

A Flicker of

Conscious

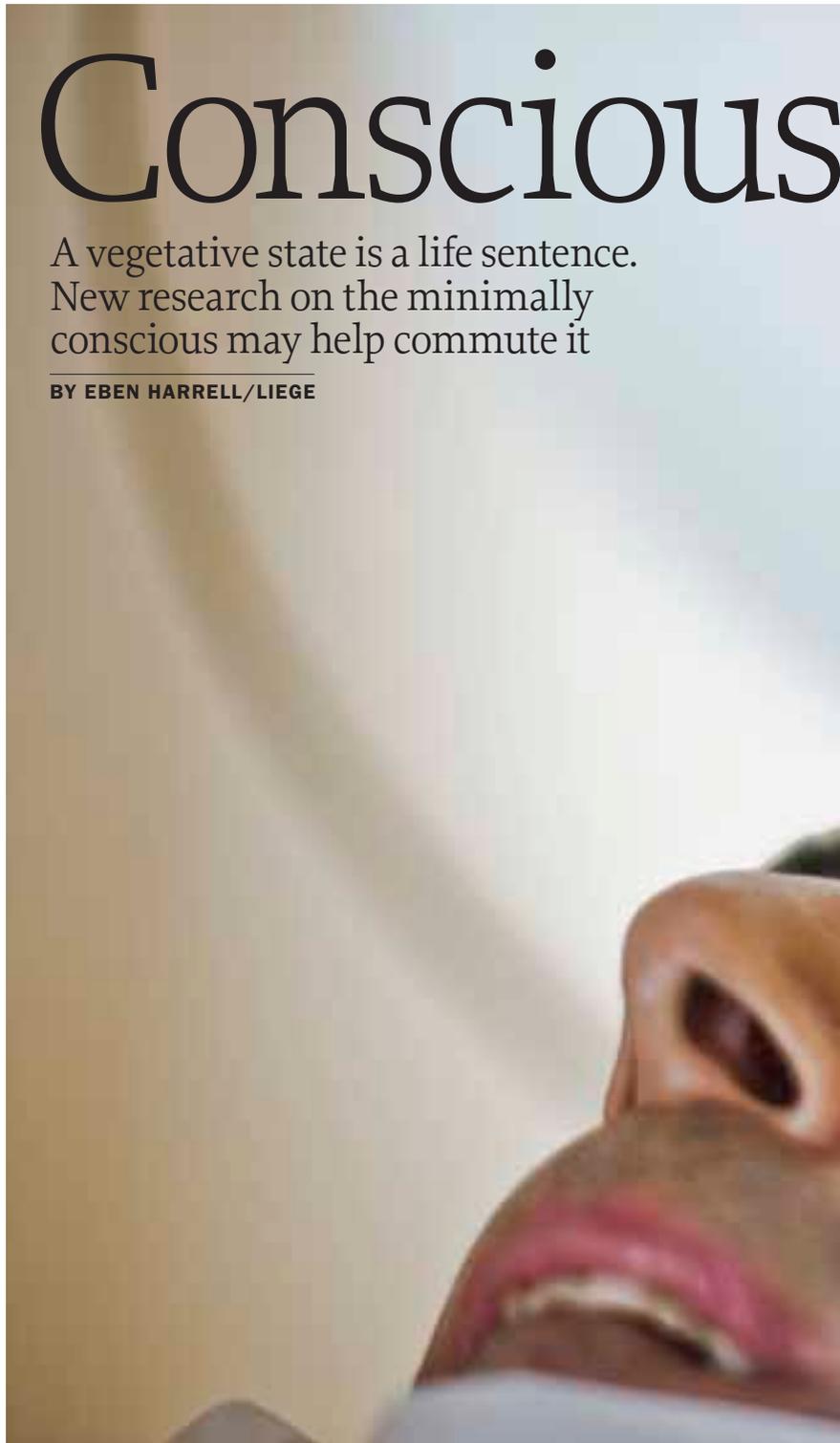
A vegetative state is a life sentence. New research on the minimally conscious may help commute it

