke up in my law school parking lot unsure how I got there. I remembered getting in the car and feeling sleepy on the highway, but could not recall driving onto campus or parking. How had a 15-minute drive in the *morning* after getting 9 hours of sleep become dangerous? “Maybe I have a sleep problem,” I thought for the first time. A month later, I visited a primary care doctor, announcing, “I’m tired all the time and have trouble studying and driving, even short distances.”

The doctor responded, “Everyone gets tired driving. Even I have to pull over to get a coffee sometimes.” The smallest voice inside me said, “I don’t *think* she understands what I’m talking about.” Next, I brought up my knees buckling with laughter. I suggested perhaps it was neurological. The doctor said she’d never heard of anything like this. “I’ll let you go to a neurologist but it’s probably something you’ll have to get used to.” I’d asked family members and friends, and another primary care doctor a year earlier, but to no avail. I was more lost than ever.

The following week, I randomly mentioned my knee-buckling laughter to my sports therapist who thought she’d heard of something like that. She wrote “cataplexy?” on a piece of paper and handed it to me. Once home, I googled “cataplexy” and knew within seconds that this was it. Cataplexy was associated with narcolepsy; a word I’d heard but thought was a joke. The dots began connecting.

For individuals with sleep disorders, finding the right diagnosis is life-changing. In my recent memoir ¹, I describe this moment: “It was as if someone was holding a mirror up to show me the last few years of my life for the first time. My understanding of who I was and how I was living was changing rapidly... I shook in the silence of this lonely self-discovery.”

I subsequently visited a sleep specialist who ordered the 24 hour sleep study and, I was diagnosed with a classic case of “narcolepsy with cataplexy.” In the six years since diagnosis, treatments, naps and life-style adjustments have helped to live successfully with narcolepsy. Diagnosed within five years of symptom onset, I am considered “one of the lucky ones”.

Introduction to Symptoms of Narcolepsy by Julie Flygare

The four major symptoms “tetrad” associated with narcolepsy are excessive daytime sleepiness, cataplexy, hypnagogic (occurring at the onset of sleep) hallucinations, and sleep paralysis ². Patients with narcolepsy experience episodes of excessive sleepiness throughout the day. The severity of the sleepiness is comparable to that experienced by a healthy individual who has been sleep-deprived continuously for 48–72 hours ³. Patients with narcolepsy cannot stay awake for long periods of time, which is problematic in most school and work conditions ⁴. In addition, this extreme exhaustion may threaten a person’s ability to safely drive a motor vehicle ⁵. The public may perceive that people with narcolepsy sleep all the time, but this is not true. Actually, people with narcolepsy don’t sleep any more than average people. When they do sleep, they awaken multiple times at night and may also suffer from other sleep disorders such as leg jerking (periodic leg movement disorder) or sleep apnea.

Cataplexy is a symptom unique to narcolepsy. It is the sudden loss of skeletal muscle tone without the loss of consciousness, often triggered by strong emotions such as laughter, surprise, or anger. Cataplexy varies in intensity; a person with severe cataplexy may collapse to the ground, unable to move or speak for a few seconds to a few minutes. Cataplexy can be extremely debilitating, and can devastate a person’s personal and professional life. Cataplexy can sometimes be confined to facial muscles, arms or legs; and could last from a second to minutes; in rare cases of “status cataplecticus” last for hours following withdrawal from antidepressant drugs ⁶.

The hallucinations during sleep onset experienced by patients with narcolepsy can be auditory, visual, or tactile and can be quite distressing to the patient as they are disorienting and create self-doubts about their sanity. These are due to dissociated “dream” (rapid eye movement [REM]) sleep and can occur even when the patient is awakening. Such hallucinations could lead to such patients being mislabeled as having schizophrenia.

Sleep paralysis is experienced by patients with narcolepsy when they are falling asleep or awakening and is the inability to move limbs, lift head, or even breathe and can be quite frightening. The symptoms of sleep paralysis, hypnagogic hallucinations, and excessive daytime sleepiness are not specific for narcolepsy and, unlike cataplexy which is specific to narcolepsy, can occur with severe sleep deprivation in healthy humans or in association with other sleep disorders. Narcolepsy’s impact upon an individual’s life varies depending on the severity of the symptoms and the patient’s response to available treatment options. Narcolepsy can affect health-related quality-of-life comparably to epilepsy and Parkinson’s disease ⁷.

