## A Physician's Journey into the Minds of Coma Patients

In studying people with severe brain injuries, Columbia neurologist Jan Claassen hopes to better identify those likely to regain consciousness.

By David J. Craig | Spring/Summer 2024 Isabel Seliger

## Nick LaRock was going to pull through. Physically, at least.

A thirty-three-year-old high-school history teacher, LaRock had been discovered by his girlfriend sprawled out on the floor of his Manhattan apartment late one Sunday evening, moaning incomprehensibly. Rushed by ambulance to Columbia University Irving Medical Center, Columbia's shared medical campus with NewYork-Presbyterian Hospital, he arrived unconscious and unresponsive, fighting for his life. Doctors in the neurocritical-care unit recognized that LaRock had suffered a massive brain hemorrhage and took extraordinary measures to save him, even bringing in surgeons to drill a hole in his skull to relieve pressure that threatened to irreparably damage his brain. Their efforts paid off. A few days later, LaRock was stable but in a coma, his motionless body surrounded by a humming nest of life-support machines that regulated his breathing and other vital functions.

Now, looking back on that time in January 2021, LaRock's parents recall the relief they felt at learning that Nick would survive, but also the troubling questions that soon weighed on them. "I remember asking one of the doctors, 'Are we past the point where he's going to die?' and she said, 'Yes, I think so.' That was obviously a big moment for us," says Joseph LaRock, Nick's father. "Of course, you're next wondering, When is he going to wake up? And what is he going to be like when he does?" says Beth LaRock, Nick's mother. "I mean, is he still going to be our Nick? Is he still going to be my boy, or is he going to be a shell of himself?"

Nick's parents couldn't bring themselves to ask the doctors those questions. Afraid of the answers they might receive, they distracted themselves by searching for clues that their son might be mentally present. Every morning, having driven three hours from their home on Long Island, where Joe works as a restaurant manager and Beth runs a program for adults with developmental disabilities, they would slip quietly into their son's room, kiss him on the forehead, and perch themselves on chairs beside his bed. They would stroke his chilly hands, whisper reassurances, and wait for any glint of recognition — a tilt of the head, the flutter of an eyelid, the squeeze of a finger. When these signs didn't come, they would talk to him nonetheless. "I would give him updates about his younger sister, my job at the restaurant, the New York Jets, the weather — anything I could think of," says Joe. "I'd tell him that we knew he was in there. And that we needed him back."

By any standard neurological assessment, their son's prospects for recovery did not look good. Nick had experienced immense bleeding in his brain and now, nearly a week later, had still not opened his eyes. He appeared to be slipping into a longterm coma — a state that few patients with brain injuries ever awaken from with their personalities and mental faculties intact. "Nick's injury was severe, and time was not on his side," says Jan Claassen, a Columbia neurologist who directs CUIMC's neurocritical-care unit and helped coordinate Nick's treatment.



Jan Claassen (Jörg Meyer)

The longer a patient remains unresponsive, Claassen explains, the less likely they will achieve a good cognitive recovery, if they do awaken. Instead, they might emerge in a semiconscious, cognitively diminished state, requiring round-the-clock care. Many such patients spend the rest of their days hooked up to ventilators and feeding tubes, battling respiratory and urinary-tract infections. "If a person doesn't regain consciousness within a week or two, we get very concerned," Claassen says, noting that brain-injured patients who don't awaken within that time frame are often taken off life support to prevent their prolonged suffering.

Yet Claassen, who is a leading authority on brain injuries, also believes that not all coma patients are as mentally incapacitated as they appear to be. At the time of Nick's injury, he was conducting an unusual clinical trial at CUIMC in which every brain-injured patient who seemed to be in a coma was, with their family's permission, given a series of sophisticated tests designed to reassess their brain function. Joe and Beth LaRock agreed to have Nick evaluated. They were told that the results of the test would not inform Nick's care, since the technique was experimental, but that his participation could eventually help others. So once or twice a day, in the morning and afternoon, members of Claassen's research team gently put earbuds into Nick's ears and played a series of recorded messages that asked him to perform simple physical tasks, like squeezing and relaxing his right hand. A collection of electroencephalogram (EEG) sensors stuck to Nick's scalp then recorded the electrical pops and crackles of his neurons, which were transmitted to a supercomputer located down the hall. There a team of Columbia data scientists and biostatisticians would analyze the millions of resulting data points using an artificialintelligence program, looking for clues that Nick might have heard the commands, understood them, and attempted to respond. Gradually, a pattern emerged. The computer detected what no neurologist could have: *Nick was in there*.