BY EBEN HARRELL/LIEGE

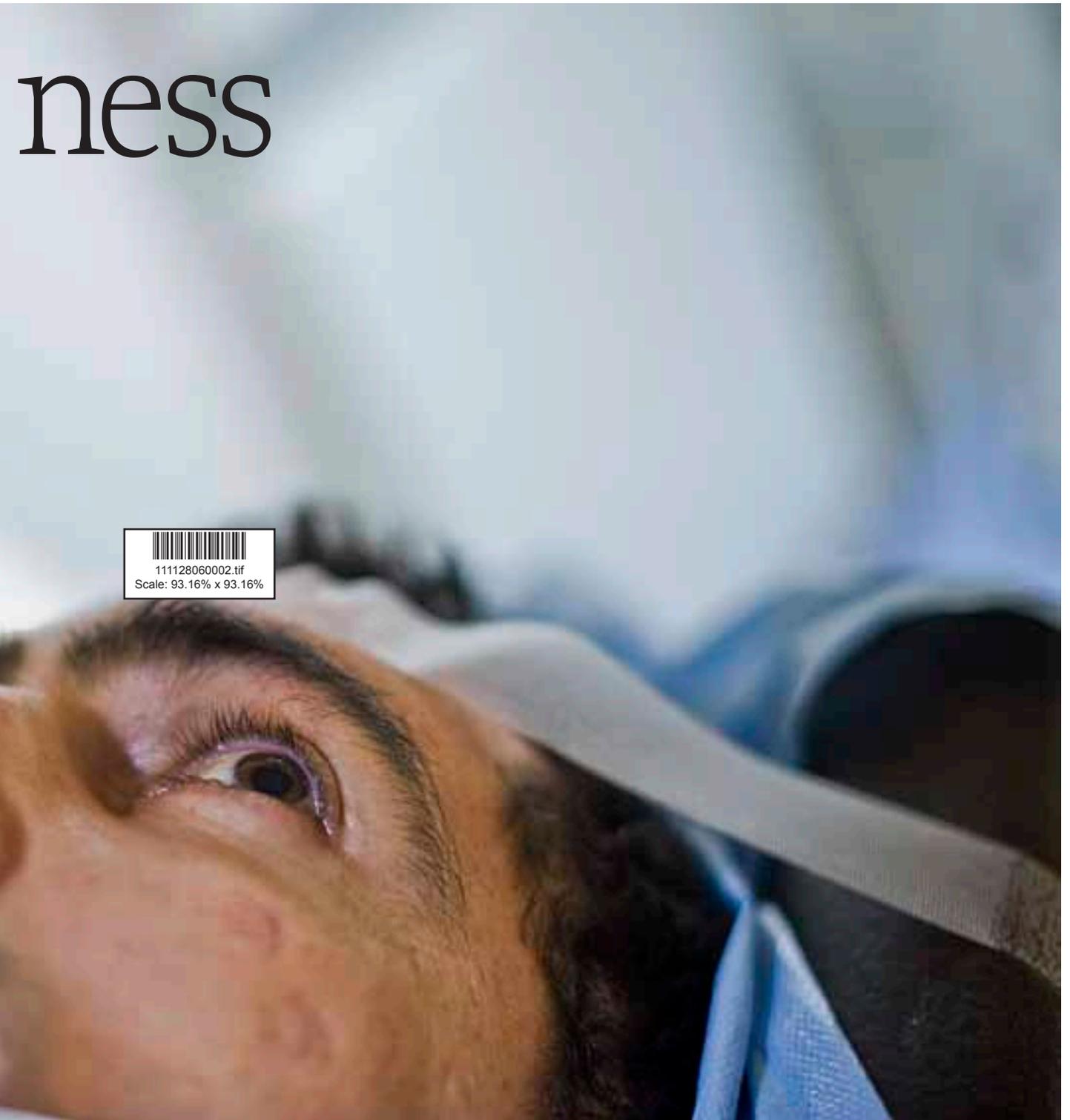
O

ON SUNDAY, AUG. 9, 2009, VALENTINE Filipov, a handsome and energetic manager at a refrigeration factory in Pazardzhik, Bulgaria, decided to change a burned-out lamp in his garden. His daughter Anna refers to what happened next as “my father’s ridiculous accident.” Filipov lost his balance on the 3-ft. (0.9 m) stepladder and fell, hitting his head on the pavement. The blow put him in a coma for five days. When he opened his eyes, doctors determined that the damage he sustained had left him in a vegetative state, a condition defined by unresponsive wakefulness, in which patients follow a normal sleep-wake cycle, breathe without assistance and make reflexive movements such as swallowing, yawning, grunting and fidgeting but have

Photographs by Peter van Agtmael for TIME



ness



Window into the soul *Valentine Filipov's eyes follow a mirror during a test doctors used to confirm he has retained some level of consciousness*

no awareness of their environment and can't respond to commands.

