Walled up consciousness

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At the Cyclotron Research Centre of the University of Liège, the researchers in the Coma Science Group put new technology to work in order to determine a level for residual consciousness in cerebral injury patients and techniques for trying to establish contact with them. They showed that patients in minimally conscious states could feel physical pain. Around the borders of their research, a question about the status of consciousness as such is indicated. And this theme is also at the centre of a book co-edited by Steven Laureys.

Consciousness is a notion that lacks clarity, inasmuch as there is no real consensus about how to define it. Sometimes this dispute retards the unification of the major concepts involved, but sometimes it seems worth it in order to stimulate debate. This lack of consensus is a reflection of the degree to which consciousness is relatively badly understood. It is the weakness, although by the same token the richness of the book, Neurology of Consciousness(1) which will appear this fall, published by Elsevier Academic Press and edited by Giulio Tononi, of the School of Medicine
of the University of Wisconsin and **Steven Laureys**, research coordinator - FNRS and leader of the **Coma Science Group** at the **Cyclotron Research Centre** (CRC) of the ULg.

The book contains twenty-eight chapters. Each was written by eminent specialists concerned with the question of consciousness and the pathologies that affect it. The book maintains an alternation between the perspectives of clinical neurologists and researchers in neuroscience, sometimes combined in one person. A contrast between the two approaches is evident when one makes reference, for example, to the suggestions of Antonio Damasio, whose research is carried out from an almost philosophical perspective, and then to Hal Blumenfeld, whose concerns are more directly focused on his patient.

"For books like that, the hardest thing for an editor is to get great authors, who get asked to do lots of things, to participate in a project," Steven Laureys tells us. "Another thing was to try to get the book to have a guiding thread, to make sure it has a certain structure and logic that give it some unity." Bringing about the second objective might seem almost impossible because *Neurology of Consciousness* is not an article but a sort of kaleidoscope where over 30 authors look at consciousness from different angles, and do not all come to an agreement. One thing is certain: in the changing state of the assertions and the questions of the moment, this work gives us a very complete account of the state of our knowledge at present concerning consciousness and its neuronal correlates.

A few examples of the subjects covered: the neurological assay of consciousness, functional neuroimagery, the relationship between consciousness and attention, sleeping and dreaming, sleep-walking, general anaesthesia and consciousness, coma, cerebral death, minimally conscious states, consciousness and dementia, epilepsy and consciousness, "brain-computer" interfacing for paralyzed patients, neuroethics and disturbances of consciousness, the hippocampus, memory and consciousness, transitory amnesic syndromes, near-death experiences...


**Boundary zones**

Steven Laureys is a co-editor of this book and also the author of one of the essays in it, which draws our attention again to the research he is doing as director of the Coma Science Group inside the CRC. He also took an active part in the preparation of two other new articles, one published in *Nature Clinical Practice Neurology*, the other in *The Lancet Neurology*. Entitled, "The changing spectrum of coma" (2), the NCP Neurology article emphasized the contribution of functional neuroimaging (PET and fMRI), electroencephalography (EEG), cognitive evoked potentials and *magnetoencephalography* (MEG) to establishing a diagnosis that accounts for observed circumstances as regards a residual level of consciousness in patients who suffer grave cerebral lesions - particularly those who emerge from comas, and find themselves in a boundary zone between a vegetative state and a minimally conscious state.

Up to now, this kind of diagnosis was based on a subject's motor responses, which might be very limited, inconsistent, and easily exhausted. Under such conditions one should not be surprised at the conclusions of two studies, carried out in London by Professor Keith Andrews and in Austin by Dr. Nancy Childs: the diagnosis made "at the patient's bedside" is wrong a third of the time. What happens is that some patients are declared to be in comas or vegetative states, when in fact they are in *minimally conscious states* (near non-relational)
or suffering from LIS, locked-in syndrome (see the inset entitled "Trapped in a paralized body"). We recall that in such a state, the subject is normally aware, but completely immobile.

Steven Laureys points out that a study carried out for the French association ALIS(3) showed that in more than half of all cases, families rather than medical staff become aware of signs of consciousness in LIS patients. On average, 78 days pass between the onset of immobility and the diagnosis of this syndrome.

The delicate point is the distinction between a vegetative state and a minimally conscious state. The second was for long reduced to the former, but was shown as something separate in 2002, in the work of Joseph Giacino of the New Jersey Neuroscience Institute. In a minimal state of consciousness the subject is incapable of following simple instructions in a consistent manner, but the subject is aware of his or her environment. For example, the subject might carry out voluntary movements from time to time, or smile at loved ones, or only at them. However, the subject here might never manage to communicate his or her thoughts. In contrast to the patient who is minimally conscious, a patient in a vegetative state is not conscious of the outside world.

