

What if There Is Something Going On in There?

By CARL ZIMMER

Daniel Rios is 24 years old, with wavy black hair, a thick mustache and a glassy stare that seems to look both at you and through you. One day almost four years ago, while he was taking a shower, a blood vessel ruptured in his brain, and he collapsed on the bathroom floor. After emergency surgery, he lay in a coma for three weeks. When he finally opened his eyes, he could not speak or move his body; his head simply lolled. In the months that followed, the doctors monitoring him at the Center for Head Injuries at the J.F.K. Johnson Rehabilitation Institute in Edison, N.J., saw few signs that he had any meaningful mental life. Sometimes he looked as if he were crying. Other times his eyes would follow a mirror passed before his face. On his best days he was able to close his eyes on command. But those days were rare. For the most part he lay unresponsive, adrift in a neurological twilight.

One morning just over a year after his accident, Rios was taken to the Sloan Kettering Institute on Manhattan's East Side. There, in a dim room, a group of researchers placed a mask over his eyes, fixed headphones over his ears and guided his head into the bore of an M.R.I. machine. A 40-second loop of a recording made by Rios's sister Maria played through the headphones: she told him that she was there with him, that she loved him. As the sound entered his ears, the M.R.I. machine scanned his brain, mapping changes in activity. Several hours afterward, two researchers, Nicholas D. Schiff and Joy Hirsch, took a look at the images from the scan. They hadn't been sure what to expect -- Rios was among the first people in his condition to have his brain activity measured in this way -- but they certainly weren't expecting what they saw. "We just stared at these images," recalls Schiff, an expert in consciousness disorders at Weill Medical College of Cornell University. "There didn't seem to be anything missing."

As the tape of his sister's voice played, several distinct clusters of neurons in Rios's brain had fired in a manner virtually identical to that of a healthy subject. Some clusters that became active were those known to help process spoken language, others to recall memories. Was Rios recognizing his sister's voice, remembering her? "You couldn't tell the difference between these parts of his brain and the brain of one of my graduate students," says Hirsch, an expert in brain imaging at Columbia University. Even the visual centers of Rios's brain had come alive, despite the fact that his eyes were covered. It was as if his sister's words awakened his mind's eye.

To the medical world, Rios and the hundreds of thousands of other Americans who suffer from impaired consciousness present a mystery. Traditionally, there have essentially been only two ways to classify them: as comatose (eyes closed and responses limited to basic reflexes) or vegetative (eyes opening and closing in a cycle of sleeping and waking but without any sign of awareness). In either case, it has been assumed that they have no high-level thought. But Schiff, Hirsch and a small group of like-minded researchers are studying people like Rios and finding that the truth is far more complicated. Their

evidence suggests that even after an injury that leaves a brain badly damaged, even after months or years with little sign of consciousness, people may still be capable of complex mental activity. "If I say, 'Touch your nose,' and you touch your nose, and then I say 'Touch your nose' six more times, and you don't do it, how do we account for the one time you did?" asks Joseph T. Giacino, a neuropsychologist who collaborates with Schiff and Hirsch.

Last year in the journal *Neurology*, Giacino and 10 co-authors accounted for that touch of the nose -- and other enigmatic hints of awareness they have observed -- by proposing a new category of consciousness: the minimally conscious state. By their reckoning, a vast number of people who might once have been considered vegetative actually have hidden reserves of mental activity. And as the study of Rios suggests, brain scans may be able to help scientists eavesdrop on their inner world. "It's free speech for people who have no speech," Hirsch says.

The implications of this research, both for medical ethics and practical policy, are potentially huge. Traumatic brain injuries are a significant health problem in the United States, but the study and treatment of them are clouded with a sense of hopelessness, a feeling that consciousness is too mysterious to be understood. When faced with patients in a vegetative state, doctors can do little more than wait to see if they wake up. No treatment has ever been definitively shown to help patients recover consciousness, and doctors can't predict which patients will emerge from a vegetative state and which won't. If patients don't show signs of recovery in a few weeks, they usually wind up at home with their families or in nursing homes, and they rarely see a neurologist again. In 1976, in a famous court case, the parents of Karen Ann Quinlan, a woman who had been in a vegetative state for about a year, won the right to take her off a ventilator (after which she lived until 1985). "There's a point where people give up" and discontinue aggressive treatment, says Joseph J. Fins, chief of the division of medical ethics at Weill Medical College. "The question is, Are we giving up too soon on the ones who might become more functional?" Schiff and his colleagues say that the answer, in too many cases, may be yes.