After Filipov spent a month in the hospital, the doctors discharged him. They told his family there was nothing more they could do, that he would be in a vegetative state for the rest of his life.

But Filipov, who was then 45, seemed less lost to the world than the doctors assumed. He would sometimes laugh with family members. He would sometimes cry with them—especially with Sofiya, his wife of 23 years. Vegetative patients have been known to cry, but their outbursts are typically spontaneous and not associated with external stimuli. Filipov's seemed triggered by things going on around him.

Desperate for a reappraisal, his family took him to see Dr. Steven Laureys, head of the Coma Science Group at the University of Liège in Belgium, one of the few centers in the world that study vegetative patients. Laureys asked the Filipovs if they could make Valentine cry. They circled his bed, and Sofiya approached him. She bent over him, cradling his cheeks in her hands. "Will you cry with me, my love?" she whispered. "Will you weep with me, my dear?" His face began to contort. His eyes fixed on his wife's face. He started crying, loudly.

The Consciousness Conundrum

THERE'S AN ODD CIRCULARITY TO STUDIES of consciousness—a curious exercise in the brain investigating the brain. Nobel laureate Francis Crick took a reductionist view of things in the 1970s, coining the term "the astonishing hypothesis": the idea that all feelings, thoughts and actions are just the products of a mass of brain tissue and that we all exist only one well-placed head trauma away from the irrevocable erasure of the self. Most people choose to see things more lyrically; consciousness is the ineffable ghost in the machine that distinguishes us from plants and bacteria and perhaps even other animals—the quality that makes us wondrously special. But scientists aren't lyricists, and Crick's mechanistic view has prevailed, with scientists treating the brain as merely another organ, albeit a highly complex one.

Nowhere is that complexity more evident than in our understanding of how consciousness works—and fails to work. Minor accidents like Filipov's can lay waste to cognitive processes. Major traumas like the shooting wounds of Congresswoman Gabrielle Giffords can

leave remarkable room for recovery. Patients labeled vegetative typically stay that way—but sometimes they don't. So where's the line between resignation and hope? Various studies in the past decade, including one by Belgian and U.S. experts in 2009, have found that about 40% of patients diagnosed as vegetative are actually conscious and fall into a category adopted in 2002 called minimally conscious, a state in which some awareness exists and improvement is possible.

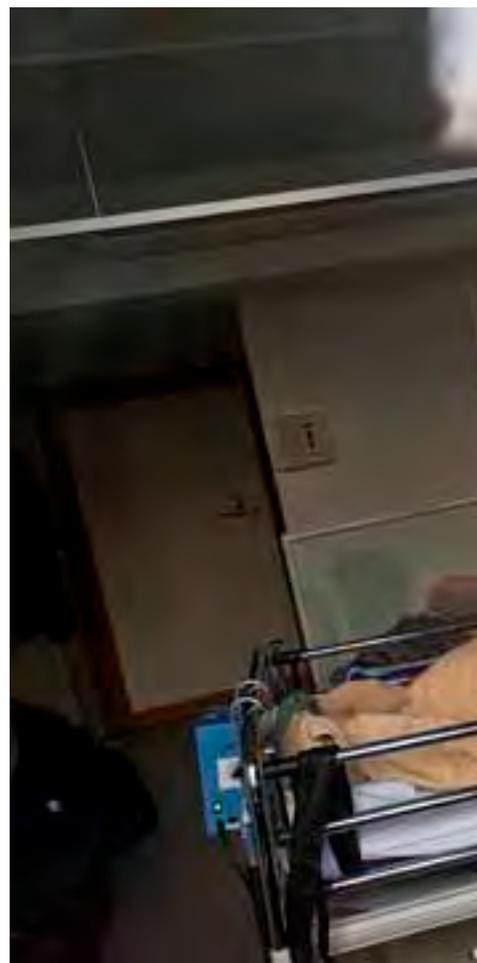
In the Nov. 10 issue of the medical journal the *Lancet*, a research team that included Laureys illustrated this point starkly. They studied 16 patients diagnosed as vegetative, hooking them up to an electroencephalogram (EEG) and asking them to imagine squeezing their right hand and wiggling their toes on command. Three of the subjects apparently imagined it well, with the proper EEG tracings appearing in the premotor cortex of their brain. Did they hear? Were they conscious?

