

SLEEP AND DEPRESSION

by Brigitte Delange

“Human beings seem to be fighting the evolutionary pressure to sleep. Despite the fact that sleep plays a vital part in our health and our efficiency, we seem out to abolish sleep. The first step in this process was the invention of the electric light bulb, which eliminated our main excuse for stopping our work at the end of the day, namely, that it was too dark to function. Next came the continuous conveyor belt, which encouraged factories to operate 24 hours a day. Now the continuous access to information provided by the Internet and other computer communication links keeps us from our beds at all hours of the night. The work ethic we have adopted today says we should do away with sleep, or at least eliminate as much sleep time as possible. The movers and shakers of the world don’t waste their time sleeping. Yet too little sleep can kill us outright or can cause a gradual deterioration in our health. Too little sleep can make us clumsy, stupid, and accident-prone. Too little sleep can destroy our psychological motivation and put us into a deep depression.”

Stanley Coren, psychology professor and neuropsychological researcher

Sleep still is one of the greatest biological mysteries. After many decades of research, we know all about what causes us to feel sleepy, different types of sleep, electrical activity in our brains while we sleep, and the mechanisms of waking up after sleep, but we still don’t know why we sleep.

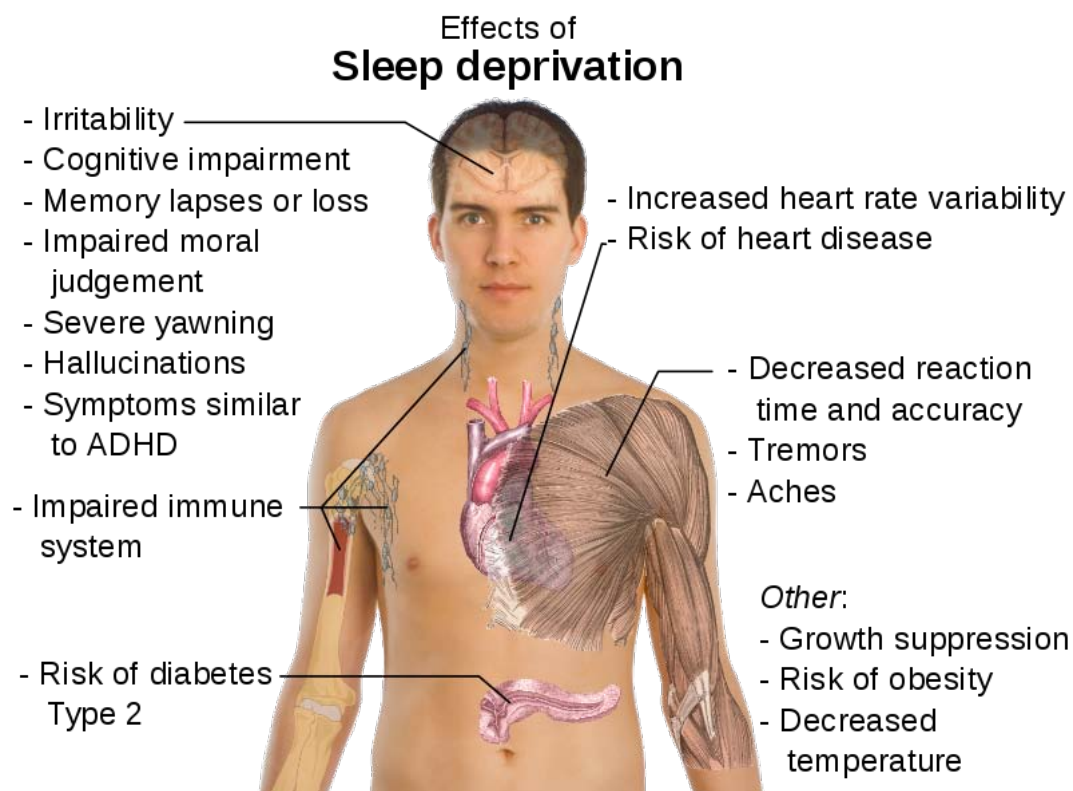
It is clear we do need regular and normal sleep for our overall health. It has persisted during evolution. All animals have some form of sleep, so far as researchers have been able to test. Sleep is strictly regulated. Sleep loss is inevitably followed by a rebound.

Not sleeping leads to unstable moods, impaired cognition, and eventually death. Sleep deprivation elevates the body’s production of stress hormones, raises blood pressure and boosts blood levels of substances that cause inflammation. It is linked to serious diseases such as heart disease, psychosis, anxiety disorders and depression. Recent research even showed that people, who don’t sleep enough, become more obese. Sleep deprivation may disrupt hormones that regulate glucose metabolism and appetite. Less sleep results in higher levels of ghrelin, an appetite-stimulating hormone, and lower levels of leptin, an appetite-suppressing hormone.

