Safely Switching Consciousness Off and On Again

What can we learn about consciousness from anesthetized patients?

BY CHRISTOF KOCH

Two studies of anesthetized patients' brain activity offer intriguing —if somewhat conflicting—clues about the seat of consciousness.

WE TAKE IT for granted that any kind of surgical procedure, whether extracting a wisdom tooth or replacing a heart valve, will be painless and won't leave any bad memories. Every year tens of millions of patients worldwide remember being prepared for an operation—then nothing, until they wake up in the recovery room. This is the magic of general anesthesia, which safely knocks out that most precious of life's possessions, conscious experience, then reliably restores it without any lasting consequences. Of course, it was not always thus. Until the discovery of nitrous oxide as an anesthetic in the mid-19th century, surgery was an extreme and dangerous intervention of last resort whose effects could, at best, be blunted by opium or alcohol.

Today anesthesiologists can choose from an astonishing variety of chemicals to separately and independently eliminate pain (analgesia), memory (amnesia), mobility and responsiveness to the cutting, scraping, drilling or cauterizing of the surgical procedure, and, most important from the point of view of the patient, awareness (loss of consciousness). Two types of anesthetics exist: intravenous agents that are injected into the bloodstream for the rapid induction and maintenance of anesthesia, such as barbiturates, propofol and ketamine, and inhalation agents, such as laughing gas (nitrous oxide) or vapors of volatile liquids, including isoflurane and sevoflurane.

Much is known about the molecular action of these substances. With the singular exception of the dissociative ketamine (abused at low doses as a street drug known as vitamin K or special K and not further discussed here), anesthetics strengthen neuronal inhibition either by activating inhibitory chemical synapses, which constrain activity in the neurons they are connected to, or by binding to membrane proteins that keep the electrical activity of neurons—and therefore their ability to transmit information and command—in check. Their net effect is to reduce overall brain activity. Every functional brain- imaging study carried out to date proves this point. For anesthesiologists, the technique of choice is positron emission tomography (PET), in which a small amount of radioactive tracer is injected into the bloodstream of the subject. Brain regions that are more or less active than neighboring areas consume metabolic resources in the same ratio. This metabolic activity can be reliably measured in a PET device, albeit with a crude temporal (on the order of tens of seconds) and spatial (on the order of the size of a pea) resolution.

PET imaging demonstrates that essentially all anesthetics decrease global cerebral metabolism in a dose-dependent manner. The more of the anesthetic dispensed, the bigger the activity reduction in regions of the brain stem responsible for promoting wakefulness and in the neocortex and the closely allied thalamus underneath it. The neocortex is the most recently evolved part of the cerebral cortex, the folded layers of neurons that constitute the proverbial gray matter. It occupies most of the forebrain and is a unique hallmark of mammals. The thalamus is a quail egg–size structure in the middle of the brain that regulates all input into the neocortex and receives massive feedback from it.

Cortex Off, Consciousness Off

This dramatic reduction in brain activity after loss of consciousness is scarcely surprising. The link between consciousness and this organ is tight, as expressed in the adage "No brain: never mind!" Yet neuroscientists are trying to track the footprints of consciousness to its actual lair. Which region in the cortex, the thalamus or elsewhere is essential to be conscious at all? Consider the following two experiments.

CREDIT TK TK TK

Neuroscientists are **trying to track** the footprints of consciousness to its actual lair.

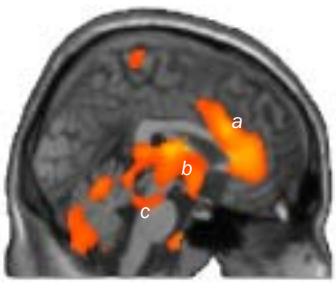
Twenty-five patients with Parkinson's disease were anesthetized with propofol or sevoflurane while the electrical activity of both cortex and thalamus were monitored by a group under François Gouin of the Timone University Hospital Center at the University of the Mediterranean in Marseille, France. Their neocortex was monitored by a conventional electroencephalograph (EEG) electrode placed on the scalp on top of the head, whereas thalamic activity was recorded by an electrode implanted deep inside the brain in the subthalamic nucleus. This electrode stimulates the brain to alleviate the shaking that is the hallmark of Parkinson's. Experimenters assessed consciousness by tapping patients on the shoulder and asking them every 20 seconds to open their eyes.