Those are terrifying questions. Patients wrongly diagnosed as vegetative are sentenced to a life of being tended to by caregivers (who may never take the trouble to engage them because it seems pointless) even as a partly functioning mind weeps or dreams or rages within. "The notion of a conscious person treated as not conscious—to me that's the ultimate portrait of isolation," says Dr. Joseph Fins, chief of medical ethics at Weill Cornell Medical College in New York City. "It's solitary confinement of the most troubling kind." The *Lancet* study and others suggest that with the right technologies and therapies, at least some of these confined minds may conceivably be set free.

A Look in the Mirror

EACH YEAR IN THE U.S. AT LEAST 14,000 victims of brain damage are diagnosed as vegetative. If the 40% misdiagnosis figure is correct, that means 5,600 of them are in better shape—perhaps far better—than their records show.

There are a lot of reasons the error rate is so high, not least that truly reliable tests for consciousness have not been developed. To date, the only accepted diagnostic method remains a bedside exam. Clinicians ask patients to respond to commands like "Squeeze my hand" and "Look at the ball." But many postcoma patients suffer from aphasia, the inability to understand language. Brain damage



may leave other patients deaf or blind or so severely spastic, epileptic or paralyzed that they cannot control their movements. They may be severely amnesiac and unable to remember what is asked of them. They may suffer from akinetic mutism, in which the part of the brain responsible for decisionmaking and drive is damaged.

What's more, minimally conscious patients almost always suffer from fluctuating vigilance; for them, consciousness flickers on and off like faulty Christmas-tree lights. "A doctor goes to the bedside, gives five commands, gets no response and pronounces the patient vegetative. But a different doctor might see the patient at a different time and come away with a totally different impression," says Joe Giacino, director of rehabilitation neuropsychology at Boston's Spaulding Rehabilitation Hospital, who led the effort to have the "minimally conscious" diagnosis accepted by the medical community.



To improve diagnostic accuracy, Giacino designed a rigorous, standardized bedside assessment called the coma recovery scale—revised (CRS-R), which Laureys and others promote as the gold-standard exam. Some elements of the old method have been retained in the CRS-R, including object recognition, in which the examiner holds two objects and asks the patient to fixate on one. But the CRS-R requires each test to be repeated multiple times to allow for fluctuating vigilance.

The primary reason for the CRS-R's improved accuracy, however, is a simple but revolutionary innovation. The test measures patients' eye-tracking ability by moving a mirror in front of their face rather than a finger or pen—the method most neurologists use. "Patients respond powerfully to their own image," Laureys explains. "It's remarkable to witness."

Indeed, Filipov's awareness became indisputable as soon as a mirror was cir-

40%
SHARE OF PATIENTS
DIAGNOSED AS
VEGETATIVE WHO
ARE MINIMALLY
CONSCIOUS

The long wait
*Anna Filipova struggles
with her father's uncertain
prognosis*

culated in front of him. While he failed to respond to nearly every other test in the CRS-R, he became transfixed by his reflection and avidly followed it with his eyes. "If every doctor in every emergency room carried a mirror in their pocket, it would immediately and significantly reduce the misdiagnosis rate," Laureys says.

Even the most rigorous neurological exam cannot circumvent another diagnostic obstacle, though. Many vegetative patients do not emerge into minimal consciousness until several months after waking from a coma, by which time they have been discharged from the hospital. "A family might tell a nurse in a care home that something's changed, but the nurse sees the *vegetative* label and dismisses this as wishful thinking," Laureys says.

The irony—a cruel one—is that often doctors give up on recovery at the worst stage possible. The first few months after an injury can be a quiescent time for a damaged brain, with all its energy going to recovering from the wound it suffered. It's only later that it has the luxury to begin recovering some of its lost faculties.