**The word "coma"** is derived from the ancient Greek *koma*, meaning deep sleep, but the condition that it describes — a prolonged state of unconsciousness caused by injury or illness — has only become common in the modern era. Before the mid-twentieth century, most people who experienced severe brain injuries, whether from strokes, oxygen deprivation, or blows to the head, quickly died. That is because the brain, when traumatized, loses its ability to coordinate essential bodily functions. Most critically, it stops transmitting motor signals that control reflexive muscle movements, including those in the diaphragm that draw air into the lungs; without them, a person asphyxiates. Only when mechanical ventilators became widely available in hospitals, in the 1950s and 1960s — a development inspired by the polio epidemic — did it become possible to sustain large numbers of brain-injured patients in comas. "Around then, modern emergency medical services also proliferated," says Claassen, "which meant that people could be stabilized at the scene of injury and transported to hospitals quickly enough to be saved by the new equipment."

Soon the study of brain injuries was among the most rapidly evolving and intellectually vibrant areas in medicine. By carefully observing patients who emerged from comas, physicians discovered previously unknown "disorders of consciousness," including the vegetative state, a condition in which patients may open their eyes but are otherwise unresponsive and unaware; and the minimally conscious state, in which they may show intermittent awareness and attempts at communication. These disorders were initially thought to be chronic, but researchers eventually realized that some patients improved over time, which contributed to a new understanding of the brain's capacity for reorganization, repair, and regeneration. There were other surprises too. In the 1960s, the American neurologists Fred Plum and Jerome Posner noticed that a tiny percentage of patients who appeared to be in a vegetative state were actually fully conscious and intellectually intact. Paralyzed except for their eyes, they could not respond to their examiners and so had been written off as mentally vacant. Plum and Posner called the condition "locked-in syndrome." These patients could be taught to communicate by blinking and glancing from side to side — a method that the French journalist Jean-Dominique Bauby famously used to dictate his 1997 memoir about living with the syndrome, *The Diving Bell and the Butterfly*. Neurologists say that the discovery of locked-in syndrome had a profound impact on their field, impressing upon clinicians the need to be exceptionally vigilant when conducting exams, lest they miss the desperate human peering back into their penlights.

*"I was taught that someone who remained in a coma for more than just a couple of days after a brain injury was basically hopeless. But I saw for myself that wasn't true."* 

Claassen, who grew up outside Cologne, Germany, began his career at the University of Hamburg's teaching hospital, caring for coma patients, in the late 1990s. At that time, he recalls, neurologists who treated people in the earliest stages of brain injury had to be masters of improvisation. Because only a few decades of clinical history had been amassed on the topic, doctors received little guidance from textbooks or senior colleagues on important matters such as how to improve a comatose patient's chances for recovery or when to speak with family members about the possibility of withdrawing life support. Those clinical guideposts that did exist, Claassen says, often underestimated patients' prospects. "As a young doctor, I was taught that someone who remained in a coma for more than just a couple of days after a brain injury was basically hopeless," says Claassen, a tall and slender fifty-five-year-old with piercing blue eyes and a gentle demeanor. "But I saw for myself that wasn't true."

Despite the stressful, fast-paced, and sometimes chaotic nature of his work — the nonstop decisions about continuing or withdrawing life support, in particular, are said to contribute to high rates of burnout among doctors in neurocritical-care units — Claassen thrived, seeing endless opportunities to advance both clinical care and scientific knowledge. "I'll never forget the first time I saw a patient who'd appeared to be lost forever wake up," he says. "One day he was completely unresponsive, and

the next time I saw him he was sitting at a table playing cards. There was something about that transformation that left me awestruck. I knew I had to devote my life to helping these people. And I had to learn everything possible about what their experiences revealed about human consciousness — what it is, why it breaks down, and how it can arise again."