A coma is what people tend to think of when they think of impaired consciousness. But most comas don't last long. After a few weeks, those who manage to survive a brain injury either wake up or shift to a vegetative state. Last year, Pedro Almodovar's movie "Talk to Her" introduced many viewers to the vegetative state, centering its story on two women suffering from brain injuries. Their peaceful slumber, unfortunately, doesn't capture the reality of the condition. People in vegetative states may keep their eyes open for much of the day, sometimes appearing to fix their gaze on you. They may startle their loved ones with an occasional groan or sob. Their limbs may curl up in spasms or swing around in constant motion. Some people eventually leave the vegetative state and regain consciousness, while others live for decades without showing any sign of awareness.

Nine years ago, when he was a young resident at New York Presbyterian Hospital, Schiff began working under Fred Plum, one of the neurologists who first recognized the "persistent vegetative state" in 1972. By the early 90's, technology was becoming

powerful enough to offer a glimpse of what was happening in the vegetative brain, and Plum put Schiff in charge of a project to scan vegetative patients. After a long, often frustrating struggle to find patients to study, filling out reams of paperwork and coping with suspicion and indifference, Schiff and his colleagues published their results last year in the journal *Brain*.

Their findings were remarkable. Among other tests they conducted, they used a technology known as positron emission tomography (PET) to estimate how much energy the brains of their subjects were using. One subject, a 49-year-old woman who had been in a vegetative state for 25 years, would say something every few days -- often a curse word. Overall, the woman's brain was using less energy than the brain of someone under deep anesthesia, but some regions of her brain were running at close to normal, including the neural network that produces language. Those regions were still producing words, long after the woman's consciousness disappeared. Another subject was a 42-year-old man who had been in a vegetative state for seven years; he would groan and clench his teeth when he was touched or heard a loud noise but appeared to be soothed on occasion by his mother's voice or soft music. Schiff discovered that one area still functioning in the man's brain was associated with listening to music and recognizing a voice's emotional inflections. And in the truly exceptional case of one 25-year-old man who exhibited no physical responses at all, Schiff found that the patient's brain used almost as much energy as that of a conscious person.

The results of the study offered hints about the nature of consciousness. High-level thought -- like language and memory -- occurs in networks of neurons located at the surface of the brain in a thin layer of tissue called the cortex. These networks also form loops, however, that dip deep within the brain, where they converge and then return to the surface. According to a theory proposed by Rodolfo Llinas of New York University, a special set of neurons deep in the brain synchronizes the activity of the loops of higher thought. The harmony of all the different thought processes gives rise to a coherence that we call consciousness. Schiff and his colleagues say they suspect that when a number of these loops or the region that synchronizes them is damaged, the brain slips into a vegetative state. Yet even after extensive brain damage, they argue, some of the loops may still function, though in isolation -- like fragments of mind.

In searching for subjects for his study, Schiff discovered the Center for Head Injuries in Edison, where Rios is treated. Neuropsychologists there have specialized in tracking how patients recover from brain injuries, moving from comas toward consciousness. Joseph Giacino, the lead author of the *Neurology* paper that defined the minimally conscious state, is the center's associate director of neuropsychology. He is one of the few doctors who focus on both the study and the long-term treatment of patients with impaired consciousness. "You come in a coma, and you can get your treatment all the way to when you're back at work and you still need some follow-up," he explained to me on a visit to the center in July.

Giacino has spent the past 15 years developing ways to measure objectively how people recover from comas. It's not enough for a father to declare that his daughter is

understanding everything he says; a turn of the head or a squeeze of the hand can just as easily be an unconscious reflex as an act of will. And pessimism can be just as misleading as optimism: if a doctor overlooks a legitimate sign of consciousness, he may peg a patient as a hopeless case.

At Giacino's center, patients repeatedly go through the same standardized battery of tests. They are asked to look at objects -- a plastic banana, for example -- and identify them. They are shown a hairbrush and asked how to use it. They answer with a glance at cards marked "yes" and "no," with a thumbs-up or, when possible, with their voices. Giacino records whether his patients can communicate and whether they communicate reliably. "If I ask you, 'Are you a man?' and you say yes, and a few questions later I ask you if you're a woman, and you say yes, you're not a reliable communicator," he says. Adding up the results of his tests, Giacino gives each of his patients a score indicating a diagnosis somewhere on a spectrum between coma and consciousness.