"You want to change the world?" asks Nicholas Schiff, a neurologist at Weill Cornell Medical College who, along with Laureys and a Canadian research group, is in the middle of a three-year project to study 500 patients with consciousness disorders. "Get these patients a six-month follow-up by experts who can do a behavioral assessment. Give them a safety net."

The Eye of the Scanner

WHILE BEHAVIORAL EXAMS REMAIN THE primary diagnostic tools for assessing consciousness, a handful of neurologists around the world are using brain scans to try to map what they call the neural correlates of consciousness, the cerebral mechanisms that make us aware. For years, doctors assumed that consciousness was a diffuse and global brain process. But studies of sleeping, anesthetized and vegetative brains have shown that it is instead localized in a network consisting of three discrete parts: a section of the prefrontal cortex; a section of the parietal cortex; and the thalamus, a structure deep in the brain that acts as a sort of traffic cop, mediating signals between the two other parts of the consciousness triad. Should connections among the three sections be severed—or should one be destroyed—consciousness ceases. "You don't need a lot of gray matter

to be conscious. You only need the right parts of the brain to function together. That was a huge surprise,” Laureys says.

With this knowledge, neurologists are getting better at developing imaging tests that can conclusively capture consciousness onscreen. Last year in the journal *Neuroimage*, Spanish neuroscientist Davinia Fernández-Espejo published a study of 25 patients with disorders of consciousness in which she used magnetic resonance imaging (MRI) to differentiate patients identified with the CRS-R as vegetative from the minimally conscious and achieved 95% accuracy. Similarly, Laureys’ group has developed software that can interpret results of positron emission tomography (PET) scans, which measure metabolic activity in various regions of the brain. Last year the group published a study in *Neuroimage* in which the program was able to distinguish fully conscious patients from vegetative patients with 100% accuracy. And while the just-published EEG findings were not as dramatic, they showed that promising diagnoses can be made with simple, inexpensive hardware too.

A Rich Inner Life

WHAT SUCH TESTS CAN’T ANSWER IS THE question that intrigues—and frightens—people most: What is life like for minimally conscious patients? Is it silent agony, or is there a primal serenity to their muted interior world? The answer may depend on their quality of care. PET scans show that when minimally conscious patients are thought to be in pain, parts of the brain associated with emotion light up, just as in healthy volunteers. Vegetative patients show no such response. Yet, Laureys says, minimally conscious patients often don’t receive basic pain medication, which he calls “very disturbing” given these results.

There are also tantalizing signs that minimally conscious patients may sometimes be capable of experiencing a rich inner life. A recent study by Laureys of sleeping minimally conscious patients showed brain waves associated with REM sleep, which suggests they could have dreams. In 2006, Laureys and Adrian Owen at Cambridge University published a study in *Science* in which they performed a functional MRI (fMRI) scan on the brain of a 23-year-old woman diagnosed as vegetative. When she was asked to imagine playing tennis, her brain activated supplementary motor areas in precisely the same



way as a healthy volunteer’s. She also activated spatial brain networks associated with navigation when she was told to imagine walking around her home.

Kate Bainbridge, a former schoolteacher who was similarly misdiagnosed in the 1990s in England, has since recovered enough to communicate by using a computer. “It really scares me to think what might have happened to me had I not had the scans,” she wrote in an e-mail to a journalist in 2007. “They show it was worth carrying on even though my body was unresponsive.”

This year, Laureys further challenged presumptions of the quality of life for postcoma patients with a survey in the *British Medical Journal* of locked-in patients. Such people sustain a brain injury that results in paralysis so severe they can control only their eye movement, even as their consciousness network remains intact. The journalist Jean-Dominique Bauby, perhaps the most famous such patient, earned fame through a memoir, *The Diving Bell and the Butterfly*, which he dictated by blinking.

In the immediate weeks after their injury, locked-in patients show intense activity in a region of the brain associated with anxiety and emotion, but they eventually adjust. Laureys’ survey of 168 locked-in patients found that while a minority—just 7%—reported life to be “miserable” and

were lobbying to be euthanized, a vast majority said they were “happy” despite their condition. “That result showed that we should be very careful not to presume that we know the subjective experience of a noncommunicative patient,” Laureys says. “That has profound implications for families and doctors considering whether to withdraw life-sustaining treatment.”

