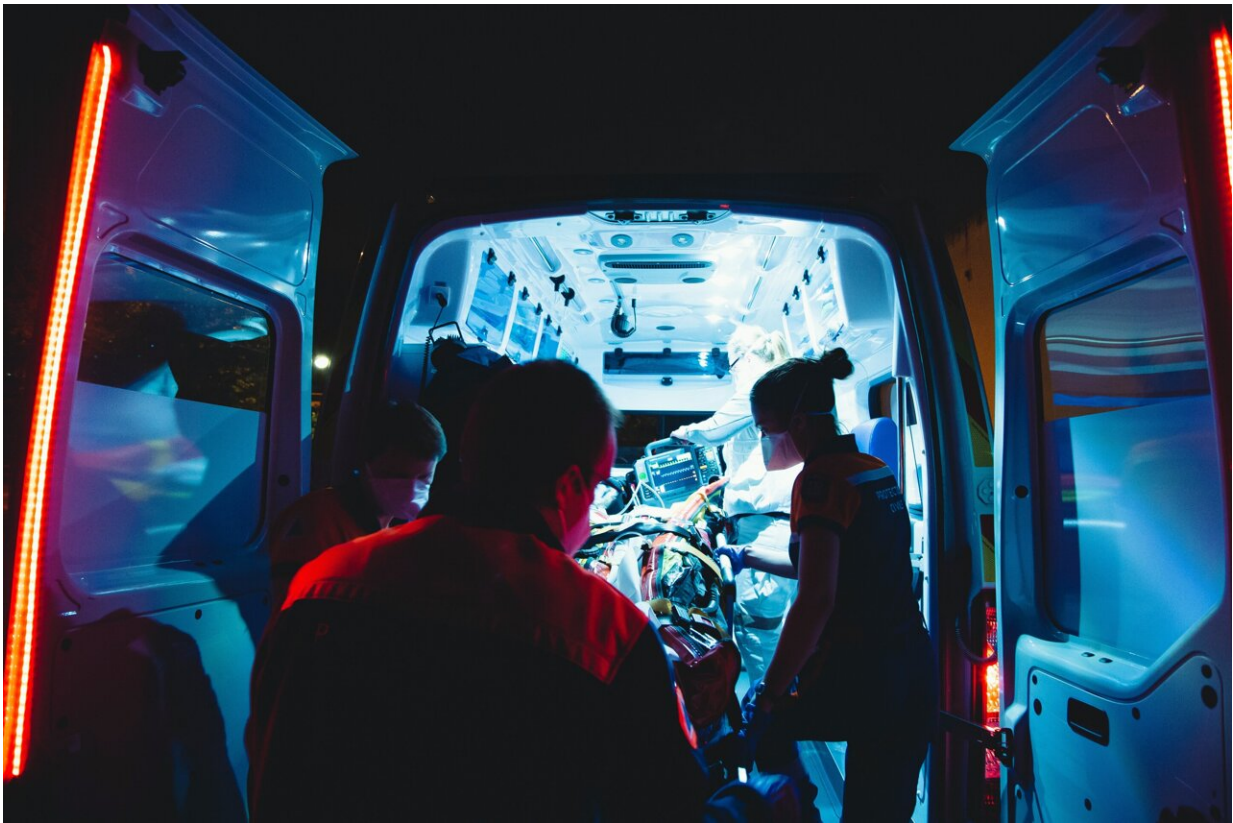


New theory explains recovery delays in COVID-19 and cardiac patients

November 7 2022



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COVID-19 patients placed on ventilators can take a long time to regain consciousness. New research from Weill Cornell Medicine, New York-Presbyterian, MIT, and Massachusetts General Hospital is now

illustrating that these delays may serve a purpose: protecting the brain from oxygen deprivation.

The existence of such a brain-preserving state could explain why some patients wake up days or even weeks after they stop receiving ventilation, and it suggests that physicians should take these lengthy recovery times into account when determining a patient's prognosis.

