

Researchers uncover altered brain connectivity after prolonged anesthesia

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A body of evidence supports the association between prolonged anesthesia and cognitive impairment, but the Columbia study is first to address the effect of the procedure on neural connections. Credit: Michael Wenzel

Prolonged anesthesia, also known as medically induced coma, is a life-saving procedure carried out across the globe on millions of patients in intensive medical care units every year.

But following prolonged anesthesia—which takes the [brain](#) to a state of deep unconsciousness beyond short-term anesthesia for surgical procedures—it is common for family members to report that after hospital discharge their loved ones were not quite the same.

"It is long known that ICU survivors suffer lasting cognitive impairment, such as confusion and memory loss, that can languish for months and, in some cases, years," said Michael Wenzel, MD, lead author of a study published in *PNAS* this month that documents changes associated with prolonged anesthesia in the brains of mice.

Wenzel, a former postdoctoral researcher at Columbia University with experience as a physician in neuro-intensive care in Germany, said

reports of post-hospital cognitive dysfunction will likely become even more prevalent because of the significant number of coronavirus patients dependent on ventilators who have taken days or weeks to awake from medically induced comas.

Until now, despite the body of evidence that supports the association between prolonged anesthesia and cognition, the direct effects on [neural connections](#) have not been studied, said Rafael Yuste, a professor of Biological Sciences at Columbia and senior author of the paper.

"This is because it is difficult to examine the brains of patients at a resolution high enough to monitor connections between individual neurons," Yuste said.

To circumvent the problem, Yuste and Wenzel developed an experimental platform in mice to investigate the connections between neurons, or synapses, and related cognitive effects of prolonged anesthesia.

Inspired by Wenzel's experience in neuro-intensive care, the researchers established a miniature ICU-like platform for mice. They performed continuous anesthesia for up to 40 hours, many times longer than the longest animal study to date (only six hours).

The researchers performed in vivo two-photon microscopy, a type of neuro-imaging that Yuste helped pioneer and that can visualize live brain structures at micrometer resolution. The technique enabled them to monitor cortical synapses in the sensory cortex, the area of the brain responsible for processing bodily sensations, an approach they combined with repeated assessment of behavior in the cortex.

Contrary to the notion that the connections between neurons in the adult brain remain stable during short-term anesthesia, the researchers found that

prolonged anesthesia significantly alters the synaptic architecture of the brain regardless of age.

"Our results should ring an alarm bell in the medical community, as they document a physical link between [cognitive impairment](#) and prolonged medically induced coma," Wenzel said.

As this study is only a pilot in mice, further study is needed, the researchers said. They added that it will be important to test different, widely used anesthetics, as well as the combination of anesthetics administered to patients. Currently, anesthetics are not individually tailored to patients in a systematic fashion.

"We are well aware that anesthesia is a life-saving procedure," Wenzel said. "Refining treatment plans for patients and developing supportive therapies that keep the brain in shape during prolonged [anesthesia](#) would substantially improve clinical outcomes for those whose lives are saved, but whose quality of life has been compromised."

More information: Michael Wenzel et al, Prolonged anesthesia alters brain synaptic architecture, *Proceedings of the National Academy of Sciences* (2021). DOI: [10.1073/pnas.2023676118](https://doi.org/10.1073/pnas.2023676118)

Provided by Columbia University

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