"In clinical practice we are faced with a gray zone, since the limits of the two clinical profiles are difficult to distinguish through an examination of motor response," Laureys explained. "So we have an obligation to
develop objective markers for consciousness that are irrefutable, especially inasmuch as a diagnosis of minimal consciousness, in terms of the patient's future and his or her chances of recovery, is more favorable."

(3) Locked-in Syndrome Association.

**Match point**

The necessity of shedding light upon this mystery is even more pressing, since Steven Laureys and Mélanie Boly, another researcher in the Coma Science Group, had shown in 2006(4) (in collaboration with neuropsychologist Adrian Owen, of the University of Cambridge) the presence of residual consciousness in a young English female patient, 23 years of age, someone who, based on clinical criteria had fit the profile of a person in a vegetative state.(5) The basis for this discovery was fMRI (functional Magnetic Resonance Imagery) as well as a change in methodology. Up to that time all experiments based on patients in altered states of consciousness relied on passive forms of stimulation - noises, pains, saying the subject's name, etc. These attempts produced interesting results that were nonetheless hard to interpret. In other words, cerebral regions were experiencing activity without anyone realizing that it had to be the result of either automatic behavior or conscious processes.

In order to solve this puzzle, researchers from the universities of Liège and Cambridge thought up the following experiment: to speak phrases that make sense, such as "I put some milk in my coffee," and some that don't, like "I put milk in my shoe," in the presence of patients in altered states of consciousness, and record their cerebral activity via fMRI. Why do it this way? Because one must understand the phrases in order to distinguish them from each other, and to bring into play the cerebral regions that would normally handle each phrase. The study examined 60 patients. The result was that activation of cerebral regions recorded did not indicate any coming to awareness of the difference between phrases that made sense and those that didn't. With one exception, just the same!... As recorded by fMRI the brain of the young English woman mentioned above "lit up" in a way much like that of normal subjects put through the same experiment.
In Steven Laureys’ view, connection to appropriate cerebral regions in response to statements that make sense or that don’t indicates conscious behavior, but does not absolutely prove its operation. Thus the group of researchers decided - and here we reach a methodological turning point - to ask the young woman, verbally, to try to perform a task of mental imagery. Two sequences were chosen: a request to imagine that she was playing tennis; and a request to imagine that she was walking through her house.

Once again, the English patient provided a surprise, because the cartography of her cerebral activity coincided perfectly with that measured in about 30 healthy volunteers - activation of pre-motor areas during the attempt to mentally imagine playing tennis, in a network that included among other areas the parahippocampic regions (during the second task, that of imagining walking around in one’s house. Today this patient has definitely regained consciousness and is able to communicate with those around her. It is striking that for the first time, a preserved consciousness was demonstrated in a person diagnosed as being in a vegetative state according to regular clinical standards. We have the right to go further and ask the question: is it not the case that in the course of the experiment, fMRI imagery by nuclear magnetic resonance has revealed a sign of a prognosis, of the future changes in the patient's state?

In the light of this discovery, and considering the diagnostic errors that have occurred, it appears at this point indispensable, for obvious ethical reasons that hospitals and other medical institutions should have available the means to detect signs of residual consciousness in cerebral injury victims, and personnel should know how to try to establish communication with them. That is what is recommended by Steven Laureys and Mélanie Boly in their article on *The changing spectrum of coma.*

(5) The patient was on the edge of minimally conscious state - she could for instance briefly stare at a moving object.

Direct dialogue

New techniques of functional neuroimagery provide a way to measure brain activity at rest, during a "passive stimulation", or (even more revealing) in response to an "order". These techniques are marking out a new path in the direction of more rigorous diagnoses, differing in some cases from those which are based on clinical criteria alone. In addition, there are indications that these techniques will make it possible to enter into a dialogue with patients that still have residual consciousness, but are unable to express themselves through words or gestures. "Allowing them to exercise their autonomy, making it possible for them to communicate their desire to live or to die, as well as their wishes regarding their own treatment, all this is in accordance with an essential principle of bioethics," according to Steven Laureys. "For too long, doctors have underestimated residual faculties and the quality of life of certain cerebral injury patients; they have assumed authority over them and have made decisions in their place."

Researchers at the ULg and the University of Cambridge wanted to use real time fMRI in order to attempt to communicate with the young English woman. The idea was to ask her a series of yes or no questions. However, fMRI is at this time not sufficiently precise to allow making a distinction between a specific cerebral activation profile for "yes" and a different one for "no". So, the neuroscientists arranged a code for communicating with this patient: they asked her to imagine that she was playing tennis when she wanted to say "yes", and that she was walking through her house when she wanted to signal "no".