In Hamburg, Claassen dove into clinical research, exploring new ways of diagnosing and assessing the severity of brain injuries. He came to CUIMC in 1999, lured in part by the medical center's embrace of new electrophysiological and neuroimaging technologies that he believed were poised to revolutionize his field. For example, physicians in Columbia's neurocritical-care unit had just begun to use computational analysis of EEG signals to peer inside patients' brains in real time and better diagnose and treat their injuries. They had also started to compile an unusually large database of patient outcomes, which they studied for insights into the effectiveness of their treatments. "I thought this was critically important, because although we'd gotten very, very good at saving the lives of people who'd suffered brain injuries, we still knew little about how to improve their chances of having a good recovery," Claassen says. "To make progress, we had to observe the brain in new ways."

Over the next few years, Claassen achieved a number of breakthroughs using EEG and other brain-monitoring techniques. In one series of influential studies, he and colleagues discovered that some comatose patients experience life-threatening brain seizures that are only detectable with EEG. They showed that administering anti-seizure drugs to these patients may save their lives. In a related line of research, Claassen's team demonstrated that miniaturized EEG sensors implanted in the heads of coma patients can help identify when they need interventions to adjust their blood pressure, oxygen levels, and other vitals. Many of the protocols that the Columbia team developed are now followed by physicians around the world.

In 2014, Claassen was named the head of CUIMC's neurocritical-care unit, an eighteen-bed facility that treats all types of brain injuries, from strokes to blunt traumas to side effects of heart attacks. He quickly set about expanding its research operations, hiring data scientists, investing in supercomputing technology, and encouraging its physicians to innovate whenever possible. "We also cultivated partnerships with faculty in other Columbia units, including the Department of Biomedical Informatics, the Department of Neurological Surgery, and the Data Science Institute," he says. "I thought that if we brought the full weight of the University's intellectual resources to bear on studying brain injuries, we could really

move the needle on the quality of care that's available."

Claassen soon saw an opportunity to make a big impact. Around the time he was appointed chief of the neurocritical-care unit, the field of neurology was abuzz with speculation about several anomalous case studies that had cropped up in the medical literature. The cases all involved patients who appeared to be unconscious but whose brain activity suggested they were alert. One British woman diagnosed as being in a vegetative state was slid into a functional magnetic resonance imaging (fMRI) machine and asked to imagine that she was swinging a tennis racket. She exhibited patterns of neuronal activity that indicated that she was enthusiastically playing along. Similar results were found in others who had suffered different types of brain injuries and since shown no outward signs of awareness. The neurologists behind the accounts had given the phenomenon a name — "covert consciousness" — but knew little about it.

"Some compared it to locked-in syndrome, except that these patients couldn't even move their eyes, so they seemed to be really locked in," says Claassen. "Which is obviously terrifying."

But how conscious were these people, exactly? Were they fully aware of themselves and their surroundings or only faintly so? And how common was the phenomenon?

Many neurologists were skeptical that it would be possible to gain a proper understanding of covert consciousness because of practical constraints. The fMRI scanner, which produces highly detailed brain images and was therefore the first choice of many scientists studying the condition, was only suitable for observing small numbers of patients with severe brain injuries. People hooked up to lifesupport machines and those with metal implants could not easily go into the scanner. Meanwhile, an EEG, although easier to administer, was seen as poorly suited to detecting signs of covert consciousness in bustling hospital settings, where its sensors tended to pick up stray electrical signals from other medical equipment.

"You can deal with that kind of electrical interference pretty easily when using EEG to observe broad patterns of neuronal activity, which is how the tool has traditionally been used, but if you're attempting to observe a person's individual thoughts, as when looking for signs of covert consciousness, it would be more difficult," says Claassen. "Then you'd face a serious analytic challenge." Yet as someone who had been working with EEG his entire career and knew its strengths and limitations, Claassen thought that he could adapt the technology for this purpose. He saw advantages in using the relatively cheap tool, which was widely available in hospitals around the world. "If we developed a test that worked, we wanted patients everywhere to have access to it," says Claassen, noting that he drew inspiration from earlier research by Cornell neurologist Nicholas Schiff, who had shown that EEG could be used to detect covert consciousness in quieter settings. So in the summer of 2014, Claassen and his colleagues launched the first major effort to identify people with the condition in a neurocritical-care unit.

