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Two different neural pathways regulate loss and regain of consciousness during general anesthesia

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University of Pennsylvania School of Medicine researchers have answered long-running questions about the way that anesthetics act on the body, by showing that the cellular pathway for emerging from anesthesia is different from the one that drugs take to put patients to sleep during operations. The findings will be published this week in *Proceedings of the National Academy of Sciences*.

The research focuses on orexins, the small, specialized fraction of the brain's 100 billion neurons that play a key role in regulating the body's wakeful state. Studying mice whose orexin systems had been genetically destroyed – a state similar to humans suffering from narcolepsy, a neurological condition that causes unusual daytime sleepiness – Max B. Kelz, MD, PhD, an assistant professor in Penn's Department of Anesthesiology and Critical Care and the Mahoney Institute of Neurological Sciences, found that these mice took much longer to emerge from general anesthesia than those with normal orexin signaling systems. However, the mice with faulty orexin systems did not appear to fall asleep faster during anesthesia, which suggests that different processes are at play when transitioning to and from the anesthetized stated.

"The modern expectation is that anesthesiologists can simply flip a consciousness switch as easily as we might turn the room lights on or off," says lead author Max B. Kelz, MD, PhD, an assistant professor in

Penn's Department of Anesthesiology and Critical Care and the Mahoney Institute of Neurological Sciences. "However, what patients do not realize is that despite 160 years of widespread clinical use, the mechanisms through which the state of anesthesia arises and dissipates remain unknown."

Kelz became interested in these questions after treating a narcoleptic patient who took more than six hours to regain consciousness after anesthesia, compared to the typical six minutes or so. By probing what's different about the narcoleptic brain, the Penn study has established for the first time that the process of entry into and exit from the anesthetized state are not mirror images of one another.

Source: University of Pennsylvania