Apparently, some benefits emerge from the environmental disconnection

sleep produces that cannot be provided by quiet wakefulness. Sleep is largely under genetic control. It can serve many functions or just one, until now unknown function. Several theories have been proposed.

The null hypothesis claims sleep is merely a way to impose a quiet, immobile state and not important by itself. It's just an extreme indolence animals indulge in when they have no more pressing needs. All the important things we could do if we didn't have to lose so much time of our lives sleeping, besides all the health problems not sleeping generates, does away with this theory rapidly.



Sleep might be to save energy, but the facts prove otherwise. The amount of energy used during sleep is just a bit less from the amount necessary during wakefulness. Hibernation is an excellent example of a way to save energy. But animals come out of hibernation at regular intervals to fall asleep, which indicates sleep has another function than saving energy.

Sleep may have an adaptive function. During its sleeping time an animal stays out of harm's way and thus sleep may help in preservation. But animals losing sleep because they are being chased by a predator are even more at risk the

next day when their sleepiness makes them less alert. Neither does this theory explain important processes going on during sleep.

The immune system surely is positively influenced by sleep. Research among mammalian species came up with a higher number of white blood cells, the building blocks of the immune system, the more total hours of sleep a species enjoys. Practically, this results in a reduced impact of parasites. Wound healing also is shown to profit from sleep. Sleep deprivation in rats showed a twenty percent decrease in their number of white blood cells.

Sleep functions may change over time. Sleep deprivation in children is known to affect the development of the central nervous system. This results in apoptosis (programmed cell death), decreased brain mass, behavioral problems, and permanent sleep disruption.

On a cellular basis, sleep may be a behavior for recovery and return to homeostasis. During wakefulness, many metabolic processes are pushed to their maximum levels. Most of the brain and peripheral organs appear to be recovering during non-REM sleep. The basic locomotor, sensory, and thermoregulatory circuits do the same during REM sleep. Macromolecules are restored and used transmitter vesicles replenished. Enzymes can repair brain cell damage caused by free radicals.

Sleep may also be essential for the brain's plasticity. During the day, neurons' synapses increase in strength. Sleep may be used to damp down to baseline levels and protect the body from the negative effects of prolonged wakefulness, such as the build-up of adenosine (an important neuromodulator) during daytime. Receptors get a 'rest' and regain their sensitivity. If the process of synaptic homeostasis is prevented by sleep deprivation symptoms occur related to synaptic overload of neocortical and limbic circuits.

Memory

The relationship between memory and sleep is one of the most evident. Many studies have shown that while sleeping the brain is busy consolidating memories. The neurons in rat brains firing while learning a new task are active exactly the same way during the following sleep period, as if to imprint the path necessary for performing the task. The simultaneous reactivation of

coherent memory traces takes place in the hippocampus and in the neocortex. Rats allowed to sleep after learning perform significantly better thereafter than their colleagues who were prevented from sleeping. A study among adolescents also reported better academic performance with more high-quality sleep, whereas increased sleep onset latency over the weekend worsened academic performance.

The most fascinating and clear theory about memory and sleep hints at the existence of an intermediate memory system next to the short-term and long-term memory systems (Zhang, 2004). Memories aren't transferred from short-term storage to long-term storage during waking time, but go into temporary memory storage. The function of sleep would be to process, encode, and transfer data from this temporary to long-term memory. To ensure an uninterrupted memory transfer process it is necessary to shut off temporary memory from the environment.

The two types of sleep, non-REM and REM sleep, can be linked to the two kinds of memories that need to be stored. During non-REM sleep information belonging to explicit memory is stored. During REM sleep implicit memory information is processed.

Atonia during REM sleep has to do with this processing of procedural data, as it prevents the sleeper from reacting to these data. It is not related to the content of dreams, as dreaming also occurs during non-REM sleep when the body isn't paralyzed.

The fact that sleep requirements are far greater in babies and children than in adults has to do with the amount of data that need to be transferred and with the transfer speed that becomes faster later in life as more connections have been formed. Babies spend more time in REM sleep, because they have to master a huge amount of new skills.

Sleep deprivation fills up the temporary memory store, which hampers cognitive skills. Sleep rebound is necessary to empty temporary memory and therefore takes up far less time than the actual time of sleep loss.

That we forget most of our dreams and sometimes only remember short fragments of dreams can be explained by the fact that intermediate memory isn't available for storage during sleep and only short-term memory is taking in new information.

It would be an interesting challenge to look for the neural circuits involved in intermediate memory and thus test this theory of sleep by reality.

Depression

An intriguing link exists between sleep and depression. It is evident depressed people don't sleep well. But sleep and the neural processes going on in the brain during sleep can actually cause depression. Several hormones and neurotransmitters that play a role in depression are also important in the sleep process.

