

Origins of brain wave patterns seen in sleep suggest answer to old question: Why do we sleep?

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To learn more about the biology of sleep, a team of neuroscientists has turned to one of nature's foremost authorities on the subject: the cat.

By studying sleeping cats, researchers from Quebec, Canada and San Diego sought to determine the origins of certain oscillating brain wave patterns recognized as the transition from being awake to falling asleep, the so-called "sleep spindles."

Understanding how sleep spindles form, the researchers believe, could uncover an important clue into a long-held mystery: why do we sleep?

"It's really phenomenal that we know so much about the brain, but we can't answer this simple question that a layman asks," said Terrence Sejnowski, professor of biology and physics at UCSD and director of the UCSD Institute for Neural Computation, who also heads the System Neurobiology Laboratory at The Salk Institute and is an investigator of the Howard Hughes Medical Institute at The Salk.

The collaborative study was conducted at the Laval University School of Medicine, with the analytical component performed in San Diego. The results in today's edition of the journal *Science*, suggest that these brain wave patterns are generated in part by a communications cable whose function was previously unknown. This cable links cortex to the thalamus.

What are these two brain areas talking about?

According to Sejnowski, they're probably sharing information about the day's events, and how best to organize or file that information.

"What we think is happening during sleep is that the cortex goes off line and reorganizes all the information that came in during the day," said Sejnowski. "To do that, it has to compare notes--different parts of the cortex have to link together to figure out where these pieces of information should be stored. This is all speculative, but all the evidence we have points in that direction."

Despite popular impressions, the brain during sleep is a busy place with a life of its own, independent of the sensory world. At the hub of this activity is the thalamus, located at the top of the brain stem. While awake,

the thalamus functions as a type of gateway to the cortex through which all visual, auditory and other sensory information must pass. When the sensory world shuts down during sleep, the thalamus remains quite active, however. Relying on the electroencephalogram (EEG) which records electrical activity in the brain, researchers have found that the thalamus generates sleep spindles. These brain waves fire in cyclical bursts every three to 10 seconds, lasting from one to three seconds each.

In a series of experiments with sleeping cats, described in *Science*, Sejnowski and the Laval University researchers--Diego Contreras, Alain Destexhe and Mircea Steriade--concluded that the spindle pattern generated by the thalamus, and synchronized in the cortex, is determined by long neuronal projections called axons leading to-and-from these areas of the brain.

During the experiment, conducted in the Laval University laboratory, eight electrodes were connected to eight different sites on the surface of the cortex of anesthetized cats. EEG recordings showed that large parts of the cortex appeared to be tuned into, or synchronized to, the same spindling pattern of waves generated in the thalamus.

The researchers then sought to determine if the synchrony in the cortex resulted from communications within the cortex itself, or if it came from deep within the brain, in the thalamus.

To find out, they surgically sliced a small area of the cortex, leaving four electrodes on one side of the cut, and four electrodes on the other side. If there were any lines of communication between these areas of the cortex, they would have been severed. However, if the lines of communications were directed to-and-from the thalamus, they would be intact.

According to the *Science* paper, the electrodes right next to the cut were silenced, resulting from the damage to the surrounding cortex. But only a short distance away from these damaged sites, the researchers saw synchronous activity across the slice. Since the only remaining connection between these sites in the cortex were long axonal projections to the thalamus, the researchers concluded this communication link was responsible for the synchrony.

It's possible, Sejnowski says, that groups of similar cables form a neurochemical communications' network over which large parts of the cortex and thalamus exchange information with each other during sleep. Instead of acting like a relay station, as it does in the waking state, the thalamus now acts more like a feedback loop or mirror, reflecting information back-and-forth to different parts of the cortex.

"Our hypothesis is there's a feedback connection that goes from one part of the cortex, down to the thalamus, and then returns back to the cortex," said Sejnowski, who performed the analysis part of the experiment. "In this manner, these two areas get synchronized.

"This mechanism could allow one part of the cortex to talk to another part."

To study spindles in greater detail, an international team of scientists led by Sejnowski--supported by a grant from the Human Frontiers Science Program, based in Japan--is using this and other experimental data to create a computer model that simulates this firing pattern. The model already is offering insights into what turns the spindle pattern on and off, and what causes the synchronization between cortex and thalamus.

With the help of the computer model, the researchers also have mimicked events in the thalamus responsible for a form of epilepsy called petit mal seizures, characterized by brief periods of unconsciousness. Such events are represented by a brain pattern generally seen during deep sleep, in which the thalamus is cut off completely from the outside world. Except with petit mal, the events come suddenly and without warning.

Sejnowski said he plans to extend his computer models to learn more about normal sleep, why some have trouble sleeping, and even why we dream.

"The model is a framework or structure to help you think," said Sejnowski, "and the computer is an engine that allows you to take the pieces and say, okay, here's where we're starting from-- these are the essential components, and here's how they are connected--and discover the hidden implications of these facts."

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