This attempt failed. Why? According to Steven Laureys, the failure was caused by the experimental conditions. In fact, the patient had to be transferred in an ambulance to a laboratory where the necessary equipment was located in order to participate. She was tired when she got to the site of the experiment, and this ruined the chances of success and a positive result. Because of this problem, the possibility of using the much less constraining technique of cognitive evoked potentials was considered. The project was started up, then abandoned, because the patient had in the intervening period recovered the ability to communicate via small movements of the feet.

Just the same, the ULg team continued to work on these problems. A soon-to-appear issue of the journal Neurology will contain an article showing that the technique of cognitive evoked potentials is a means of detecting signs of consciousness in cerebral injury patients that is portable, cheap, and reliable (primary author: Caroline Schnakers, researcher in the Coma Science Group). Work is also underway to validate this technique as a means of communication between these cerebral injury victims and the outside world.

Signs of consciousness

Some time ago, Fabien Perrin, a researcher at the Université Claude Bernard (Lyon 1) who works with the Coma Science Group, proposed a technique using cognitive evoked potentials in which one compares the cerebral electrical activity of a patient while hearing his or her own first name spoken, with that obtained when
another name is spoken. Despite the promising nature of this method, it appeared finally that it did not provide a good "marker" or sign of consciousness, especially because the cerebral activations recorded after the speaking of a person's first name could after all be produced by automatic processes, and be unrelated to the existence of consciousness.

Since then the concept of an active paradigm has been substituted for passive stimulation. At Liège, cerebral injury victims were asked to listen for one particular first name out of a list of eight. "If we ask patients to focus on the name Jacques, and if we get a different cerebral activity profile when the subject hears that name and only that name, we must conclude that the request was understood and to that extent, the patient was conscious," Steven Laureys argues.

The results of the test were all negative for patients in a vegetative state, but positive for 9 of 14 patients declared to be in a minimally conscious state in terms of classic diagnostic criteria. Even individuals who only demonstrated the ability to look steadily at a particular object or to follow an object with their eyes - behavioral indicators of consciousness that are still quite controversial - were able to perform the task, thus demonstrating that their consciousness persisted.

Today, neuroscientific research in Liège is being undertaken with the objective of successfully employing the cognitive evoked potentials method as a means of communication. The director of the Coma Science Group
explains it this way: the first problem has to do with testing the method by asking the patient ordinary questions. For example, we might ask, "Do you hear a man’s voice or a woman’s voice?" If the method appears to be effective and dependable, we can ask other questions that actually matter, such as whether the subject is experiencing physical or mental suffering, whether that person wishes to live or not, etc. As in the experiment with the young English woman, the patient’s responses have to be "formulated" indirectly, that is, via the request to imagine one thing for yes and another thing for no.

Most recent advances in the scientific approach to altered states of consciousness depend upon single case studies or on a very small number of cases. Steven Laureys reminds us that only multi-centred studies of large patient populations can authorize the definitive acceptance of diagnostic and communicative tools that are tested, and enable them to be used widely on patients whose state and level of consciousness is in question.

**Not insensible to pain**

On September 14, 2008, *The Lancet Neurology* published an article produced by the researchers of the Coma Science Group and the Department of Neurology of the ULg: *Perception of pain in the minimally conscious state with PET activation : an observational study*(6). The authors breach the delicate question of pain in patients judged to be in a vegetative state or in a state of minimal consciousness. In order to approach this question they have measured, using positron emission tomography (PET), the cerebral activity of injury victims and healthy subjects in response to stimuli judged to be painful by the latter group - electrical stimulation of the median nerve in the wrist.
In normal subjects, activation of these areas was observed: cerebral trunk, the thalamus and the somesthesic cortex, as well as hierarchically superior areas: the anterior singular cortex, cortical insula, frontal and parietal regions...Contrary to an idea that had been widely accepted up until this time, brain activation was recorded among patients considered to be in a vegetative state. Beyond the cerebral trunk, not involved in the injury leading to this pathology, the thalamus and the primary somesthesic cortex "lit up". A connectivity study revealed however that this area of the cortex was functioning as an isolated island, without any connection to the hierarchically superior cerebral regions. "What meaning should we give to these results? asks Steven Laureys. "Can we be conscious of neuronal activation that does not go beyond the primary regions? The controversy has been going on since Nobel Prize winner Francis Crick raised the problem in 1995 in the journal Nature."

The most instructive case was that of the patients judged to be minimally conscious. Nociceptive stimuli generated in their brains patterns of cerebral activation very similar to those of normal subjects. In other words, they can feel pain. "Therefore we need to review our approach; they should be given pain medication, particularly when they are receiving care," Steven Laureys concludes. This reality has consequences on both the ethical and the therapeutic level.