



WHITEPAPER

Understanding the Science of Sleep

The Sleep Genius Solution

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sleep genius

Overview

Understanding sleep is one of the great challenges to biomedicine of the 21st century. Sleep is as important to life and health as breathing, eating or drinking, and yet despite decades of research by thousands of dedicated scientists and physicians, it is still one of the least understood behaviors. It is estimated that 40 million people in the US have chronic sleep problems and 20 million more experience temporary sleep problems at some point in their lives. These disorders broadly include:

- Insomnia, the inability to fall or stay asleep
- Disturbed sleep, in which the sufferer fails to achieve all the required stages of sleep
- Excessive sleepiness, such as narcolepsy or chronic fatigue syndrome.

However, simply lumping sleep problems into diagnostic categories does very little to help figure out their underlying causes. Sleep can be affected by factors as fleeting as the amount of coffee or tea consumed, or by those as basic as age, gender, genetics or health. Discovering ways to allow everyone to get the sleep they need at every stage of their life requires a major rethinking of how we approach sleep and sleep disorders.

What is Normal Sleep?

Sleep is a complex neurological behavior found in all vertebrates, from fish to humans. While there are differences in the stages and forms of sleep in different species, it is a critical part of health in all of them. In humans, sleep is broadly broken into Rapid Eye Movement (REM) and three stages (N1, N2, N3) of non-Rapid Eye Movement (NREM), defined by electroencephalographic (EEG) measures.

- N1 sleep is often called “drowsy sleep,” and represents the transition from the waking (W) alpha state, with brain rhythms of 8-13 cycles per second (Hz) to slower theta waves of 4-5 Hz.
- N2 sleep is when muscular activity and all conscious awareness of the outside world decrease, and is detected by the emergence of K-complex bursts often followed by sleep “spindles” — bursts occurring between 12-14 Hz. This stage constitutes about 50% of the entire sleep cycle in normal human sleep.
- The N3 stage is termed deep or “slow wave sleep,” with oscillations appearing at 0.5 to 2 Hz.
- REM sleep is the “dream stage,” taking up about 25% of normal sleep time. It is characterized by rapid movements of the eyes under the closed lids and low amplitude, fast EEG signals.
- Normal sleep in adult humans usually progresses through several cycles of N1-N2-N3-N2- REM-N1, etc. each night.



There is no single place in the brain that controls sleep. Sleep behavior is based on the interactions of multiple sleep-related centers throughout the brain. These include elements of the “global sleep system,” based on direct and indirect retinal input to the mammalian master clock, the suprachiasmatic nucleus, and brainstem sites such as the dorsal raphe nuclei and locus coeruleus that provide specific neurotransmitter input to modulate thalamic and cortical regions involved in sleep. In addition, input from all sensory systems, from light to smell, can interrupt or help sleep, with certain modalities such as hearing and balance providing critical maintenance or disruption abilities.

As there is no single sleep control center in the brain, there is no single function for sleep. Proper sleep is required for behaviors ranging from cognitive and memory function to adequate immune responses and metabolic maintenance. Failure to achieve proper sleep has been implicated in health issues as wide-ranging as dementia, delayed wound healing, obesity and diabetes.

What are Sleep Disorders?

As of today, there are more than 70 separately described sleep “disorders” — some irritating and temporary, some literally life threatening. These can be broadly characterized as insomniac (interfering with or limiting sleep duration and quality), or excessive sleepiness, with sleep or physical malaise interfering with normal daytime activities.

Complicating matters is that the two often interact — sleep loss during the night can induce excessive daytime sleepiness. Furthermore, there are major demographic differences in sleep needs. The “normal” 7-8 hours sleep required by healthy young adults is completely inappropriate for an infant, who needs 16 hours, or even a young child, who will need 10 hours. The idea that it is “normal” for elderly people to need less sleep is actually a reflection of the increased issues that can negatively affect sleep as we age.

Different age groups tend to express differences, not only in normal sleep patterns, but in the problems they face. The sleep patterns of very young infants can be highly erratic, as their brains are still entraining to standardized patterns. They may need 16 hours, but they often get it in very changeable periods of time, inducing sleep deprivation in their parents. Children and teenagers are also undergoing significant brain and behavioral development, and are often much easier to disrupt than adults. The consequences of sleep disorders in children and teenagers is as far-ranging as in adults, with insufficient or poor quality sleep being implicated in everything from depression to poor scholastic performance. Young adults tend to have more problems falling asleep, whereas older adults more often have trouble staying asleep.

