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► To cite this version:

Benjamin Rohaut, Frédéric Faugeras, Lionel Naccache. Neurology of consciousness impairments. Brain Disorders in Critical Illness: Mechanisms, Diagnosis, and Treatment, 2013. hal-01865867

HAL Id: hal-01865867

<https://hal.science/hal-01865867>

Submitted on 9 May 2024

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Chapter

7

Neurology of consciousness impairments

Benjamin Rohaut, Frédéric Faugeras, and Lionel Naccache

SUMMARY

Probing consciousness in non-communicating patients at bedside can be very challenging. In this chapter, we describe some of the key goals, caveats and pitfalls of the evaluation of consciousness in non-communicating patients. First, we will address the importance of neurological and behavioral examination, and then briefly outline the current developments of functional brain-imaging tools able to provide important additional evidence. Current approaches include both: (i) active paradigms in which a patient is asked to perform a specific cognitive task; (ii) “resting state” conditions in which the spontaneous patterns of brain-activity can be instructive of patients conscious state; and (iii) passive paradigms in which cortical functional connectivity can be explored by recording, for instance, EEG in response to focal transcranial magnetic stimulation (TMS) pulses.

Introduction

In this chapter, we intend to summarize the key goals, caveats, and pitfalls of the evaluation of consciousness in non-communicating patients, and in particular in awake patients in whom this issue is the most difficult to solve. Distinguishing minimally conscious (MCS) and conscious states from vegetative (VS) and comatose states can be extremely challenging at bedside. We will first address the importance of neurological and behavioral examination, and then briefly outline the current developments of functional brain-imaging tools able to provide important additional evidence. Far from being systematically categorical, we will also try to provide the reader with the current weights of (un)certainly associated with each clinical sign or neurophysiological measure mentioned in this chapter.

Caveats and pitfalls of consciousness examination

Examining an awake, eyes open, and yet non-interactive patient with no clear evidence of consciousness can be a very awkward situation. For instance, both MCS and VS patients can perform behaviors such as laughing, crying, grimacing, and they can demonstrate withdrawal movements to nociceptive stimulation. All these rich behavioral, and sometimes emotional, manifestations are difficult to interpret in relation to the conscious status of the patient, and the observers can easily overestimate them as univocal evidence of a voluntary conscious state. This problem is frequent in clinical practice, and can be the source of contradictory interpretations within a team of caregivers, and with patients’ relatives. Assessing consciousness and/or residual cognitive abilities of a disorders of consciousness (DOC) patient obviously requires neurological expertise. We will adopt here the classical definition of consciousness as a “state of full awareness of the self and one’s relationship to the environment” [1].

Do not overestimate consciousness

Visual fixation

Visual fixation is defined by at least two consecutive ocular saccades to a target followed by a fixation longer than two seconds (see for instance the Full Outline of UnResponsiveness (FOUR-score) [2] and the revised version of the Coma Recovery Scale (CRS-R) [3] (see Tables 23.2 and 7.1). It is admitted that visual fixation does not require conscious access to the visual target, given that it can be observed for instance in some patients with cortical blindness (“blindsight” phenomenon), but it is still not clear

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Table 7.1 Coma Recovery Scale – Revised

<ul style="list-style-type: none"> • AUDITORY FUNCTION SCALE <ul style="list-style-type: none"> 4 – Consistent movement to command* 3 – Reproducible movement to command* 2 – Localization to sound 1 – Auditory startle 0 – None
<ul style="list-style-type: none"> • VISUAL FUNCTION SCALE <ul style="list-style-type: none"> 5 – Object recognition* 4 – Object localization: reaching* 3 – Visual pursuit* 2 – Fixation* 1 – Visual startle 0 – None
<ul style="list-style-type: none"> • MOTOR FUNCTION SCALE <ul style="list-style-type: none"> 6 – Functional object use** 5 – Automatic motor response* 4 – Object manipulation* 3 – Localization to noxious stimulation* 2 – Flexion withdrawal 1 – Abnormal posturing 0 – None/flaccid
<ul style="list-style-type: none"> • OROMOTOR/VERBAL FUNCTION SCALE <ul style="list-style-type: none"> 3 – Intelligible verbalization* 2 – Vocalization/oral movement 1 – Oral reflexive movement 0 – None
<ul style="list-style-type: none"> • COMMUNICATION SCALE <ul style="list-style-type: none"> 2 – Functional: accurate** 1 – Non-functional: intentional* 0 – None
<ul style="list-style-type: none"> • AROUSAL SCALE <ul style="list-style-type: none"> 3 – Attention 2 – Eye opening without stimulation 1 – Eye opening with stimulation 0 – Unarousable