Melatonin is a hormone produced by the pineal gland. It governs the entire sleep/wake cycle. The neurotransmitter norepinephrine, also pinpointed in depression disorders, regulates the activity of the pineal gland. Binding of norepinephrine to its receptors in the pineal gland triggers a cascade of second messengers. Among these second messengers is cyclic adenosine monophosphate (cAMP), which contributes to the synthesis of serotonin – another suspect in depression disorder- from its precursor tryptophan.

Serotonin in turn is used to synthesize melatonin.

Melatonin binds to its receptors on neurons of the suprachiasmatic nuclei in the hypothalamus, which take care of the functioning of the body's biological clock. The levels of melatonin in the brain vary in a daily cycle. Its secretion peaks in the middle of the night. The production of melatonin is inhibited by light.

A specific type of depression, seasonal affective disorder (SAD), is caused by a deficiency of the system that produces melatonin. Fooled by winter's darkness, the production of melatonin continues. This results in an inability to shake off the night's slumber.

The neurotransmitter serotonin also contributes to the onset of sleep due to a build-up of serotonin in certain parts of the brain during wakefulness. But the tasks of serotonin are more specifically than those of melatonin. Serotonin is involved in wakefulness, in triggering sleep, and in REM sleep.

During REM-sleep, levels of serotonin in the brain drop as clusters of neurons within the locus coeruleus in the brain stem stop firing.

During non-REM sleep these cells turn on again. In general, low serotonin levels lead to problems falling asleep and make the brain stay less time in

non-REM sleep, two deficiencies that are part of depression disorders. Sleep deprivation can alleviate symptoms of depression, especially if REM sleep is prevented. The natural decrease in serotonin during REM sleep doesn't occur and thus serotonin levels that are low in depressed persons are elevated. Unfortunately, symptoms return if the patient's sleep cycle is back to normal. Treatment of depression with tricyclic antidepressants happens to suppress REM sleep.

Another hormonal alteration during depression involves cortisol, produced by the adrenal gland. Cortisol is also referred to as the stress hormone as it is involved in response to stress and anxiety. Depression is characterized by raised levels of cortisol, but levels of cortisol normally also rise gradually in the course of the night.

Clear evidence exists for a strong link between mood and sleep, not in the least because in most cases symptoms of depression are felt most intensely in the morning after waking up. Individuals with mild episodic depression and seasonal affective disorder have lower than normal melatonin levels. People who suffer from major depression or panic disorder also have low levels of melatonin clinical studies have shown. Administration of melatonin, which possibly causes a surge in serotonin levels, may help alleviate the symptoms of depression. It may also improve sleep patterns in patients with depression. Further studies are necessary to confirm this.

In the end, it may turn out that it's not the depression that causes patients to sleep badly, but disturbed sleep patterns that cause the depression.

Specifically too much or prolonged REM sleep seems to be a promising culprit, as lengthening REM periods result in progressively lower levels of aminergic neurotransmitter release during the night. All the substances until now identified in participating in creating a depression are important players in sleep processes as well. Only melatonin has stayed out of the spotlight so far. Due to its very tight-knit relationship with serotonin, it would deserve a more central role in future sleep and depression research.

References

- Cirelli, Chiara and Giulio Tononi. *Is sleep essential?* PLoS Biology, August 2008.
Coren, Stanley. *Sleep Thieves, an eye-opening exploration into the science and mysteries of sleep.* New York (US): Free Press Paperbacks, 1997, pp ix-x, 139 and 210.

Dubuc, Bruno. *The brain from top to bottom*. <http://thebrain.mcgill.ca>

Gazzaniga, Michael S. and Richard B. Ivry and George R. Mangun. *Cognitive neuroscience, the biology of the mind* 3rd ed. New York (US): W.W. Norton & Company, 2009, p 331-332.

Howard, Pierce J. *The owner's manual for the brain, everyday applications from mind-brain research*. Atlanta (US): Bard Press, 2001, pp 48, 139, 147 and 344.

Ji, Daoyun and Matthew A. Wilson. *Coordinated memory replay in the visual cortex and hippocampus during sleep*. Nature Neuroscience, January 2007.

Kandel, Eric R. and James H. Schwartz and Thomas M. Jessell. *Principles of Neural Science* 4th ed. New York (US): McGraw-Hill, 2000, pp 936-947.

Mignot, Emmanuel. *Why we sleep: the temporal organization of recovery*. PLoS Biology, April 2008.

Opp, Mark R. *Sleeping to fuel the immune system: mammalian sleep and resistance to parasites*. BMC Evolutionary Biology, 2009.

Tononi, Giulio and Chiara Cirelli. *Sleep function and synaptic homeostasis*. Sleep Medicine Reviews, 2006.

Weil, Andrew. www.drweil.com

Wikipedia, www.wikipedia.com

Zhang, Jie. *Memory process and the function of sleep*. Journal of Theoretics, December 2004.

Zillmer, Eric A. and Mary V. Spiers and William C. Culbertson. *Principles of Neuropsychology*. Belmont (US): Thomson Wadsworth, 2008, pp 454 and 458-459.

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