SCIENTIFIC AMERICAN™

The Brain May Disassemble Itself in Sleep

By Jason Castro | May 24, 2012

Slumber may loosen the links that undergird knowledge, restoring the brain daily to a vibrant, flexible state

In Brief

1. Most scientists agree that sleep has significant benefits for learning and memory.
2. Conventional wisdom holds that recently formed memories are replayed during sleep and in the process become more sharply etched in the brain.
3. Emerging evidence suggests that sleep also serves as a reset button, loosening neural connections throughout the brain to put this organ back in a state in which learning can take place.

Compared with the hustle and bustle of waking life, sleep looks dull and unworkmanlike. Except for in its dreams, a sleeping brain doesn't misbehave or find a job. It also doesn't love, scheme, aspire or really do much we would be proud to take credit for. Yet during those quiet hours when our mind is on hold, our brain does the essential labor at the heart of all creative acts. It *edits itself. And it may throw out a lot.*

In a provocative new theory about the purpose of sleep, neuroscientist Giulio Tononi of the University of Wisconsin–Madison has proposed that slumber, to cement what we have learned, must also spur the brain's undoing. As the conscious mind settles into sleep, the neural connections that create a scaffold for our knowledge must partially unravel, his theory suggests. Although this nightly dismantling might seem like a curious act of cerebral self-sabotage, it may in fact be a mechanism for enhancing the brain's capacity to encode and store new information.

The benefits of sleep for learning and memory are widely accepted in the scientific community. The prevailing view holds that recently formed memories are replayed during sleep and in the process become more sharply etched in the brain [see "Quiet! Sleeping Brain at Work," by Robert Stickgold and Jeffrey M. Ellenbogen; *Scientific American Mind*, August/September 2008]. As Tononi surmised, however, the neural circuits buttressing those memories can be fortified only so many times before reaching their maximum strength. He and his colleagues have gathered evidence that sleep also serves as a reset button, uniformly ***loosening neural connections throughout the brain to put this organ back in a flexible state in which learning can take place.***

The theory is still controversial. Some sleep researchers consider the evidence for it too preliminary, favoring the conventional wisdom of sleep as a time of memory consolidation and reinforcement. Still, **if Tononi is right**, sleep may not be just for curating memories of the recent past. It may also set aside space for memories of experiences we have not yet had.

Saturated Pixels?

Learning occurs when an experience—listening to new music, say, or navigating an unfamiliar city—imposes a pattern of activity on groups of neurons. The pattern alters the cells' interconnections: ties among co-active neurons grow stronger, and those among out-of-step neurons weaken. In this way, the cells become functionally lassoed together. This coalition becomes dedicated to preserving a specific fragment of experience—a memory. During later offline periods—sleep in particular—the pattern stamped in by experience gets replayed, leading to cellular changes that stabilize the pattern.

A decade or so ago most psychologists conceived of sleep as this recap of daytime learning. **Yet Tononi sensed a potential problem**: if the junctions among neurons—synapses—were being ratcheted tighter and stronger over consecutive nights and days, they would eventually plateau. As with the saturated pixels of a too-bright image, a set of maxed-out, uniform synapses would provide little information. Equally problematic, such a brain would have no way of storing new experiences.

Tononi also noted some interesting properties of the brain waves he and many other researchers had recorded in sleeping people. Scientists had long known that "slow-wave" sleep—that stage of rest when people are hardest to rouse—was necessary and restorative. Even so, he took note of **two more specific phenomena**. First, he recognized that when people are deprived of slow-wave sleep, they tend to make up for it with longer and more intense bouts of this type of sleep later on.