** Denotes emergence from minimally conscious state (MCS).

* Denotes MCS.

whether visual fixation needs primary visual cortex, or may be mediated through the superior colliculus pathway [4]. In the CRS-R the presence of this behavior rules out the diagnosis of VS, while it is not the case according to the Multi-Society Task Force on the persistent vegetative state (PVS) [5], and to the Royal College of Physicians' report [6]. Accordingly, a recent PET study did not report any difference in brain metabolism between VS patients with preservation of visual fixation and VS lacking this behavior. Similarly, both groups shared the same 1-year outcome [7]. From a theoretical point of view, a long-lasting intentional behavior is a gold standard criterion of

consciousness [8]. As a consequence, one may consider that a fixation sustained over several seconds belongs to this category of conscious behaviors. However it is highly notable that fixation is dependent of the continuous presence of the visual target, and may therefore correspond to a continuously stimulated visuomotor reflex, rather than to a long-lasting internally generated behavior. A patient able to fixate a target, and to maintain fixation on instructions even after the disappearance of the stimulus, and even if presented with competing stimuli, would demonstrate a much stronger evidence of conscious processing.

Blink to threat

In contrast with auditory startle – or maybe also of visual fixation – blink to visual threat (BVT) probably requires cortical processing [9–11]. Functional integrity of primary visual cortex is a mandatory stage, but note that patients with cortical lesions located away from cortical pathways (e.g., frontal or parietal) can lose BVT [10]. The Multi-Society Task Force stated that the diagnosis of persistent VS (PVS) should be extremely cautious in the presence of BVT [5]. However, BVT is not a criterion taken into account to distinguish VS from MCS [12]. In terms of consciousness recovery, BVT does not seem to be a predictor of a better outcome [11]. Therefore, while BVT requires richer cortical processing than visual fixation, it does not guarantee a patient to be conscious, or even minimally conscious. However, presence of a BVT requires the examiner to be even more cautious to look for additional signs of cortical integrity, and for the presence of more reliable signs of consciousness. To close with that sign, note that it is highly important not to confound it with corneal reflex elicited by an air puff caused by target motion.

Oro-facial behaviors

Oral reflexes such as chewing, teeth grinding, or swallowing are not problematic but other behaviors such as facial movements (smiles or grimaces), tears, grunting, or groaning sounds could be easily considered as conscious behavior. In this case, a possible adapted emotional behavior should be carefully searched for, and for example if a patient cries only in the presence of one of his or her relatives, one has to look for the presence of more univocal signs of MCS or of conscious state. Clearly, current knowledge is insufficient to provide any strong claim about these complex and sometimes specific emotional responses.

Additional signs

Noxious or noisy stimuli can elicit arousal responses, with autonomous reaction (e.g., increases of respiration and heart rates), grimaces or limb movements, and cause the extensor or flexor withdrawal of a limb. None of these signs should be confounded with a conscious behavior. Similarly, gaze or head orientation toward a loud sound is considered as reflex, and does not exclude VS [6,12]. In the same vein, grasping reflex and triple withdrawal should not be confounded with intentional movements.

Do not miss consciousness

While it is crucial not to overestimate consciousness (the “false positive” issue), it is even more dramatic to miss conscious patients. However, many factors can lead to such an error. Consider a conscious but non-communicating patient. On the basis of clinical observation and testing, consciousness is never probed as a “pure” and isolated process but rather in relation to many distinct cognitive abilities, to sensorimotor processes, and to mental contents [13]. Therefore, trivial or subtle impairments in any of those abilities, processes, or contents may lead to the absence of clinical evidence of conscious processing in a conscious but severely disabled patient. Illustrations of “trivial” impairments correspond to deaf, blind, or paralyzed conscious patients. Note that even these “trivial” or “easy” cases are not that easy to deal with. An astonishing study on locked-in syndrome (LIS) patients reported that the mean time of LIS diagnosis since the initial event was around 2.5 months [14]. One has to take into account that at the initial stage of a massive brainstem stroke, patients are usually in a genuine comatose state during a variable period. Recovery of consciousness from this initial comatose state may be missed if clinical evaluations are not repeated very regularly. Therefore, this long diagnostic delay emphasizes the need of repeating these evaluations, and of varying the ways of assessing consciousness.