**On a recent Thursday morning,** in a small, sparsely furnished office in CUIMC's neurology department, Qi Shen, a Columbia data scientist, is looking at two large computer screens. Her eyes dart back and forth between the brightly colored digital images of human brains. "Most of the time, it's like we're looking into mist," says Shen, who is a member of Claassen's research team. "And then if we're persistent, we may see a picture emerge — very faintly at first. We can then examine the data in many different ways to determine if we're truly detecting a signal amidst the noise."

The signal that Shen is hunting for? Consider it the shadow of a human thought. It will appear as a distinct and consistent difference in the levels of neuronal activity in various brain regions as a person hears commands played for them over headphones. For someone who is conscious but immobile, this could be an attempt at communication. A tiny salutation back from the void.

"We're looking specifically at regions that are responsible for higher cognitive functions, including language comprehension, to make sure we're detecting signals that represent active engagement with the stimuli," says Claassen, who is seated beside Shen.

This work is challenging in part because of the brain's sheer complexity. Even when it is injured and functioning at a reduced level, its hundred billion neurons are still firing constantly. The imprecision of EEG sensors adds to the challenge. "They'll detect electrical activity in brain regions other than the ones we're interested in and even in other parts of the body, including the heart," says Claassen. "We need to do a lot of creative analytics to weed out artifacts from our data."



Claassen with research-team members Qi Shen and Ángela Velázquez. (Rudy Diaz / CUIMC)

Despite these challenges, Claassen's team has managed to produce the most detailed descriptions to date of covert consciousness in acutely brain-injured patients. This research, based on observations of hundreds of CUIMC patients and published in numerous papers, suggests that the phenomenon is real, surprisingly common, and a useful indicator of a patient's potential for recovery.

"We're still a couple of years away from incorporating this into practice, because our technology needs fine-tuning," Claassen says, "but we've certainly demonstrated that covert consciousness is a major clinical concern and that detecting it has great potential to guide patient care."

The Columbia researchers' first big discovery on the topic came in 2019, when they showed that about 15 percent of brain-injured patients in comas exhibit signs of covert consciousness, which is also known as cognitive-motor dissociation, or CMD. They also found that these patients are much more likely to awaken from a coma and achieve a robust recovery. Then last year they found evidence that covert consciousness is caused by a communication breakdown between the brain regions responsible for higher-order cognition and the brain regions that control muscle movement.

Still, major questions remain unanswered. Claassen's team has yet to determine, for example, the level of consciousness of the patients who respond to their commands. The scientists can only say for certain that these patients are sufficiently aware to distinguish between prompts like "start opening and closing your right hand" and "stop opening and closing your right hand." The Columbia scientists have attempted to communicate with these patients in more meaningful ways, inviting them to open or close their hands to convey meaning in the style of Morse code, but the results so far are difficult to interpret. "We're not sure if they're cognitively incapable of participating in a higher-level interaction or if something else might be getting in the way — like they're confused, distracted, or simply frustrated," says Ángela Velázquez, a Columbia physician involved in the project. "But we're continuing to improve our methods and remain optimistic that we may reach them."

Claassen says that he has spoken to patients who regained their mental faculties after testing positive for covert consciousness, and he's found that so far none can recall their time in the neurocritical-care unit. From Claassen's perspective, this is a mixed blessing. "Of course, it's fortunate that they don't seem to remember a possibly traumatic experience," he says. "On the other hand, it means that this phenomenon remains a mystery, a black box that we cannot peer into." He still operates on the assumption that some coma patients may be fully conscious and that memories could be formed. "The human mind is very adept at blocking out terrible experiences," he says. "That certainly could be happening here."

Joseph J. Fins, a Cornell physician and medical ethicist who has written extensively about covert consciousness, says that the prevailing opinion among scientists who study the phenomenon is that people who test positive for it likely possess a wide range of cognitive abilities. "I think it's possible that some of these patients are fully aware, others barely awake, and still others somewhere in between," he says. "Clearly it's a moral imperative for us to try to reach them if possible."

Today, the Columbia researchers are pressing forward in their attempts to make contact with patients who are unresponsive. Their most ambitious plan is to develop a brain-computer interface similar to those that have been used to decode the thoughts of paralyzed people and to help them control keyboards and other communication devices. Claassen imagines that such a technology, by detecting distinct patterns of brain activity, could enable patients to answer yes-or-no questions and even summon hospital staff when they need help. "Are they in pain, uncomfortable, feeling hot or cold, or extremely anxious?" he says. "Being able to express themselves would dramatically improve the care we provide and make them feel less isolated."