Prevalence and Detection

Narcolepsy affects an estimated 250,000 individuals in the US, but only 20% of them are correctly diagnosed. Many remain undiagnosed or are even misdiagnosed with other conditions such as sleep apnea, idiopathic hypersomnia, schizophrenia, depression or sleep deprivation. Many patients report experiencing narcolepsy symptoms for many years before receiving an accurate diagnosis. There are many reasons for such delayed diagnosis. First,

many people may not recognize their own “sleepiness” as a sign of an ailment especially when the disease is of insidious onset. Symptoms may progress to the point of losing their jobs or getting into life-threatening situations before they realize that they need medical attention. Second, public perception of narcolepsy is inaccurate and incomplete with social mores associating narcolepsy with sleepiness that is harmless or even humorous rather than a medical condition requiring medical attention. Consequently, people experiencing the cardinal symptoms of narcolepsy for the first time have no prior knowledge that these symptoms are associated with narcolepsy. People with undetected narcolepsy are often unable to perform on par with their peers and cope by lowering their self-confidence and expectations. Furthermore, those individuals surrounding people with narcolepsy often misinterpret the disorder. Authority figures like teachers, employers and parents may associate these symptoms with laziness, lack of motivation, depression, or the result of late-night partying. Inaccurate preconceptions and lack of basic knowledge about narcolepsy perpetuate the delays in proper detection and diagnosis. Lastly, primary care doctors may miss indicators of narcolepsy, leaving this serious illness undiagnosed. In part, this may be due to the fact that narcolepsy is not adequately emphasized within the average medical school curriculum. In 2006, the Institute of Medicine report stated that the “[t]ime devoted in medical school curriculum to sleep medicine is limited.”⁸ In 1993, only 63 percent of medical curriculums included sleep disorders. Of the programs that included sleep disorders, an average of 2.1 hours of class time was devoted to covering all sleep disorders. Since 1993, “[s]imilar analysis has not been performed, but there is no evidence to suggest that medical schools are placing increased emphasis on sleep-related content in their curriculums.”⁸ Increased emphasis on sleep disorders within the medical curriculum and in continuing medical education extension programs may facilitate quicker detection and diagnosis of narcolepsy.

Scientific basis and diagnosis of Narcolepsy

In 1999, the cause of canine narcolepsy was attributed to disruption of the hypocretin (orexin) receptor gene⁹. Subsequently, post-mortem brain tissue of narcoleptic patients helped identify the cause of narcolepsy to a selective loss of hypocretin neurons that are normally found as a mere few thousand cluster of cells in the lateral hypothalamus^{10,11}. Such selective loss of cells may be due to an autoimmune disorder, with genetic and environmental factors as additional contributors. Diagnosis of narcolepsy is made by referral to a sleep center wherein an overnight sleep study (polysomnography) followed by a multiple nap test (multiple sleep latency testing [MSLT]) is performed to establish a diagnosis of narcolepsy as outlined in table 1.

Treatment

Currently, there is no known cure for narcolepsy. Treatment of patients with narcolepsy is primarily symptomatic. Excessive daytime sleepiness is commonly treated with wakefulness-promoting drug Modafinil. Studies indicate that Modafinil reduces fatigue and improves quality of life for people with narcolepsy. Modafinil at a dose of 200 to 400 mg per day has been used in such studies and common side-effects include headaches, nausea, and anxiety. Armodafinil, at a dose of 150 to 250 mg has also been approved for use in

patients with narcolepsy. Side effects of armodafinil are similar to modafinil. Other stimulants such as Methylphenidate and amphetamines may be used in patients with narcolepsy. However, these medications are associated with hypertension, tachycardia, irritability, aggressiveness and insomnia. Unlike administration of stimulant medications during the day, the administration of sodium oxybate at nighttime is a different approach that aims to help improve daytime wakefulness by making sleep more restorative at nighttime. Sodium oxybate is a highly controlled medication requiring centralized pharmacy with the patient requiring frequent monitoring by a sleep physician. Sodium oxybate requires a first dose immediately before bedtime and a second dose about 2–4 hours after first sleep bout aided by the patient awakening to a preset alarm clock. Sodium oxybate has a high sodium content which limits administration in patients with hypertension, heart failure, and renal disorders. Common side effects are nausea, enuresis, and sleepiness the morning after. Nighttime sodium oxybate should not be administered with alcohol and other sedative-hypnotics, but may be prescribed concomitantly with modafinil taken in the morning. The widespread prescription of this otherwise effective agent is limited by the abuse potential for non-medical illegal use as a euphoric agent or for transient amnesia as a date rape agent.

For cataplexy, besides sodium oxybate, antidepressants (Serotonin-specific reuptake inhibitors [e.g., citalopram] and tricyclic antidepressants [e.g., protriptyline]) are prescribed off-label because of their ability to suppress REM-associated symptoms of narcolepsy such as cataplexy and hypnagogic hallucinations. Norepinephrine reuptake inhibitors such as Viloxazine or agents with multiple actions such as venlafaxine have also been used to effectively treat cataplexy. For now, patients manage symptoms with multiple medications, daily naps and diligent personal attention to their symptoms and healthy lifestyle modifications. More research into disease-modifying (rather than symptom-based) therapies for narcolepsy is direly needed.