Visual pursuit

When looking for visual pursuit, the use of the patient’s own eyes (and even own face) as a visual target seems to be the most powerful stimulus, probably due to self-referencing (e.g., the “cocktail party effect” which corresponds to the powerful ability to react to one’s own name when heard in a complex auditory scene) [15]. Indeed, the utilization of a mirror

to detect visual pursuit has been shown to be more sensitive than any other visual stimuli (other faces, contrasted, or colored targets) [16]. As mentioned below, visual pursuit is one of the most informative signs to classify a patient as MCS or conscious.

Cognitive impairments

Less trivial situations are encountered in DOC patients suffering from aphasia, or from massive anterograde amnesia, or severe dysexecutive syndrome impacting attentional, working memory, and strategic abilities. In many of the clinical tests used with DOC patients, one may miss some form of conscious processing. Obviously, there is no easy solution to this point. However, a rigorous examination using both verbal and non-verbal instructions and stimulations (e.g., imitation or automatic behavior) may help to overcome some of these limitations. Additionally, systematic assessment of any possible movement (hands, feet, eyes, blinks, mouth and tongue movements) will maximize the probability to detect an intentional response. Repetition of clinical evaluations is particularly important in the “acute” stage (first days and weeks), given the presence of frequent and major fluctuations in arousal and also possibly in consciousness, in particular in MCS patients.

Neglect

Attentional disorders such as spatial hemi-neglect – observed in patients with a non-dominant hemispheric lesion – could explain both perceptual difficulties (culminating in the neglect of instructions delivered in the neglected hemi-space) and behavioral responses impairments (motor neglect) in the absence of any central or peripheral motor neurons dysfunction. Patients have to be stimulated and observed from both sides (right and left).

Aphasia

Patients with dominant hemispheric lesions could be expected to have language impairments. In this case intentional and voluntary behaviors should be tested using non-verbal communication and instructions. This consideration is not yet implemented in standard behavioral scales, but most verbal commands could be delivered by gestural description. For example the examiner can show the movement of a handshake to the patient with one hand, while testing the patient’s response with the other hand [17].

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Taken together, these elements contribute to explain that up to 40% of patients considered as VS demonstrate univocal evidence of MCS when examined by expert teams used to current detailed scales [18].

Finally, one has to be aware of the possible persistence of sedative agent effects. Electroencephalography and, most importantly, pharmacological measurements and pharmacological antagonistic tests (e.g., for benzodiazepines and morphinic agents) are sometimes extremely valuable here, in particular in comatose patients. Similarly one has to systematically check body temperature and hemodynamic constants when examining a DOC patient, and in particular when examining a comatose patient and a suspicion of brain death.

Overview of clinical and behavioral assessment of consciousness

Consciousness first requires a minimal level of arousal, the absence of which is observed in comatose states.

Arousal and basic neurological assessment

Arousal depends on the ascending arousal system distributed within the tegmentum of the upper pons and midbrain, and in paramedian diencephalic structures along with the basal forebrain. These structures widely project onto the cortex including the thalamo-frontoparietal network which plays a major role in consciousness, as theorized for instance in the conscious “global workspace” model [19]. Therefore coma can result from diffuse bihemispheric lesions (e.g., anoxia, trauma) or dysfunction (e.g., status epilepticus), or from focal brainstem lesions affecting in particular the pontomesencephalic tegmentum, or paramedian diencephalic structures bilaterally.

In front of a comatose patient, neurological examination aims at three major goals: (1) to confirm the diagnosis of comatose, and therefore to discard differential diagnoses such as locked-in syndrome, for instance; (2) to estimate the functional depth of the comatose state from profound and poorly reversible comatose to “diencephalic” comatose associated with a better prognosis of consciousness recovery; and (3) to provide potential cues to the etiological diagnosis (e.g., presence of discrete palpebral myoclonus in a status epilepticus; fever and meningitis syndrome in an acute meningo-encephalitis). Here, we will only underline the “functional depth” issue: basically, comatose is probably the clinical condition in which Hughlings Jackson’s seminal concept of the central nervous