The scientists are also fine-tuning their EEG test to make it more accurate. For now their methods are adequate for studying covert consciousness and estimating its prevalence but not for informing the care of individual patients. For example, people who are conscious but unable to comprehend language — a common result of brain injuries — will slip through the cracks, since their brains will be unable to process spoken requests and demands. (To identify such patients, Claassen's team is now expanding the test to include a nonverbal component that looks for brain signals that indicate a person is aware of other types of stimuli.) False positives are also a concern. The key to improving the diagnostic, Claassen says, is to build a much larger database of patient results. To this end, the Columbia doctors continue to screen their own coma patients for covert consciousness, while also making their data-gathering methods and analytic algorithms freely available to the research community, to encourage others to join the effort. Claassen has also helped found an international nonprofit, the Curing Coma Campaign, in part to promote research on covert consciousness.

"This is a topic of such urgency that we need to break down institutional barriers and pool our knowledge and resources, so that we can get this technology out into the world as rapidly and safely as possible," says Claassen. The team recently helped physicians at the University of Miami's teaching hospital implement their testing methods, and it is in conversation with several other institutions that are interested in collaborating.

Perfecting the EEG test is critical, Claassen says, because its results are likely to inform the agonizing decisions that many families confront about whether to take their loved ones off life support. In the US and Europe today, the majority of people who remain comatose for more than a couple of weeks following a brain injury are removed from life support. "It's around that point that you need to perform surgical procedures, including a tracheotomy and the insertion of a feeding tube, to sustain patients," Claassen says. Decisions about withdrawing life support in such circumstances are ultimately made by families in close consultation with physicians, who often struggle to provide guidance, since an individual's chances for recovery are difficult to assess. "Clearly some patients will have no chance of waking up," he says, "and we can identify them early on." These include people with catastrophic injuries to the midbrain and brainstem. "But in other patients, it's extremely difficult to predict recovery," he says. "It's as much art as science." For families, he says, the lack of clarity can be exasperating. "These are people who are facing one of the most difficult decisions they'll ever have to make. What they would like to do is know the future."

The picture is clouded by a lack of long-term epidemiological data. Since at some hospitals people are kept on life support for less than a week, it's difficult to know how many of them might ultimately awaken and recover if they were sustained for longer. Claassen and his colleagues have conducted research aimed at addressing this question, too. In one study, published in the journal Neurocritical Care in 2022, he and several Columbia colleagues tracked the lives of people who had slipped into comas after suffering severe brain injuries in Japan, where, for a variety of cultural and legal reasons, comatose patients are rarely taken off life support. The Columbia team's findings offered a measure of reassurance to Western neurologists, showing that Japanese physicians' initial assessments of their patients' long-term chances for recovery usually proved accurate. "In other words, patients who might have been removed from life support early on if they'd been in the US, based on the apparent severity of their conditions and other factors, did not, in fact, end up faring well on the whole," says Claassen. Yet the Columbia researchers also discovered that a small minority of Japanese patients who were initially predicted to have no chance of meaningful recovery did eventually wake up, with some regaining a high level of cognitive function and even managing to live independently. It is the promise of identifying patients like these, whose inner life and potential is hidden from conventional diagnostics, that drives Claassen. Yet he insists that his test for covert consciousness must be made foolproof before it can be introduced in the clinic. Imagine, he offers, if a patient were to be disconnected from life support simply for having been erroneously labeled as not having covert consciousness. Or if someone were to be kept alive for months or years in an unresponsive state, possibly suffering, on the faulty belief that she did.

"We have to get this absolutely right, so that we don't mislead people in either direction," Claassen says.

In some ways, the Columbia team's research has already influenced the clinical care that they provide. With a deepened appreciation for how unpredictable brain injuries can be, Claassen says, he and his colleagues have rededicated themselves to helping family members navigate the difficult process of serving as surrogates for their loved ones' care decisions. "We encourage a lot of open conversations about how comatose patients would likely regard the uncertainties surrounding their prognosis and the available care options, and how they would wish to proceed," he says. And at the bedside, doctors and nurses in Claassen's unit are careful to avoid speaking about patients as if they are not there. "We always operate on the assumption they can hear us speaking," Claassen says. "And we encourage their loved ones to do the same."