But those implications can cut two ways. Truly vegetative patients who remain awake but unresponsive for more than 12 months following traumatic brain injury or three months after cardiac arrest or stroke are classified as permanently vegetative. The U.S. Supreme Court ruled in 1990 that such patients may have their feeding tube withdrawn if they have a living will, if their legal proxy so desires or if there is strong evidence that the patient would want to die.

There is no known time limit, however, for when a minimally conscious patient might suddenly return to full awareness. In 2003, 39-year-old Terry Wallis of Arkansas emerged from minimal consciousness and regained fluent speech after lingering in a nursing home for 19 years after a car crash. Using diffusion tensor imaging, a novel brain-scanning technique that maps the intact internal cables in the brain, Schiff found in 2006 that Wallis’ brain had undergone axonal sprouting. New connections had been made among existing neurons.



All families with a vegetative loved one imagine that he or she will be the next Wallis, though few are. So even with the dignity and perhaps comfort of the patient on the line—not to mention the welfare of the family’s wallet—it can be agonizingly difficult to pull the plug. “The right to die is an important principle,” Laureys says. “But doctors must also be clear that we can’t always give a certain prognosis.”

Making things worse, even the best scanners are still just inferential machines. They reveal brain activity, and neurologists must decide if that suggests thoughts. In a healthy patient it typically does, and it’s easy enough to confirm the premise: just ask the subject. There’s no such proof possible with the minimally conscious. “Opening up a communication channel with these patients is the holy grail from an ethics point of view,” explains Weill Cornell’s Fins. “Right now the debate about what these patients feel is missing the one voice it needs most—that of the patient.”

The Stirring of the Silent

THAT VOICE COULD SOON BE HEARD. LAST year Laureys and the Cambridge team reported using the methodology of the 2006 tennis study to show that some minimally conscious patients can use mental visualization within an fMRI to communicate. Laureys asked patients to imagine playing tennis if the answer to a question

19 YEARS

TIME THAT AMERICAN TERRY WALLIS SPENT IN A MINIMALLY CONSCIOUS STATE BEFORE REGAINING SPEECH AND FULL AWARENESS

Vital signs

Dr. Steven Laureys, far left, searches for signs of consciousness on brain scans like the one administered by Caroline Schnakers, center

was yes and to imagine navigating their home if the answer was no. One otherwise unresponsive minimally conscious patient was able to answer five of six questions correctly. Many of the patients did not respond, and the paper is admittedly merely a proof of concept, since fMRIs are hardly affordable household appliances. But Laureys’ *Lancet* study published this month shows that inexpensive EEGs could work too.

Other far less expensive techniques may also help patients make the most of their residual communication powers. Zolpidem, a popular sleeping pill, seems to make a minority of minimally conscious patients immediately more alert. Preliminary evidence suggests that amantadine, a Parkinson’s drug, may be beneficial too. Many Parkinson’s patients enjoy dramatic symptom reduction through deep brain stimulation (DBS), a surgical procedure in which a fine wire is threaded to the mis-firing region in the brain and regulated through a cardiac-pacemaker-like device. This has also been shown to have potential benefits in some minimally conscious patients. Laureys recommended that Filipov’s family try to enroll him in a DBS trial after trying amantadine as well.

Before Laureys communicated this treatment plan to Filipov’s family, he and a team of doctors, neuropsychologists and Ph.D. students crammed into a small meeting room in Liège to review the results of his tests. The group peered at a large screen at the front of the room. The areas of Filipov’s PET scan that showed functional activity glowed with a purple aurora reminiscent of distant galaxies. The rest was as gray as wet concrete. Laureys discussed what the scans suggested and then asked a far deeper, more important question: “What is it like to be Mr. Filipov?”

No one in the room knew, of course. Nor could they say if Filipov himself knew. Eight months later, he has shown no improvement. But Sofiya, his wife, puts faith in the possibility that her husband’s essence remains. And inside her head, in a way, it does. Each evening as she prepares him for bed—as she checks his tubes, cleans out his sores, pulls the covers over his shoulders—she says silently to herself, “Good night, my dear, my love, good night.” She is working to keep two Valentines alive: the one lying before her, and the one working peacefully in the garden. ■