



Part two of a series exploring sleep and its effect on the body. This time we focus on brain activity and hormone function.

# The Biology of Sleep

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*In the first of this four-part series, we covered the basic mechanisms of sleep—how the body initiates it and the different stages we experience throughout the night. We also touched on a few of the important physical processes impacted by sleep. In this installment, let's look more closely at how sleep, and the lack of it, affect some of the body's internal processes—particularly brain activity and hormone regulation.*

As sleep science advances, researchers are discovering that sleep plays a critical role in keeping many of our body's internal processes intact and functioning. The sense of rest and rejuvenation we feel from sleeping is tied to specific cellular and biochemical processes that help the body restore and adjust itself.

Repair and regulation occur in multiple ways. In the brain, repair and rejuvenation is primarily related

to metabolism and neurotransmitter activity. In the body, regulation is affected by the way sleep impacts endocrine function and hormones.

## Repairing and refreshing the brain

Recent studies have suggested that the brain, so active during the day, may use the downtime of sleep to repair damage caused by our busy metabolism, to refresh neurotransmitter activity and even to grow new neurons. For starters, sleep appears to detoxify the brain.

Scientists noticed long ago that larger animals require less sleep than smaller ones. Ferrets, for example, need nearly 15 hours of sleep per day while elephants need only 3 or 4 hours. (Humans should get 7 to 9 hours.) Research has connected this need to the energy conversion process called metabolism. The smaller the animal, the higher its metabolic rate and the more sleep it needs. But why?

Metabolism generates highly reactive chemicals (free radicals) that damage cells in a process called oxidative stress. Sleep helps repair the damage, particularly in the brain. The lower metabolic/energy needs of the brain during the slow-wave (non-REM) stages of sleep provide an opportunity to deal with the cellular damage done during waking hours. Sleep is also when the brain produces more of a specific enzyme (superoxide dismutase) that works to neutralize free radicals. When deprived of sleep, the brain produces less of this enzyme and has less non-REM sleep time to repair cells.

For people with CFS, a connection between poor sleep and oxidative stress is significant. Studies using brain imaging, exercise testing, genomic analysis and examination of spinal fluid protein have all uncovered indications of excessive oxidative stress or mitochondrial dysfunction in CFS—pointing to cell damage and

problems with energy conversion. With more oxidative damage, more cellular repair may be needed, making it even more important to treat CFS-related sleep dysfunction—particularly since in some cases of CFS it's the slow-wave sleep that shows disruption.

It appears that REM sleep, characterized by rapid eye movement and brain activity resembling that of waking hours, may also play a role in refreshing certain parts of the brain. Though much of the brain is very active during REM sleep, the brain cells that release certain neurotransmitters—the chemicals that physically carry signals from one brain cell to another—shut off. During REM sleep the transmitters (serotonin, norepinephrine and histamine) that would activate movement and produce awareness of surroundings cease. Beyond keeping us still while dreaming, it's thought that this cessation is vital for the function of these brain cells and their receptor counterparts, letting them rest and regain proper sensitivity.

This also could be important to people with CFS, since studies have shown irregularities in serotonin transport (5-HTT) function (see page 19) and other serotonergic mechanisms. Norepinephrine, too, has been implicated in the pain associated with CFS and fibromyalgia.

The formation of new nerve cells in the brain is also affected by sleep. We now know that some parts of the brain continue to produce new cells throughout life. But recent evidence shows that sleep deprivation can impede new neuron growth, and that the brain cells that are formed during sleep deprivation often don't mature normally.

Sleep is important to brain cell repair, restoration and rejuvenation, probably in ways that complement each other. But sleep also impacts the system that regulates many of the rest of the body's functions: the endocrine system.

### Regulating body functions; releasing hormones

Hormones are substances produced to trigger or regulate particular body functions.

The release of hormones by the pituitary gland—the “master” endocrine organ that governs secretion from the peripheral endocrine glands—is often timed to correspond with sleep. Growth hormones, for example (vital to growing children, but also for restorative processes like muscle repair), are released during sleep, and corticotrophin-releasing hormones (involved in the stress response) are inhibited. Loss of sleep can short-circuit this timing, throwing off the hormone levels in the body.

Another way sleep affects peripheral endocrine function is through variations in autonomic nervous system activity. During sleep the sympathetic nervous system, governing the stress response, is less active, and the parasympathetic nervous system, governing rest and digestion, dominates. Most endocrine organs are highly sensitive to this balance. Lack of sleep or reduced sleep can reverse the dynamic, resulting in dysfunctional hormone production.