What do you think are the obstacles confronting early identification and prompt treatment of sleep disorders?

Julie: Currently, many primary care doctors are unfamiliar with sleep disorders. We need to better identify the barriers to the implementation of screening, evaluation and treatment [of sleep disorders] in primary care.”¹² As a community, we can increase awareness for sleep disorders.

What can Primary Care Physicians do to overcome such obstacles?

Julie: There are currently no standards for addressing sleep disorders at the primary care level. A succinct primary care sleep inquiry could include just two simple questions:

1. “Do you have trouble sleeping at night?”
2. “Do you have trouble maintaining wakefulness during the day?”

These questions would help doctors and patients explore signs of sleep disorders and take action by referring such patients to a sleep specialist for further evaluation.

I urge the physician community to promote sleep disorders screening that can be easily administered by primary care physicians. Greater awareness of sleep health and disorders by primary care physicians can save lives and connect patients with sleep doctors to receive proper diagnosis and treatment. Major public education campaigns and incorporation of sleep medicine into medical school and continued medical education curricula are crucial. Change won't happen overnight, but our collective voice will gain momentum and make a difference. I believe that the day will come in the future when primary care physicians will uniformly ask patients about their sleep health and our society will value sleep as much as they value diet and exercise as essentials for healthy living.

What can Sleep Physicians do to overcome such obstacles?

Julie: Sleep physicians and researchers need to increase their efforts in conducting outreach opportunities in order to spread understanding about sleep health and sleep disorders.

Patient-centeredness

Julie voices a simple straight-forward request. We, as healthcare providers should listen and implement Julie's "two sleep-related questions" in our review of systems in the primary care physicians' office visit. But, the dissemination and implementation of Julie's request is fraught by competing needs, access to healthcare, busy practice settings, or plain lack of awareness.

Delivering on such "patient-centeredness" has been slowly gaining momentum for the past six decades with the advent of the guidance-cooperation model of patient-physician relationship, informed consent, and the greater emphasis being placed on humanistic skills of physicians-in-training¹³. However, medical research has traditionally focused on "hard" biomedical outcomes rather than the "soft" patient-centered outcomes such as pain, sleep, health-related quality of life, and patient satisfaction^{14,15}. Although the Agency of Healthcare Research and Quality has made strong strides in the area of patient-centered research, the birth of Patient-Centered Outcomes Research Institute (PCORI), propels us toward realizing the elusive goals of true patient-centered care¹⁶. Patient-centered outcomes research that embrace mhealth and web-portals for better assessment of patients – that can bypass the "impossibly cramped" physician office visit – by sending patients' responses to sleep-related questions to their healthcare provider *should* become a reality. Moreover, societal awareness of the importance of sleep is further enabled by the advent of innovative self-monitoring devices for sleep that have become available. Such a multitude of resources, however, needs harnessing and better direction in order to improve public health. As Goethe said, "Knowing is not enough; we must apply. Willing is not enough; we must do."

Julie's initial experiences reveal the frustrations faced by many patients with sleep problems. Let the patient's voice awaken us!

Acknowledgments

Support from Patient Centered Outcomes Research Institute (IHS-1306-02505) and National Institutes of Health (Grant No. HL095748).

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Clinical Significance

The diagnosis of narcolepsy and other sleep disorders are often overlooked and could be attributed to other medical or even psychiatric conditions with years of missed diagnosis. This is a “patient-centered” review about narcolepsy that aims to awaken the reader to the narcolepsy condition and to the trials and tribulations of patients with sleep problems in general. This may patient-centered review may engender healthcare providers to better detect, diagnose and treat narcolepsy and other such sleep problems.

Table 1**Diagnostic criteria for Narcolepsy with cataplexy**

Excessive daytime sleepiness occurring almost daily for at least 3 months.

Definite history of cataplexy -- sudden and transient episodes of loss of muscle tone, generally bilateral, triggered by emotions (usually laughing and joking).

Diagnosis confirmed by nocturnal polysomnography (with a minimum of 6 hours of sleep) followed by a daytime multiple sleep latency test (MSLT) *:

Mean daytime sleep latency 8 minutes or shorter, with two or more sleep onset REM periods (SOREMP; the time interval between onset of sleep and onset of dream "REM" sleep < 15 minutes).

Hypocretin-1 concentrations in the cerebrospinal fluid < 110 ng/L or less than a third of mean control values.

The hypersomnia is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

* Concomitant medications that can affect sleep or suppress REM sleep would need to be withheld before testing can be performed in a reliable manner.