Trying to treat all these diverse issues under a single diagnosis of “sleep disorder” is likely to result in frustration for both the sleepers and those close to them, sometimes even exacerbating the issue.



But while the differences in sleep problems across age are at least basically understood, differences in sleep between the sexes are often ignored. Even in basic research studies, scientists tend to select male subjects in order to avoid the complex effects that can appear based on cyclical changes in hormone levels in females. The problem is that these hormonal changes are, in fact, normal for half the population. Changes in hormone levels, particularly around puberty and menopause, have profound effects on every biochemical system in the body, and have been shown to severely impact the duration and quality of sleep in women. Yet even a basic search of medical publications shows that studies on sleep in men outnumber those on sleep in women by about 2:1.

Treatments

So how to best treat problems with a system universal in scope, critical to health and life, but with so many variables? A major problem has been the manner in which sleep issues have been treated as medical disorders. Early treatments for insomnia primarily focused on the administration of sedatives to induce relaxation or unconsciousness, and this technique is still widely used. However, more recent studies have demonstrated that sedatives and hypnotics not only do not induce normal sleep, they can cause more long-term problems than they solve, including dependence, reactive insomnia or even drug-related deaths due to improper dosage and mixing with alcohol or other drugs. Sleep is, in fact, a complex multistage process, and failure to go through all stages of sleep can have just as devastating an effect as being entirely sleepless.

Drugs, such as Ambien or Lunesta, that purport to target sleep-related biochemical systems, can have greater efficacy without some of the side effects of more general sedatives, but also have mixed effectiveness in the greater population. These drugs target the nervous system's gamma-Aminobutyric acid (GABA) receptors. GABA is a very widespread inhibitory neurotransmitter that does much more than induce sleep. Over-the-counter dietary supplements are often effective for some people, but their unregulated nature allows for wide variance in strength and purity, as well as the fact that users are taking very complicated compounds whose mechanisms are poorly understood. Melatonin in particular, while generally considered safe in low dosages for short periods, is associated with diminished libido, headaches, nausea, grogginess and weight gain when taken in higher dosages.

On the other hand, hundreds of thousands of people suffer the reverse problem of being unable to stay awake. Many of these people suffer from daytime sleepiness, sometimes as a by-product of insufficient nighttime sleep, others due to underlying medical conditions such as narcolepsy or chronic fatigue syndrome.

But for many, daytime sleepiness is due to environmental factors such as low frequency, low amplitude vibration, which causes a form of motion sickness called "Sopite syndrome" (Graybiel & Knepton, 1976; Lawson & Mead, 1998). Sopite syndrome is the underlying cause of many vehicular accidents where an otherwise healthy individual nods off at the wheel. Again, in many cases, the treatments given for excessive daytime sleepiness can be as much of a problem as the disorder they are trying to fix, with pharmaceutical and natural stimulants having effects that last much longer than the daytime period, interfering with normal sleep patterns at night. This is why many people who begin trying to medicate their way out of sleep issues end up in a long-term roller-coaster of inappropriate sleepiness and wakefulness, leading often to serious psychological and medical problems.



Non-pharmaceutical Treatments

A common alternative for aiding sleep is using sound. This is because sound (and its related sense, balance) are two sensory systems that easily penetrate the brain's natural sensory damping during deeper sleep stages. Sound is the only sensory system that remains truly active during sleep (Velluti, 1997). This sensitivity to sound, even while trying to sleep, is a two-edged sword (especially for women who have greater hearing sensitivity from birth until after menopause). While it means that sounds are the most likely distracters to interrupt or prevent sleep (Vallet and Mouret, 1984), it also provides a way to more thoroughly mask the environment, allowing someone to fall asleep. This is why some people try to fall asleep to ambient or soft classical music, and is also the basis for the success of "sleep machines," which play quiet repetitive sounds, usually of something familiar and calming, such as ocean waves. Neither music nor sleep machines induce sleep, but they are often useful for masking noises from the environment, and sometimes thought from within the sleeper's mind, although there is some evidence that overly loud white noise significantly reduces REM sleep in a variety of animals (Velluti, 1997).