**After one week in a coma,** Nick LaRock began to move his fingers. Then he tilted his head slightly, toward a window. And his breathing changed: rather than inhaling in sync with his ventilator, he suddenly seemed to be battling it, insisting on his own rhythm.

"He sounded like he was gasping at first, and I hollered for the nurse," remembers his mother, Beth. "But she told me it was a good sign — it meant that he was starting to breathe on his own."

The next few days brought more surprises, for Nick's parents and doctors alike. He opened his eyes. Said his name. Held up two fingers. Picked up a cup of water and drank from it. Spoke a full sentence. "Whenever he talked, he sounded groggy, like he was still half asleep, and he was very confused," says his father, Joe. "But it was Nick. We could tell. He was coming back to us."

In the hallways of CUIMC's neurocritical-care unit that week, Claassen says, doctors and nurses walked a little lighter, smiled a little wider. "When a very sick patient starts showing signs of recovery, it's definitely something that we celebrate," he says. "Everybody is excited. You might even hear whoops of joy."



Nick LaRock and Jan Claassen reconnect recently at CUIMC. (Jörg Meyer)

By the end of his second week at CUIMC, Nick was conversing with his caretakers, albeit in a laconic drawl that his family said was new, and he was cleared for transfer to another hospital closer to his home. Soon after, he entered a rehabilitation center on Long Island, where he began the hard work of starting his life over. Paralyzed on the right side of his body as a result of the brain hemorrhage, he spent the next several months relearning how to walk, navigate stairs, climb in and out of bed, shower, and dress himself. Suffering from mild cognitive impairment, he had to be taught to read, spell, and enunciate certain words.

"In movies, we're used to seeing people come out of comas and pick up their lives right where they left off, but the reality is very different, especially for people who've suffered severe brain injuries," says Claassen. "Recovery is a very long, slow, and painful process."

Today Nick is living on his own, in an apartment in Upper Manhattan. A mildmannered, composed, and agreeable young man, he speaks reflectively about the challenges he's faced over the past three years. He is not currently working but dreams of returning to the classroom. He taught American history in New York City schools for ten years before his injury and says the job was the core of his identity. "I've actually tried to go back to teaching but found it too difficult," he says. "I don't know if that will change." Reading is still arduous for him, and he says he is self-conscious now in a way that he wasn't before the injury, when he could easily hold thirty-five boisterous teenagers in rapt attention. "I struggle to find the right words and formulate my thoughts," he says. "Other people might not notice, but I do, and it bothers me." Even if he cannot teach, he says, he will be fine. He notes that he's given up many other things as a result of his paralysis: playing saxophone and ukulele, golfing, bicycling, gaming, slicing vegetables, and wearing shirts with buttons. "And I've survived," he says. "I'm just a different person now. I'm more likely to be found sitting in the park, simply enjoying being here. I feel very lucky."

From a medical standpoint, Claassen says, Nick's recovery has been extraordinary. "Considering the severity of his original injury and the length of his coma, it's tremendous," he says. "Quite unexpected."

The supercomputer in Claassen's office predicted it, though. Back in 2021, every time Columbia researchers asked Nick to imagine opening his hand and then closing it again, they observed two distinct patterns of neuronal activity in his brain's motorcontrol center. These patterns closely resembled those seen in fully conscious, healthy subjects who had undergone the same exercise. Nick, like other former patients identified by the Columbia researchers as having covert consciousness, doesn't remember this. But he doesn't remember *anything* from three months before his brain hemorrhage until nearly four months after it. "From October 2020 until May 2021 is just kind of wiped from my mind," he says.

Even if the Columbia team's experimental new diagnostic had been in clinical use at the time, it would have had little bearing on Nick's care. He woke up several days before his Columbia doctors would have talked to his parents about long-term lifesupport options.

So the real question is this: are there many more people lying unresponsive in hospital beds right now who might similarly spring to life, if only given additional time to heal? And if so, is it possible to identify them? "It's difficult to know for sure — there are uncertainties at every turn here," says Claassen. "But we need to look, and we are making great progress."

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