

Is Sleep the Root of CFS Evil?

What role do sleep abnormalities play in chronic fatigue syndrome? Could sleep dysfunction be the cause of CFS? Or does CFS cause the sleep problems so many patients experience? Read on for highlights on what we know so far.

By Vicki Walker, MA, Guest Contributor

Unrefreshing sleep is a major symptom of CFS, with 70-95% of people with the illness reporting this symptom, making it one of the most common of the eight CFS symptom criteria.¹

Some patients experience disrupted or fragmented sleep. Others report that they are “tired but wired,” and no matter how exhausted they are, their brains won’t shut down for sleep. Still others, particularly at the onset of the illness, have hypersomnia, sleeping 12 to 14 hours a day, but waking exhausted.

It has been difficult, however, to untangle how sleep and CFS relate. Many of the theoretical causes of CFS, such as infection, immunological abnormalities, neuroendocrine irregularities and stress, as well as CFS symptoms like pain, are known to disrupt sleep. Conversely, poor sleep affects immune and neuroendocrine function and can produce symptoms of CFS, such as pain, fatigue and cognitive problems in otherwise healthy people.¹

Anyone who has experienced a few days of insomnia, restless sleep or disrupted sleep knows about dragging out of bed feeling achy, stiff in the joints and mentally foggy. Imagine experiencing sleep problems for months, even years, and the impact this would have on your health and physical and mental functioning. It’s easy then to understand why some people have speculated that sleep problems may either cause CFS or help perpetuate the symptoms.

Stages of sleep

There are two types of sleep: REM, or rapid-eye movement, which is characterized by dreaming, and non-REM, which is divided into four stages. Stage 1 is the transition between wake and sleep; stage 2 is referred to as “baseline” sleep; and stages 3 and 4 are the deepest stages of sleep, also called “delta sleep” because of the slow delta brain waves

seen in this stage.

Each night, healthy humans cycle among these stages of sleep five to six times, with each cycle lasting about 90 minutes. As we begin to fall asleep we enter stage 1, which only lasts a few minutes before stage 2 starts. About 20 minutes later, we transition into stage 3 and then into deeper stage 4 sleep. Delta sleep has been compared to a coma because our heart rate and breathing slow and our bodies are still. After 20-30 minutes in delta sleep, we briefly reenter stage 2 and then move into REM sleep, which is characterized by very high brain activity, dreaming and increased heart rate and respiration. After 10-20 minutes, we sink back into stage 2 sleep, and the cycle begins again. However, most of our sleep in stages 3 and 4 occurs during the first three hours of sleep; afterward we mainly transition between stage 2 and REM sleep. If this pattern is disrupted, we wake unrefreshed and have trouble functioning during the day. And this is integral to most of the research on sleep and CFS.

Why do we sleep?

For something that appears to be vital to life, researchers can’t seem to agree on the reason we sleep. Traditionally, most people have thought that the purpose of sleep is simply to refresh the mind and the body. Anyone who has stayed awake all night cramming for a test or tending to a sick child can agree with that theory. After all, the reaction time of people who have been awake for 20 hours straight is approximately the same as that of people drunk enough to be arrested for driving under the influence. So sleep must do something to refresh us.

However, newer research shows that sleep does much more for us than simply keep us alert and rested. Some of the more interesting findings relate to the role of sleep in developing memory, which is often impaired in CFS.

The Science & Research of CFS

During REM sleep, our brains seem to sift through the thoughts and experiences we had earlier that day and build permanent connections that help us retain and retrieve these memories later. And during delta sleep, our brains appear to prune some of the neural connections, possibly removing weaker links and creating a more efficient brain.

If this theory holds true, poor delta sleep (as has been reported in CFS) may lead to a less efficient, more energy-intensive brain.² And it suggests that the cognitive complaints characteristic of CFS, particularly the deficits in information processing speed, attention and auditory learning, may have their roots in sleep dysfunction.

Sleep abnormalities in CFS

Researchers have largely been interested in learning whether the stages of sleep are disrupted in CFS, and whether any of these disruptions might explain the symptoms. While research results have been mixed, there are several clues that sleep stages are disrupted, at least for some people with CFS, but research to date has not supported the theory that these disturbances are the cause of the illness.

The most commonly cited CFS research findings are an intrusion of fast “alpha” waves into the delta stages of sleep and a decrease in the duration of stage 4 sleep. It’s logical that both of these disruptions to the most restful stages of sleep might result in fatigue and unrefreshing sleep, but several excellent researchers have been unable to replicate these findings.

A 2004 study of identical twins, one with CFS and one without, found that the twins with CFS spent more time in stage 3 and REM sleep, even though the CFS twins reported greater problems with unrefreshing sleep.³ An interesting note is that prolonged delta sleep may result from a release of cytokines by the immune system, which may support the theory that CFS is an immunological disease. These findings, however, must be interpreted with caution, given that this study found an extraordinarily low rate (4.5%) of sleep disorders in the 44-person research group.

Primary sleep disorders such as sleep apnea, narcolepsy or restless legs syndrome are frequent abnormalities seen in fatigue illnesses, but with the current diagnostic criteria, primary sleep disorders are exclusionary conditions for a diagnosis of CFS unless treatment of the disorder doesn’t resolve the CFS symptoms. Oddly, many people with a CFS



“Evidence from studies of sleep stage disruption indicates that sleep fragmentation and sleep loss lead to negative mood. Cognitive and physical performance decrements are also noted, as well as increased muscle discomfort and pain sensitivity. Therefore, sleep pattern changes at the very least reinforce many symptoms common to CFS.”