system (CNS) described as a “hierarchical vertical axis” is the most relevant [20]. According to Jackson theory, the higher a CNS region is, the more it controls and inhibits the CNS regions located below it, and the weaker it is to CNS “aggressions.” This famous conception was the first to provide a satisfactory account of the positive signs secondary to a CNS lesion (e.g., disinhibition of medulla reflexes associated to primary motor cortex lesion). As a consequence, examination of brainstem reflexes in relation to the vertical location of their neural substrates within this hierarchical axis plays a major role: the lower reflexes are usually the most resistant, and one can frequently observe a gradient of reflexes preservation. This “neo-jacksonian” view inspired for instance the scoring of the famous Glasgow Coma Scale and its variants including brainstem reflexes scoring (such as the Glasgow–Liège scale) or the more recent FOUR-score (see Tables 7.2 and 23.2): the upper reflexes are more weighted than the inferior ones, and the scoring of motor reactivity to stimulation also follows this supero-inferior gradient: a decortication response is scored better than a decerebration response. As a matter of fact it is extremely rare to observe the presence of oculo-cephalic reflexes in a comatose patient in whom oculo-cardiac reflex would be abolished. Combining all these observations with the inspection of pupil diameter, reactivity, and symmetry, and with the spontaneous breathing pattern (e.g., from Cheynes–Stokes dyspnea to apneustic or ataxic respiration) usually allows definition of the “functional depth” of comatose, and to monitor it

Table 7.2 Glasgow Coma Scale

- Eye response
 - 4 – eyes open spontaneously
 - 3 – eyes opening to verbal command
 - 2 – eyes opening to pain
 - 1 – no eyes opening
- Motor response
 - 6 – obeys commands
 - 5 – localizing pain
 - 4 – withdrawal from pain
 - 3 – flexion response to pain
 - 2 – extension response to pain
 - 1 – no response to pain
- Verbal response
 - 5 – oriented
 - 4 – confused
 - 3 – inappropriate words
 - 2 – incomprehensible sounds
 - 1 – no verbal response

across time in a given patient. When this detailed clinical examination does not fit with this functional gradient view, one has to look for focal lesions within the brainstem, or for additional factors which may interfere (e.g., drugs, metabolic dysfunctions).

Consciousness assessment

A more subtle alteration of consciousness is the vegetative state, which is characterized by preserved wakefulness [21] – even if circadian rhythms may not be strictly normal [22] – in the absence of any purposeful behavior and of any sign of intentional reactions to the external environment. Note that VS is, by definition, a clinical syndrome and not a specific condition. For this reason, and in order to avoid too radical interpretations of patient's cognitive state only based on behavioral observations, a group of experts recently proposed the 'Unresponsive Wakefulness Syndrome' expression to describe VS [23]. The mere existence of VS demonstrates that wakefulness and consciousness can be dissociated, and therefore that they cannot be identified one with another.

Consequently, several scales have been created in order to distinguish VS patients from MCS patients. All these scales enable the clinician to administer various language, auditory, visual, somatosensory, and noxious stimuli and judge whether a patient's responses are indicative of conscious processing. Stimulations have to be repeated within the same examination session, in particular when spontaneous behavioral fluctuations are frequent. It is also important to gather all sources of observational evidence, including various caregivers and relatives who deserve a special consideration: while not being experts of behavioral assessment and being frequently the most motivated to interpret the behavior of their companion as conscious, they are also the most meaningful, or as Damasio phrases it: the most "emotionally competent" to the patient. It means that they are sometimes the most active stimuli to elicit a patient's richest behaviors. It is therefore sometimes useful to include the relatives to some stages of consciousness assessment. Furthermore, confounding variables (sedation, noisy environment, physical limitations) must be reduced to a minimum.

All these scales share a common design, combining: (1) items which appreciate coma exit [e.g., item 2 of the Wessex Head Injury Matrix (WHIM); arousal scale of the Coma Recovery Scale Revised (CRS-R)], with (2) items (see Table 7.1) probing purely reflexive behaviors integrated at a brainstem level and

indicative of a vegetative state if isolated despite repeated assessment (e.g., item 3 of the WHIM, or item 2 of the auditory function scale of the CRS-R which imply integrity of the colliculi and the tectospinal tracts), and with (3) items exploring behaviors requiring cortical integration and sustained activity, properties which are considered as specific to conscious processing (item 18 of the WHIM or items 2 and 3 of the vision function scale of the CRS-R which imply integrity of parietal and frontal eye fields area).