Over months and years of administering and readministering his tests to patients as often as every week, Giacino is able to chart patients' scores in fascinating graphs. Some are straightforward climbs to consciousness, others level off at less-than-conscious plateaus. Still others form a series of conscious peaks and vegetative valleys. These variegated landscapes were Giacino's inspiration for the minimally conscious state, which describes patients who show signs of awareness but are still far from full consciousness.

Giacino works hard to tease out hints of awareness in a patient. Sometimes he can actually coax patients into consciousness by working his fingers deep into their muscles. Neurologists have found that the stimulation of the nerve endings in the muscles can be powerful enough to arouse activity in networks of neurons in the brain. Giacino has a particular knack for the technique, and after a few seconds of muscle work, he can get some minimally conscious patients to speak. Some tell him their names, others tell him to leave them alone. As soon as he removes his hands, they slip away again.

Marie Conniff has seen Giacino work this transformation many times. On New Year's Day in 1998, her son Scott was on duty as a New York policeman when a drunken driver rammed his car. Today, Scott sits in a wheelchair, his gaze often drifting across the room. Sometimes he laughs, sometimes he growls like a bear. He gives hard kicks to a big orange beach ball hanging from the ceiling. When Giacino begins to work her son's muscles, Conniff finds herself startled at how well Giacino can bring Scott back, in the look on his face, the clarity of his movements. "I see a lot of what I had before he got hurt," she told me.

Conniff raises a profound question: Is a part of her son still there? Schiff began to gather some clues to this question when he switched from studying vegetative patients to people in minimally conscious states. He and Giacino selected a few patients at the Center for Head Injuries whom Giacino had identified as minimally conscious. They arranged for the patients to have PET scans to measure their brain metabolism, as Schiff had done in his earlier study on vegetative patients. But they also collaborated with Joy Hirsch to

probe their subjects' brains with M.R.I. scanners, which can measure moment-by-moment changes in brain activity.

Rios provided some of the first astonishing results of this second project. And when the researchers ran the same study on another minimally conscious patient, they got even better results. "It certainly raises the question that there's more 'there' than we've been giving them credit for," says Joseph Fins, who has been exploring the ethical dimension of Schiff's new research. "It's very suggestive that there's consciousness."

Schiff is reluctant to declare prematurely that these images are pictures of consciousness, but he and his colleagues are considering two important clues. One is the overall metabolism of Rios's brain. While undergoing an M.R.I., Rios's brain became active in response to sounds and touch in much the same manner as a conscious brain. But when the researchers took a PET scan of his brain at rest, they got a very different picture. A healthy brain burns a lot of calories even when not processing any particular information from its senses. Rios's brain at rest used about as much energy as someone in a pure vegetative state.

The other clue emerged when the scientists played Rios the tape of his sister's voice backward. When uninjured people hear backward voices, the regions of their brains that control language become more active than when they listen to recordings played forward. Their brains instantly recognize that the signal is unusual and respond by working harder to decode it. But when Rios heard his sister's voice played in reverse, his brain barely responded at all.

Schiff says he suspects that Rios's brain works very differently not only from a vegetative brain but also from an uninjured one. Rios still has a healthy number of loops of higher thought that the scans suggest may be able to work in harmony when he hears his sister's voice. But for some reason, it appears that these loops shut down in the absence of familiar stimuli. His brain doesn't seem to have the strength, as it were, to reflect continually on itself and its surroundings the way a healthy brain does, ready to engage the world in an instant. An ambiguous signal isn't enough to provoke him.

It's hard not to speculate about what it's like -- if that's even a meaningful notion here -- to inhabit this sort of mind. You wake up every morning but feel as if you're under a deep anesthesia. Images enter your eyes, and sounds enter your ears, but most of them reverberate through your brain without triggering any awareness. From time to time, you join the outside world at the sight of a familiar face or at the words of a loved one. Memories and meaning emerge. But as soon as that face or those words disappear, you sink back into darkness. Perhaps you can't even tell you're sinking -- perhaps your awareness leaps from one isolated moment to the next.

Still, there are plenty of neurologists who doubt whether any of this research on the minimally conscious state has any real significance. Alan D. Shewmon, chief of pediatric neurology at the Olive View-U.C.L.A. Medical Center in Los Angeles, has called Giacino's category "an inaccurate name for an invalid concept." He argues that there is no

scientific way to draw a line between full consciousness and minimal consciousness, and says he worries that the definition is so broad that it easily encompasses people who are conscious but suffer from other neurological disorders that impair their ability to communicate.