— DR. JOAN SHAVER, UNIVERSITY OF ILLINOIS AT CHICAGO

diagnosis have never undergone polysomnography, also called a sleep study, to determine whether they might have a sleep disorder that could be causing their symptoms.

Recently it was reported that 58% of people with CFS had a previously undiagnosed sleep disorder, and 86% had self-reported insomnia.⁴ Treatment of the identified sleep disorders improved the patients’ general daytime functioning and perceived quality of life, but the fundamental nature of fatigue wasn’t resolved. For this reason, the researchers concluded that sleep disorders likely co-occur with, rather than cause, CFS.

Sleep and immune function

Numerous studies, some CFS-specific and others not, have reported a link between sleep disruption or deprivation and immune function. An increase in proinflammatory cytokines and decreases in natural killer cell responses are the most common findings, supporting the role of sleep in regulating immune system functioning.

Stress has also been implicated in the relation-

ON THE FRONTIER

A Link between Sleep and Weight?

Several recent studies have investigated the relationship between sleep and weight. Researchers at Eastern Virginia Medical Center found that overweight and obese subjects slept about 2 hours less a week than normal-weight subjects.

Researchers at sleep labs found that sleep deprivation can alter metabolic functions and the activity of several hormones, including leptin. Scientists at Stanford University and the University of Wisconsin believe ghrelin, an appetite-stimulating hormone, may also be involved. In a long-term study of the sleep habits of 1,000 subjects, they found that in people who slept less than 8 hours a day, body mass index increased in direct proportion to decreases in sleep time. They also found people who slept less had reduced leptin and elevated ghrelin.

It's not yet certain that insufficient sleep contributes to weight gain, and none of these studies focused on CFS, but further study is warranted. Such research could have implications for CFS since many patients experience weight gain. While this may be due to decreased activity and other factors, a possible link to insufficient sleep is intriguing.

Serotonin, Sleep and SSRIs

Serotonin, a neurotransmitter synthesized from the amino acid tryptophan, is known to modulate mood, sleep and appetite. Two recent studies found that it may play a role in CFS.

Japanese scientists reported in *NeuroReport* that PET scans of the brains of CFS subjects showed that the density of serotonin transporters (5-HTTs) was significantly reduced. They theorize that an alteration of the serotonergic system in the brain plays a key role in the pathophysiology of CFS.

In contrast to studies reporting reduced brain serotonin levels in CFS patients, researchers in the United Kingdom found that a subgroup of CFS patients has a high level of brain serotonin. Their 2005 study, published in the *Journal of Psychopharmacology*, reports the serum ratio (free tryptophan/competing amino acids) was 43% higher in this subgroup of patients.

Serotonin-reuptake inhibitors (SSRIs) are often prescribed for fatigue, pain and depression in CFS patients. These findings suggest important implications for drug therapy since SSRIs wouldn't be indicated for the group of CFS patients who have high levels of brain serotonin, but might be useful for those patients with a serotonin deficiency.

ship between sleep and the immune system. A 2001 study suggested that the interaction of psychological factors—like the stress brought on by CFS symptoms or stressful life events—and immune changes may contribute to the chronic nature of symptoms and to altered immune surveillance function in CFS.⁵ It's possible that persistent stress, with its negative impact on sleep, alters the immune defense system.

Sleep and hormones

Deficits in the neuroendocrine system have been implicated as a cause of CFS, and sleep is both influenced by and influences the function of the neuroendocrine system. Disturbances in the hypothalamic-pituitary-adrenal (HPA) axis are some of the more robust CFS research findings. Levels of melatonin, the natural brain hormone that induces restfulness in sleep in healthy individuals, may be altered in CFS, but evidence is not conclusive. Reduced levels of the stress hormone cortisol is the most common finding of research to date. Normally cortisol rises during times of stress, and it's usually elevated in major depression. These reports and others suggest that CFS patients have an altered neuroendocrine response to stress.⁶

Sleep deprivation mimics the body's neuroendocrine response to stressful circumstances. Administering the hormones normally released during stressful exposures also impairs sleep quality, affects immune function and disturbs sleep and waking rhythms. Myrtis Fossey's research group in Quebec posits that symptoms of depression, anxiety or other mental illness in CFS may actually stem from the release of stress hormones in response to sleep deprivation.⁴

Finally, evidence of neuroendocrine-mediated disturbances in the sleep-wake cycle of CFS patients has been reported, as has a desynchronization of the temperature and melatonin circadian rhythms, which influence the sleep-wake cycle.⁴ Desynchronization of sleep-wake cycles can produce insomnia, daytime fatigue, nonrestorative sleep and memory and concentration problems, such as are seen in CFS.

We need to know more

The precise relationship between poor sleep and CFS is still unknown. Is unrefreshing sleep the cause of CFS, a result of CFS or something that co-occurs with CFS? There are many clinical and laboratory findings and intriguing links from other areas of research that associate CFS with disturbed sleep. Further research is necessary, however, to answer the many questions about how and why these conditions relate. ■

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