Note that a recent study explored a clinical sign previously described and emphasized by Plum and Posner as a marker of preserved cortical integration. The authors assessed the fast nystagmic return to mid-position of the eyes after ipsilateral tonic deviation towards the cold water-irrigated ear during testing of the oculovestibular reflexes [24]. This saccadic return – probably mediated by a long-range fronto-parietal cortical network – predicted consciousness recovery in a group of 26 clinically defined VS patients. Thirteen out of these 26 patients ultimately recovered consciousness. All patients who recovered consciousness presented a fast-component of nystagmus compared with only one of 11 patients who remained unconscious.

Using cognitive neuroscience to look for consciousness in patients

A complementary approach to clinical neurology originates from cognitive neurosciences of consciousness. Although the issue remains debated, two decades of experimental and theoretical work have led to the characterization of psychological and neurophysiological attributes that may be unique to conscious processing. Many cognitive processes may occur unconsciously either in conscious subjects, in visual neglect patients or related patients, and in non-conscious patients [25–27], reaching such complex levels as abstract semantics, phonological or emotional processing. Still, three properties seem to be exclusively associated with conscious processing of reportable mental contents [19]: (1) active maintenance of mental representations in working memory; (2) strategic processing; and (3) spontaneous intentional behavior. Similarly, while unconscious processing may engage multiple isolated cortical areas, neural signatures of conscious processing are defined by late and long-lasting brain activations that mobilize long-distance coherent thalamo-cortical networks, particularly involving bilateral prefrontal, cingulate, and parietal areas [25,28].

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On the basis of these studies, original experimental “active” paradigms can therefore be designed in order to improve our ability to diagnose consciousness in non-communicating patients, beyond clinical evaluations. For instance, at the behavioral level, Bekinschtein and colleagues [29] capitalized on the working memory property mentioned above, and used an eyeblink conditioning paradigm in which a tone stimulus can be paired with an air puff delivered on the cornea. Delayed conditioning – where the conditioned stimulus and the unconditioned air puff overlap in time – does not require conscious processing of the stimuli. In contrast, trace conditioning where a

temporal gap is inserted between the two stimuli seems to require conscious processing in working memory [30]. Interestingly, they showed that some clinically defined VS patients were able to demonstrate both conditioning and trace conditionings. Functional brain-imaging approaches are also emerging [31]. For instance, Owen and colleagues [32] probed with functional magnetic resonance imaging (fMRI) the active maintenance of task-instructed cognitive tasks, such as the ability to perform motor or spatial imagery tasks for an extended duration of 30 seconds (see Figure 7.1). Using this approach on 54 patients, they could identify five patients able to willfully modulate

