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Coma and General Anesthesia Demonstrate Important Similarities

The brain under general anesthesia isn't "asleep" as surgery patients are often told -- it is placed into a state that is a reversible coma, according to three neuroscientists who have published an extensive review of general anesthesia, sleep and coma, in the Dec. 30 issue of the New England Journal of Medicine. This insight and others reported in their review article could eventually lead to new approaches to general anesthesia and improved diagnosis and treatment for sleep abnormalities and emergence from coma.

The researchers explain that a fully anesthetized brain is much closer to the deeply unconscious low-brain activity seen in coma patients, than to a person asleep. Essentially, general anesthesia is a coma that is drug-induced, and, as a consequence, reversible. The states operate on different time scales -- general anesthesia in minutes to hours, and recovery from coma in hours to months to years, if ever. The study of emergence from general anesthesia and recovery from coma could help to better understand, how both processes occur?

Understanding that these states have more in common with each other than differences -- that they represent a continuum of activity with common circuit mechanisms being engaged across the different processes of awakening from sleep or emerging from coma or general anesthesia -- "is very exciting, because it gives us new ways to understand each of these states," says study co-author, Dr. Nicholas D. Schiff, a Professor of Neurology and Neuroscience at Weill Cornell Medical College and a neurologist at NewYork-Presbyterian Hospital/Weill Cornell Medical Center. Co-authors of the study are Dr. Emery Brown of Massachusetts General Hospital, Massachusetts Institute of Technology and Harvard Medical School, and Dr. Ralph Lydic from the University of Michigan.

Knowing more about the brain circuit mechanisms may also help researchers develop therapeutic agents to "tweak the circuits as needed, to help us in the areas where we don't do well, such as abnormalities of sleep and, especially, emergence from a coma," Dr. Schiff says. "And while use of general anesthesia is an incredibly safe technique, it can have effects on the elderly, such as slower recovery time and impaired cognitive function afterwards."

In their review, which took three years to develop, the researchers synthesized the newest studies in these three areas, including work of their own. Among their other specialties, Dr. Brown's expertise is general anesthesia, Dr. Lydic's is sleep, and Dr. Schiff's is recovery from coma.

"We think this is, conceptually, a very fresh look at phenomena we and others have noticed and studied in sleep, coma and use of general anesthesia," Dr. Schiff says. "By reframing these phenomena in the context of common circuit mechanisms, we can make each of these states understandable and predictable."

"These findings show that general anesthesia is a reversible coma, and learning about the different ways we can safely place the brain into this state, with fewer side effects and risks, could be an important advance in general anesthesiology," explains Dr. Brown. "Also, in a scientific sense, monitoring brain function under general anesthesia gives us new insights into how the brain works in order to develop new sleep aids and new ways for patients to recover from coma."

Describing the Switching Circuit

One critically important circuit the authors describe involves specific brain areas. One major player is the cortex, which is made up of layers of neural tissue at the outer edge of the brain, and another is the thalamus, a ball of neural tissue at the center of the brain. These areas are connected to each other through nerve cell axons, which act like information highways, passing signals. The cortex and the thalamus "talk" to each other in different ways over a 24-hour cycle.

Also part of the circuit is the basal ganglia, within the front of the brain, which is used to control certain actions. It does this in part by setting up two feedback loops. One is a negative feedback release on behavior, and that part of the circuit is always active when overall brain activity is reduced, Dr. Schiff says. For example, it works to stop a sleeping person from physically acting out their dreams.

The second feedback loop, however, releases the brake imposed by the first feedback loop, the researchers say. Certain drugs, such as the sleep aid zolpidem (Ambien), and propofol, a powerful general anesthetic with similar pharmacologic properties, can trigger that loop to function, producing what is known as "paradoxical excitation."

This phenomenon described in transitions observed in the early stages of general anesthesia appears to be common across all three states, because the drugs are triggering this same feedback loop, the authors explain. Most people given propofol become agitated and confused shortly after falling unconscious. Some people who use Ambien walk, eat and carry out other complex behaviors in an altered state of consciousness arising from sleep. Surprisingly, Ambien has also been reported to restore communication and behavioral responsiveness in some severely brain injured patients. The linkage of these disparate observations within a common circuit model is one of the key insights in the authors' integrative review.

Eventually the brake is switched back on in these three states -- giving way to sedation and deeper sleep, or in the case of the severely brain patient, the return to a state of diminished responsiveness.

There is another phenomenon that results from this circuit, the authors say. "Emergence delirium is the flip side," says Dr. Brown. "For example, when bringing a person out of general anesthesia, the brain is woken up enough to be active, but it is not coherent or organized, which can explain the slower recovery time we see in some patients."

It is these two areas -- losing consciousness and returning to consciousness -- that the researchers believe they might be able to target to provide better therapies for sleep, emergence from coma, and general anesthesia with fewer side effects. And it is by studying general anesthesia -- a process that can be well controlled as well as monitored and studied -- that researchers will likely make progress in understanding all three states of mind, Dr. Schiff says. For example, because coma patients each have individualized damage to their brains due to injury or stroke or hemorrhages, studying recovery from general anesthesia may offer potential opportunities for developing general strategies for intervention, Dr. Schiff says.

"The quantitative neurobehavioral metrics used to monitor recovery from coma could be used to track the emergence from general anesthesia from a functional state that can approximate brain-stem death to states similar to a vegetative state and eventually to a minimally conscious state," the authors write.

"Moreover, understanding this circuit will help us understand the relationship of brain function to consciousness in general -- what it is, how it is produced, and what the variety of brain states truly are," Dr. Schiff says. "Consciousness is a very dynamic process, and now we have a good way of studying it."

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