This could be of particular relevance to people with CFS who already experience neuroendocrine dysfunction and hormone levels off-kilter from the norm. For example, people with CFS tend to have lower than average levels of growth hormone (GH), which is primarily released during slow-wave sleep—the type of sleep shown in some studies to be disrupted in CFS. Research also shows that people with CFS experience autonomic irregularities that keep their sympathetic nervous system on overdrive—a state likely to affect normal endocrine function. More and better sleep may have the potential to help stabilize endocrine function.

Sleep and hormone production has been gaining scientific focus. A recent study by the University of Chicago Medical Center investigating the hormonal effects of a week of partial sleep loss found an increase in evening levels of cortisol, a split in the timed release of GH and a striking drop in nocturnal thyroid-stimulating hormone (TSH) and the hormones leptin and insulin. The drop of insulin and leptin levels are particularly troubling indicators that poor sleep could lead to obesity and type 2 diabetes.

In fact, an increasing number of studies are showing that the levels of



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appetite-regulating hormones are profoundly influenced by sleep duration. In the study mentioned above, just one week of restricted sleep (4 hours versus 10 hours), resulted in leptin levels so low as to signal a state of famine when, in fact, caloric intake was robust. A follow-up study also showed significantly elevated levels of ghrelin. Investigators at Stanford and Wisconsin universities reported similar results in a large scale study of 1,000 subjects. This combined drop in leptin and spike in ghrelin could feasibly lead to excessive eating and unhealthy weight gain.

In yet another study by the Chicago team—this one investigating slow-wave sleep suppression—just three nights of altered sleep resulted in 16 young, healthy study subjects exhibiting a 30 percent decrease in their ability to secrete and respond to insulin. Such impaired glucose intolerance is usually an early symptom of type 2 diabetes.

The good news is that, in all of these studies, once the participants regained healthy sleep patterns, their hormone levels returned to normal within approximately one week. While it could prove more challenging to correct damage caused by chronic sleep loss, the ability to “recover” from the immediate effects of poor sleep holds promise for people who are able to work with their physicians to address sleep problems.

### Reasons for hope

Sleep serves the brain and the body in critical ways that we understand better with each new study conducted. And as research about the effect of sleep increases, so too does research into medications and other treatments to help induce and improve sleep. For people with CFS, it’s an

area that appears to be both important and potentially treatable, with more advances and better treatments likely to emerge in the future. ■

**Coming in Part 3: How poor sleep can affect the immune system and cognitive function.**



## TALKING TO YOUR DOCTOR ABOUT SLEEP

Unrefreshing sleep is one of the major distinguishing symptoms of CFS. If you’re experiencing trouble sleeping, it’s important to begin working with a medical professional to address the issue. Here’s some advice to get that process started.

**Clearly communicate the nature and severity of your sleep complaint.** CFS physician Lucinda Bateman, MD, collects the following information from new patients. You can use this form with your physician to help describe your sleep troubles.

Sleep problems: (0=never had the symptom, 1=infrequent or mild, 2=moderate, 3=severe or almost constant)

- 0 1 2 3 Can’t go to sleep. Can’t initiate sleep.
- 0 1 2 3 Restless, light sleep. Frequent awakenings.
- 0 1 2 3 Wake up too early in the AM.
- 0 1 2 3 Can’t go back to sleep when awakened.
- 0 1 2 3 Need too much sleep. (Number of hours? \_\_\_)
- 0 1 2 3 Need to take naps during the day
- 0 1 2 3 Unrefreshing sleep. Wake up feeling tired.
- 0 1 2 3 Restless legs (creepy crawly, need to move)
- 0 1 2 3 Leg cramps (painful spasm of the muscle)
- 0 1 2 3 Myoclonic jerks (sudden jumps and jerks)
- 0 1 2 3 Snoring
- 0 1 2 3 Stop breathing during sleep

**Consider all possible cause(s) of sleep disruption.** This might take into account the type of disruptions above, but also pay attention to other possible causes, such as poor sleep habits or drugs that disrupt sleep (caffeine, decongestants, stimulants). The type of sleep problem you’re having will determine to a great extent the kind of treatment or medication that will be effective.

**Record doses and observations to share with your doctor.**

When starting a sleep medication, make notes that will help you describe how it’s working (or not). How many days did you use it? What dosage and timing did you use each day? If the drug isn’t meeting your expectations, be detailed about why. Some issues can be resolved by changing the dosage or the time of day you take it; others by switching to a different type of sleep aid.

According to Bateman, the key to effective sleep treatment is to keep a dialogue going with your doctor. The better you can describe the nuances of your sleep and of a medication’s effects, the more likely a medical professional can zero in on the treatment that will yield the best rest possible.