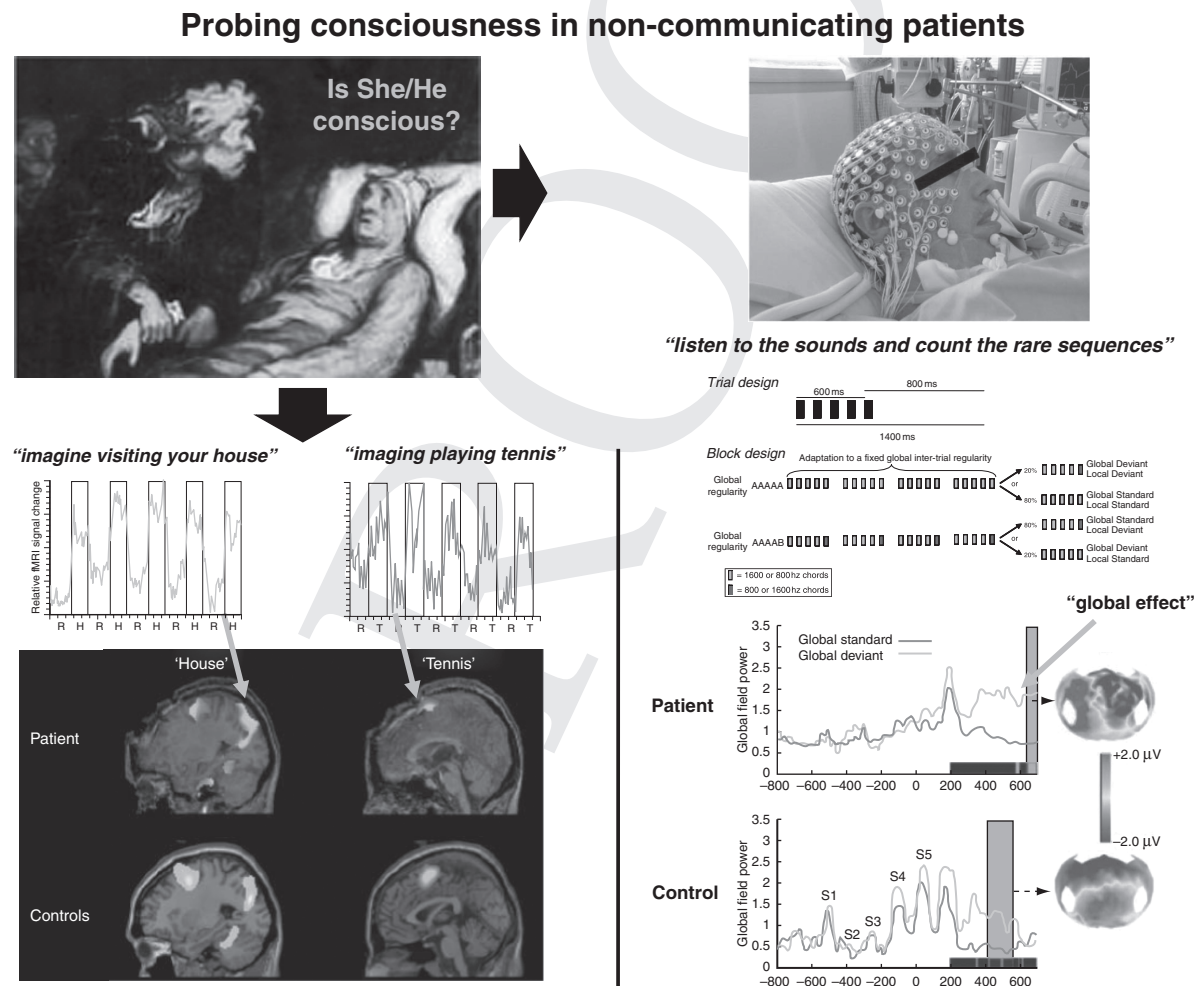


Figure 7.1 Two recent illustrations of active paradigms using functional brain imaging (EEG and fMRI) to probe consciousness in non-communicating patients. The mental navigation and mental motor imagery tasks designed by the group of Owen (left) allow the detection of sustained fMRI BOLD activations in cortical networks specific to each of these two mental imagery tasks [32]. The global regularity auditory task designed by the group of Naccache [42] allows the detection of late and sustained P3-like EEG responses when patients detect the occurrence of global regularity violations. In these two paradigms, the presence of a significant effect is highly suggestive of conscious processing.

their brain activity [33]. Among these five patients, two were clinically classified as VS. In one clinically MCS patient, fMRI could be used to define an arbitrary code and communicate a single piece of information (a yes/no answer), while such a communication was not possible behaviorally.

In parallel to such fMRI experiments, EEG paradigms may constitute a highly promising research direction for at least two reasons. First, EEG is a time-resolved tool able to sample brain activity at the millisecond scale. This offers a unique opportunity to monitor the flow of consciousness and eventually to interact with the patient in real time. Second, given that EEG is a non-invasive technique, has a relatively low cost and can be recorded at bedside, one may ultimately design dedicated systems for recurrent and even continuous daily recording of brain activity in patients. In that respect, EEG monitoring seems more likely to truthfully reflect VS and MCS patients' complex fluctuating states than a single fMRI scan lasting a few tens of minutes. Schnakers and colleagues showed the utility of using active EEG paradigms to probe voluntary brain responses to stimuli. They could confirm the presence of conscious processing in a locked-in syndrome patient and in clinically defined MCS patients [34].

Active paradigms are important because they provide a way to probe various cognitive processes by looking for their specific neural signatures. However, this very same property confers a severe limitation: if for any reason the patient does not engage in the cognitive performance requested by the experimenter, then the test will fail to identify this patient as conscious even if she or he is conscious. If the patient is not awake during the task (e.g., confusional states, sleep cycles), or is conscious but cognitively impaired (aphasia, amnesia, poor working memory, dysexecutive syndrome), or refuses to obey the instructions, active paradigms will fail to diagnose this conscious patient as conscious.