In addition, Tononi noticed that the intensity of this deep slumber—measured as amplitude in recordings of brain waves—dies down as the night progresses. Both observations **struck him as examples of homeostasis**, the *push and pull of opposing forces to maintain equilibrium in a biological system.* **Slow-wave sleep seemed to be pulling the brain back to some kind of equilibrium that being awake had disturbed.**

Tononi considered which biological process might underlie the changes in slow-wave sleep. He knew that its intensity is correlated with overall synapse strength. When neurons fire in unison, they drive groups of these neural junctions to activate in synchrony. Electric current flowing through them creates the slow-wave signal that is recorded with electrode pads on the scalp. Tononi surmised that being awake may lead to a proliferation or strengthening of synapses and that the initial high intensity of slow-wave sleep reflects these very strong cell networks. If synapses somehow weaken or break down during this period of sleep, their loss could explain why the sleep signals shrank during the night.

To support his conjecture, which he dubbed "synaptic homeostasis," Tononi wanted to look directly at how synapses differed between sleep and wakefulness. In a study published in 2008 he and his collaborators harvested brain tissue from rats, some of which had been sleeping and others that had been awake. For each tissue sample, the researchers used radioactive antibodies to selectively tag several proteins that exist only at synapses. They found that many of these proteins were significantly scarcer in snoozing rats than in awake ones. Their conclusion: fewer synapses exist in the sleeping brain, or else these synapses have, on average, less of the machinery they need for effective communication—that is, they are weaker.

Further support for this view came from a study published in 2010 by Xiao-Bing Gao of Yale University and his colleagues. In collaboration with Tononi, Gao's team recorded electrical activity from individual neurons in slices of brain tissue that they took from both dozing and alert rodents. Neurons constantly chatter with one another by way of small electric currents that shuttle through their synapses. The more current flowing through a synapse, the stronger the synapse. Neurons from previously awake rodents received more vigorous barrages of current than did those from sleeping animals, indicating that neurons in the sleeping brain are connected by fewer or weaker synapses. The results hint that the brain flips between strongly and weakly connected states on a day-night cycle.

Sleepless Flies

If sleep remodels synapses, researchers should be able to see structural signs of these changes. The synapses through which neurons communicate can vary in number and size. In general, the more synapses and the bigger those synapses are, the more electrical "information" can travel between two connected neurons.

Scientists can visualize synapses by sticking fluorescent tags onto the proteins that work at either side of the synaptic gap. In 2011 Tononi, together with Wisconsin neuroscientists Daniel Bushey and Chiara Cirelli, reported using these techniques to track the size and number of synapses in fruit flies. They forced some of the flies to stay awake by putting them in a revolving box—at the top of the rotation, snoozing flies would fall and wake up—to see if staving off sleep would prevent the shrinking and retraction of synapses. In striking agreement with Tononi's hypothesis, they saw a significantly higher density of synapses and considerably larger synapses—in some cases, twice as large—in brains of flies that had been forced to stay awake compared with brains of sleeping flies.

In an even more recent study from 2011 Tononi and his team have extended these results to mice. By labeling neurons in the cortex, or outer rind, of the mouse brain with fluorescent indicators, the researchers could watch the growth and retraction of spines—the tiny, knoblike protrusions on neurons where synapses are made. They *saw that the overall density of synapses increased with wakefulness, remained high when the mice were sleep-deprived and decreased only after sleep was allowed.*

Bedtime Tonic

Before synaptic homeostasis can be hailed as the main reason we sleep, however, investigators *must provide better proof that some measurable aspect of neural function—learning, memory or perception,* for example—*is improved by the shrinking and dismantling of synapses* and impaired when these activities are somehow curtailed. Such evidence will be difficult to dig up. If and when it surfaces, Tononi's ideas could add considerable nuance to the established notion that sleep serves to cement memories by strengthening synapses forged during the day.

Intuitively, we know that sleep is restorative, and many colorful metaphors have tried to capture this idea. Sleep is a tonic. Sleep is a balm. As Shakespeare put it, sleep "knits up the ravell'd sleave of care." He couldn't possibly have known that sleep may renew us by undoing in the brain some of what the day knits, so that we can live to learn another day.

This article was published in print "Sleep's Secret Repairs."

ABOUT THE AUTHOR(S)

JASON CASTRO is a postdoctoral fellow in the Center for Neuroscience at the University of Pittsburgh. He studies synaptic processing and plasticity in the auditory system.