In a study published Nov. 7 in the *Proceedings of the National Academy of Sciences*, the investigators connect the pattern seen among those who have survived severe COVID-19 with similar delays known to occur in a small fraction of cardiac arrest patients.

"The delayed recoveries in COVID-19 patients are very much like the rare cases we've documented in previous research. In this new paper, we describe a mechanism to explain what we're seeing in both types of patients," said study co-senior author Dr. Nicholas D. Schiff, the Jerold B. Katz Professor of Neurology and Neuroscience in the Feil Family Brain and Mind Research Institute and co-director of the Consortium for the Advanced Study of Brain Injury (CASBI) at Weill Cornell Medicine.

He found evidence for this explanation—that patients' brains are protecting themselves—in animals, most notably painted turtles, that can tolerate extended periods without oxygen.

More than a decade ago, Dr. Schiff and his colleagues first observed these delays among [comatose cardiac arrest patients](#) who received cooling therapy to reduce [brain damage](#) caused by a loss of blood flow. In one such case, a 71-year-old patient took 37 days to awaken, before ultimately making a near-complete recovery.

During the pandemic, Dr. Schiff, who is also a neurologist at NewYork-Presbyterian/Weill Cornell Medical Center, performed neurology

consultations for COVID-19 patients, and he soon began [seeing similar, delayed awakenings](#) occurring when patients were taken off ventilators and stopped receiving the sedatives given to them to reduce their movement.

In a separate analysis of a large cohort of COVID-19 patients from Weill Cornell Medicine and two other major U.S. medical centers, Dr. Schiff and his colleagues, including co-author of the current paper, Dr. Emery N. Brown, professor of anesthesia at Harvard Medical School, Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience in The Picower Institute for Learning and Memory at MIT and an anesthesiologist at Massachusetts General Hospital, found that a quarter of patients who survived ventilation took 10 days or longer to recover consciousness. The more oxygen deprivation they suffered while on the ventilator, the longer that delay.

In the prior study of cardiac patients, the researchers recorded a distinctive pattern in [brain activity](#), one also seen in patients under deep anesthesia. (Recordings from COVID-19 patients are extremely limited.) Dr. Schiff read that a similar pattern had been seen in the brains of painted turtles, which can withstand up to five months without oxygen under ice in the winter. To do so, they activate the same inhibitory system within the brain targeted by anesthetics given to human cardiac and COVID-19 patients but in novel ways developed by evolutionary specializations.

Dr. Schiff and Dr. Brown propose that, by chance, the same protective response emerges in the patients.

"It is our theory that [oxygen deprivation](#) as well as practices in the ICU, including commonly used anesthetics, trigger in humans expose elements of strategies that animals use to survive in [extreme conditions](#)," Dr. Schiff said.

"These observations may offer new insights into the mechanisms of how certain anesthetics produce unconsciousness and new approaches for ICU sedation and for fostering recovery from disorders of consciousness," Dr. Brown added.

When patients fail to regain consciousness for an extended time, physicians may recommend withdrawing life-supporting care. This threshold is typically set at 14 days or less for cardiac patients, while no such guidelines exist for COVID-19.

In light of this new research, however, so long as they lack [brain](#) injuries, physicians should avoid making negative projections about these patients' potential to recover, note the researchers.

More information: Schiff, Nicholas D., Protective down-regulated states in the human brain: A possible lesson from COVID-19, *Proceedings of the National Academy of Sciences* (2022). [DOI: 10.1073/pnas.2120221119](#). doi.org/10.1073/pnas.2120221119

Provided by Weill Cornell Medical College

Citation: New theory explains recovery delays in COVID-19 and cardiac patients (2022, November 7) retrieved 2 February 2024 from <https://medicalxpress.com/news/2022-11-theory-recovery-covid-cardiac-patients.html>

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