When consciousness was lost after anesthesia was initiated—that is, when the patients no longer opened their eyes following the command—the cortical EEG changed dramatically, switching from low amplitude and irregular activity into readings dominated by large and slow brain waves that occur about once every second. Such so-called delta band activity is characteristic of deep sleep. Furthermore, the complexity of the cortical EEG signal decreased significantly when patients stopped responding. None of these changes occurs in the thalamic electrode at the time that consciousness is lost.

Indeed, it is only several minutes later that the thalamic voltage signal matches that of the cortex. The data—consistent for two quite different anesthetic agents, one injected and the other one inhaled—argue that the drivers for the loss of consciousness are parts (or all) of the neocortex and that the thalamus follows.

Returning from Oblivion

In a second experiment, by a group primarily based at the University of Turku in Finland, involving Harry Scheinin, Jaakko W. Långsjö and Michael T. Alkire, 20 volunteers were put to sleep with two different substances, dexmedetomidine and propofol (again, to make sure that the outcome does not depend on any one specific agent). After being injected with the radioactive tracer, the subjects lay down inside a PET scanner. The anesthesiologists measured the regional cerebral blood flow when the patients regained consciousness—that is, when the subjects could open their eyes again in response to a persistent command (albeit given only once every five minutes).



Colored areas indicate the parts of the brain that first come online when patients emerge from consciousness after being anesthetized with one of two different agents. The three critical regions are the anterior cingulate cortex (*a*), the thalamus (*b*) and parts of the brain stem (*c*).

Subsequent statistical analysis fingered phylogenetically older regions in the brain stem (in particular, the locus coeruleus and parabrachial area that contains the noradrenergic neurons that project widely throughout the corticothalamic complex and exert broad effects on the brain). They mediate the arousal needed for behavioral responses—such as blinking the eyes—to occur. As consciousness returns, the thalamus is exuberantly active, whereas the cortex shows a much more circumscribed response, primarily in those frontal regions responsible for monitoring of the self.

The conjoined activation of both cortex and thalamus appears at odds with the previous study, which implicated the cortex as the driver and the thalamus as follower. Yet the two techniques (EEG versus PET imaging) measure distinct signals (voltage versus blood flow, which is 1,000 times more sluggish), compounded by the fact that the first study checked whether or not the patients were conscious every 20 seconds, whereas the second one inquired only every five minutes. Furthermore, although consciousness waxes and wanes during anesthesia, many other processes—the overall level of brain arousal, the ability to move and to remember, the experience of pain and other sensations, and so on, each with their own neuronal signature—also vary and confound the search for the sources of consciousness. Finally, just as the sequence of operations on booting up a computer are not the same as those that occur when the machine is shut down, the brain events accompanying the return of consciousness are unlikely to be identical to those that cause consciousness to cease.

These two exemplary studies point to the difficulties, but also to the progress, of the quest to unravel the mind-body riddle. M

CHRISTOF KOCH is chief scientific officer at the Allen institute for Brain Science in Seattle and Lois and Victor Troendle Professor of Cognitive and Behavioral Biology at the California Institute of Technology. He serves on *Scientific American Mind*'s board of advisers.

(Further Reading)

- **Differential Dynamic of Action on Cortical and Subcortical Structures of Anesthetic Agents during Induction of Anesthesia.** Lionel J. Velly et al. in *Anesthesiology,* Vol. 107, No. 2, pages 202–212; August 2007.
- **Returning from Oblivion: Imaging the Neural Core of Consciousness.** Jaakko W. Långsjö et al. in *Journal of Neuroscience,* Vol. 32, No. 14, pages 4935–4943; April 4, 2012.

SOURCE: "RETURNING FROM OBLIVION: IMAGING THE NEURAL CORE OF CONSCIOUSNESS," BY JAAKKO W. LÅNGSJÖ ET AL., IN JOURNAL OF NEUROSCIENCE, VOL. 32, NO. 14; APRIL 4, 2012