The Sleep Genius Solution

One solution for developing a non-pharmaceutical sleep aid is to use the brain's own sensory-sleep organization to prevent the roller-coaster of drowsiness/wakefulness from insomnia by combining the two sensory systems most capable of affecting sleep cycles. Parents the world over know that they can rock their baby to sleep. And everyone has experienced being shaken awake. Both of these are balance responses — changes in acceleration that are measured by part of your inner ear, the vestibular system. Between these two extremes, there is a psychophysical curve, with sleep on one end and wakefulness on the other, mediated by the inner ear. Advances in auditory neuroscience over the last decade have demonstrated that hearing and balance can cross talk under certain conditions (Todd & Cody, 2000). The next generation of sleep aids uses sound, but in a different way than music alone or sleep machines.

The neurosensory algorithms within Sleep Genius are based on two factors:

1. The vestibular system is profoundly interconnected with, and effects substantial control over, sleep processes; and
2. The auditory system has substantial functional and anatomical overlap with the vestibular system and is the sensory system most able to affect arousal under sleep and near-sleep conditions.

The vestibular system is important, not only for maintaining balance and orientation, but is also required for normal sleep. While the vestibular system is not part of the global "sleep regulatory system," vestibular stimulation modulates known arousal centers. Bidirectional connectivity between brainstem vestibular centers and arousal centers, as well as multisynaptic connections with the mammalian master clock, the suprachiasmatic nucleus (Horowitz et al, 2005), indicate that vestibular input may be a potent modulator of sleep and arousal. There has been continuous attention to the possibility of a direct sleep-vestibular system connection since the 1960s (Leslie et al. 1997). The problematic interaction of the vestibular system and sleep that arises in Sopite syndrome is due to regular, low-amplitude vestibular stimulation for extended periods of time, inducing drowsiness, lethargy and reduced attention (Graybiel et al, 1965; Lawson & Mead, 1998).



The noradrenergic coeruleovestibular pathway has been implicated in the sleepiness-inducing aspect of Sopite (Nishiike et al, 2001).

On the other hand, vestibular stimulation can be a boon for sleep induction when it is desired. For instance, premature infants given active rocking treatments for two weeks showed enhanced quiet sleep compared to matched control infants (Cordero et al. 1986). When adults are swung less than three inches each way in a head-to-toe direction for two nights, nocturnal sleep latency is reduced (Woodward, et al. 1990). In elderly people, low frequency bed rocking yields significantly greater consolidation of otherwise fractionated sleep patterns (Iber et al. 1989).

While acceleration is the normal stimulus used to stimulate the vestibular system, properly structured and presented sound can be effective as well under certain circumstances. Complex, broadband sounds, particularly those with harmonic structure, are capable of synchronizing large populations of neurons in the brain from the brainstem through the cortex. This allows sound or music to be used as a carrier to deliver stimuli that overlap and interact with targets of the vestibular system. Low frequency low amplitude rumbling noise can drive Sopite responses, rather than using whole body vibration or rocking, inducing sleep.

Binaural beating — structured stereo sounds that synchronize large regions of the cortex — can be used so that the beating frequency oscillates at the rates observed in different stages of sleep, simulating normal neural processes for maintaining sleep and driving the sleeper from one stage to another.

Finally, overall arousal can be reduced by auditory-facilitated relaxation. This involves the use of calming sounds, such as low amplitude pink noise, convolved with cardiac and respiratory sound envelopes which decrease in repetition rate across a physiologically appropriate range, to lower the listener's heart and breathing rates.

Our sleep-inducing technology, embedded within the acoustically-modified music created for Sleep Genius, uses all three methodologies. We've developed neurosensory algorithms that use sound to drive sleep-inducing vestibular responses instead of whole body vibration or rocking. Additional algorithms allow us to implement microsecond-scale accuracy for fine-grained binaural interactions, and let us use structured noise as a modulatory neural driver.

Ad-hoc clinical testing has demonstrated the effectiveness of our algorithms in inducing sleep by reducing sleep latency and increasing efficiency in subjects ranging in age from 1 to 62, and has been shown to decrease sleep latency, increase sleep efficiency, or both, in up to 77% of people with normal binaural hearing.



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