For all these reasons, it is therefore useful to develop additional neurophysiological measures which could escape some of the limits of active paradigms. One promising path of research consists in recording brain activity in the absence of external stimulation. This approach is grounded on the seminal work of Raichle's group on the "resting state" or "default mode" (DM) networks aims at exploring the spontaneous patterns of brain activity [35]. One of these DM networks include mesial cortical areas, including the precuneus and the posterior cingulate cortex and seems to be related to self-consciousness and to

introspective processes. Some key regions of this network may contribute to a general "projective system" enabling the individual to escape from immediate contingencies, e.g., projection in time (past and future), in space (mental navigation), and in mind (theory of mind) [36]. Functional MRI recordings of these DM networks seem to be informative about the level of consciousness in non-communicating patients [37]. It is important to note that while recording of resting state activity is not complex as compared with active paradigms, the selection of the most relevant analyses to be done on these raw data still remain a subject of research. Resting state measurements were initiated with fMRI but recent electrophysiological works pave the way to explore more finely these dynamics [38].

Lastly, a very elegant method combining EEG and TMS offers an easy way to probe the functionality of long-distance cortico-cortical networks at bedside without relying on a specific cognitive process. The principle consists in recording EEG with a fairly good spatial sampling over the whole cortex (from 32 up to 256 electrodes) immediately after the delivery of a single pulse of TMS over a local region of the cortex. By observing both early local, but most importantly late and sustained global responses, in particular over fronto-parietal regions, one may probe the existence of a functional "global workspace" network. First applications of this method during sleep [39], under midazolam anesthesia [40], and in DOC patients [41] strengthen its ability to isolate neural correlates of long-distance coherent cortical activities related to conscious states.

The 'local global' test of consciousness

We will now focus on one "active" paradigm which provides a very specific (but not a very sensitive) way to probe consciousness in patients. We recently designed an auditory paradigm that evaluates the cerebral responses to violations of temporal regularities [42]. Local violations due to the unexpected occurrence of a single deviant sound amongst a repeated train of standard sounds led to an early response in auditory cortex, the mismatch negativity (MMN) ERP component, independent of attention and of the presence of a concurrent visual task. On the other hand, global violations, defined as the presentation of a rare and unexpected series of five sounds, led to a late and spatially distributed response that was only present when subjects were attentive and aware of the

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violations (P3b ERP component). We could detect the global effect in individual subjects using fMRI and both scalp and intracerebral event-related potentials. Since the original publication [42], we reported the results obtained in 73 recordings of non-communicating patients (32 recordings in MCS, 28 VS, and 13 in conscious patients) and confirmed that only conscious individuals (MCS or CS) presented a global effect (see Figure 7.1). When focusing on the group of VS patients, we confirmed the absence of global effect in the vast majority of patients, but identified two patients showing this neural signature of consciousness [43,44]. Interestingly, these two patients showed unequivocal clinical signs of consciousness within the 3–4 days following ERP recording, strongly suggesting they were misclassified as VS due to limitations of clinical examination. Taken together, these observations were highly suggestive that the global effect might be a signature of conscious processing, although it can be absent in conscious subjects who are not aware of the global auditory regularities.

Conclusion

In this non-exhaustive overview, we tried to emphasize the crucial importance of expert and informed clinical examination. Currently, up to 40% of patients may be misdiagnosed, most often considered as VS while they show univocal behavioral evidence of conscious or minimally conscious states (e.g., sustained visual pursuit in the mirror test of the CRS-R). It is probably the case that such a high error rate also reflects a prevailing opinion that being able to distinguish VS from MCS does not impact so much on the way we manage these patients. While this opinion highlights our weak therapeutic efficacy in these patients, in particular in chronic situations, we think it is important to remember that recognizing an MCS from VS is crucial for the patient, and for the relatives and caregivers. Note also that MCS patients seem to have a better functional prognosis outcome than VS patients [45]. Several new and valuable clinical scales and procedures are now increasing the power and standardization of consciousness probing in these patients. In parallel to this emphasis on clinical observation, we also tried to briefly show some of the very promising functional brain imaging tools (in particular EEG, fMRI) taking advantage of the psychological properties of conscious processing to directly look for them in brain activity rather than in behavior. We think such tools will be integrated with the clinical assessment in these difficult

situations. Finally, in identified conscious but non-communicating patients, current developments of EEG-based brain–computer interfaces may constitute a major therapeutic improvement by restoring to these patients the ability to “action their mind.”

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