Schiff and Giacino say that as more of their studies on people like Rios are published, they will silence their critics. By understanding the biology underlying the minimally conscious state, they say, it may also be possible to help people in this condition expand their moments of awareness. Drugs that boost the brain's supply of certain neurotransmitters, for instance, might be able to keep their networks turned on longer. Schiff says he hopes that within a decade researchers will be able to experiment with implanted electrodes that act like pacemakers for consciousness. By emitting regular pulses of electricity, they could keep the brain's networks active and synchronized. "What's got me still willing to do all this is that you could help someone on the borderline to cross over," Schiff says. "To live on their own at home, to have fun, to have a life."

In the years since Karen Ann Quinlan's parents had her taken off her ventilator, courts have also acknowledged the rights of families to remove feeding tubes from vegetative patients. And as research on the minimally conscious state has emerged, the courts have been asked, in recent cases, to judge whether the category describes a life that's always worth living.

On one visit to the Center for Head Injuries this summer, I was privileged to witness firsthand why Schiff and Giacino can be so hopeful about a seemingly hopeless condition. I joined Schiff, Giacino, Fins and some of their colleagues as they made rounds, and at noon we reached Rios's room. More than three and a half years had passed since he collapsed in his shower, and he was still considered to be in a minimally conscious state. Physical therapists had been regularly working Rios's limbs, and his sister had been caring for him at home on some weekends. Even with this attention, the statistical odds were against his ever reaching a higher level of consciousness. "He hasn't crossed that line," Giacino said before we went into the room.

Rios sat in a wheelchair, his hands curled to his chest, his left eye drifting. He wore a broad, unchanging smile. Over the years, his walls had become crowded with photographs, prayers, and a map of Puerto Rico.

The doctors introduced themselves to Rios. "Do you remember me?" Schiff asked. "I'm Dr. Schiff from New York. I saw you with your sister Maria a couple times." Rios continued to smile.

Giacino stepped close in front of Rios. "So, Dan, if it's O.K. with you, we want to do a bit of examination."

With his right eye, Rios was able to track a mirror that Giacino moved in front of his face. "Dan, look toward my voice," Giacino said, stepping to Rios's left side. Rios's eye

moved left. "Now look away." He looked away. Giacino showed Rios cards marked "yes" and "no." "Now look at the card marked 'no.'" Rios looked at the card marked "no."

The other doctors buzzed with excitement. "This is three years out," Schiff said. Giacino switched the cards and asked Rios to look at the card that said "yes." Rios looked at the card. Giacino did the test a third time, and Rios got it right again.

"That's a hundred percent," Schiff said. "Let's ask him some questions."

"Dan, are you in a bathtub right now?" Giacino asked.

Rios looked at the "no" card.

"Are the lights on?"

Yes.

"He said yes, he mouthed it," Fins said.

"Do you feel sad right now?" Giacino asked.

Yes.

"Do you feel happy right now?"

Yes.

"He has both feelings," Schiff offered.

"At the same time," Fins added. "He's in the moment."

"Let me take it back down a level," Giacino said. He didn't want to rely on interpretations to pinpoint Rios's level of awareness. He asked Rios if his name was Bill. No. Giacino switched the cards between his hands. "Is your name Jason?" No. "Is your name Dan?" Yes.

"Ask him if I'm happy or sad," Schiff asked. He put on a giant pout.

"Is Dr. Schiff happy?" No.

Schiff broke into a grin. Rios broke into his grin again. "I'd say he's emerged now," Schiff said.

"O.K.," Giacino said. "I'm going to take it up a level." He wrote words on two new cards: "happy" and "sad." He held them up in front of Rios, and before he could ask a question, Rios looked at "happy." He moved his lips, silently saying the word.

"Yeah, that's it!" Schiff said.

"Well, maybe," Giacino said. He kept his eyes on Rios. "I'm going to ask you to look at the word that I say. Dan, look at the word that says 'sad.'" Rios looked at "sad." Giacino asked him twice more; twice more, Rios looked the right way.

"That's it," Giacino said. "He's reading."

He turned back to Rios. "How are you feeling inside? Look at the card how you're feeling."

Rios mouthed, "Happy."

By all measures, Rios had officially emerged from the minimally conscious state. As the doctors said goodbye to him, filing out of the room into the hallway, Schiff was already wondering aloud if Rios should be brought back to the lab for study. He wanted to know what had happened to Rios's brain, how his neural networks had reorganized themselves into something closer to full consciousness. "I was just thinking we should try to redo all those studies," Schiff said. "He's got to be different."

"He was pushing us to go to a higher level," Fins said. "He's aware of himself, he's happy, but it took a lot of skill to see it. If he ended up in a nursing home and started doing things like this, no one would have noticed."