Externalization of Consciousness. Scientific Possibilities and Clinical Implications

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Abstract The paper starts by analyzing recent advancements in neurotechnological assessment of residual consciousness in patients with disorders of consciousness and in neurotechnology-mediated communication with them. Ethical issues arising from these developments are described, with particular focus on informed consent. Against this background, we argue for the necessity of further scientific efforts and ethical reflection in neurotechnological assessment of consciousness and 'cerebral communication' with verbally non-communicative patients.

Keywords Consciousness · Disorders of consciousness · Neurotechnology · Informed consent

Contents

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1 Introduction

The instrumental investigation of consciousness has witnessed an astonishing progress over the last years. Different neurotechnological tools and methods have been developed in order to assess residual consciousness in patients with disorders of consciousness (DOCs). Functional neuroimaging technologies, such as electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), single photon emission tomography (SPECT), event-related potentials (ERPs), magnetoencephalography (MEG), magnetic resonance spectroscopy (MRS), and transcranial magnetic stimulation (TMS) (Laureys et al. 2009), give researchers the possibility to see what happens in the brain during the execution of particular tasks. These emerging neurotechnologies are very promising in regard to the study and the treatment of DOCs. Notably, identification of activated brain areas and real-time observation of cerebral activity potentially allow a new form of technology-based communication in the absence of overt external behavior or speech, thus going beyond the behavioral manifestation of awareness (Evers and Sigman 2013).

It is important to clarify and to assess some issues emerging from this kind of communication. First of all is the relationship between brain activity, which is the specific object of the neuroimaging investigation, and awareness: how to judge when the first implies the second. Another important issue concerns the kind of consciousness that patients with DOCs retain (e.g., can they perceive the same emotional meaning of the provided information?). As a further development of these analyses, the question of how to assess the capacity of patients with DOCs to make an appropriate informed decision will also arise.

In short, the new advancements in neurotechnological assessment of residual consciousness in patients with DOCs raise important ethical issues, such as how to assess residual capacity of self-determination; whether and how much a prospective ‘cerebral communication’ may be considered as valid for an Informed consent; and whether a prospective direct communication with patients with DOCs through neurotechnology implies the necessity to rethink their clinical management, particularly the role of legal guardians.

According to Laureys and Schiff, the most relevant result of the progress in the neuroimaging investigation of consciousness is the passage from a monolithic way of looking at DOCs to a more graded nosology based on a quantitative assessment of consciousness and on functional neuroimaging technologies. Neurotechnology allowed researchers to detect important neurological differences between patients that are behaviorally classified as equal: As a result, both description and diagnosis of DOCs are more detailed, and new nosographic criteria and categories have been elaborated (Laureys and Schiff 2012). Furthermore, advancements in neuroimaging research have allowed the development of novel investigational paradigms that provide an imaging indication of volition and awareness: This indication may appear but is not unanimously assumed as unambiguous (Laureys and Schiff 2012). One of the earliest studies, conducted by Owen, Laureys and colleagues in 2006 (Owen et al. 2006), is particularly relevant in showing the possible dissociation between the clinical examination based on the behavioral appearance and the results of a neuroimaging assessment (in this case, an fMRI examination). A young woman who survived after a car accident was behaviorally diagnosed as being in a vegetative state (VS) according to the international guidelines. The researchers' team pronounced some sentences (e.g., 'There was milk and sugar in his coffee') and measured through fMRI her neural responses comparing them with responses to acoustically matched noise sequences. Interestingly, the woman's neural reaction to the sentences was equivalent to the control subjects' reactions, yet this result alone is not sufficient to conclude that the woman is aware because there is the possibility of implicit processing: Some aspects of human cognition, as language perception and understanding, can go on without awareness (Fine and Florian Jaeger 2013). For this reason, the research team developed a complementary fMRI study asking the woman to mentally perform two tasks: imagining playing tennis and imagining visiting her house. The relevant result was that the brain activation of the woman was not distinguishable from that of the control subjects, a group of conscious volunteers.

Similar results were obtained in the follow-up study jointly conducted in Liege and Cambridge: 54 patients with severe acquired brain injuries were scanned through fMRI. In response to the request to perform imagery tasks, 5 of them were able to modulate their brain activity by generating blood-oxygenation-level-dependent (BOLD) responses which were judged by the researchers as voluntary, reliable, and repeatable (Monti et al. 2010). Additional tests in one of the 5 responsive subjects revealed his ability to correctly answer yes–no questions through imagery tasks, showing the feasibility of communication. These results are ethically very significant: If new diagnostic tools are available, then it is ethically warranted to use them and to give all the patients the possibility to be rightly diagnosed through them.

Given the possibility that patients with DOCs retain the capacity to communicate and express their own thoughts and preferences, the ethical question of their Informed consent arises.

In this paper, we discuss some technical aspects of fMRI and brain–computer interfaces (BCI) and their prospective use for communicating with patients with DOCs. Furthermore, we analyze the epistemological issue of the relevance of neural activation in the patient for proving or suggesting his/her ability to communicate. Against that background, we analyze emerging ethical issues of Informed consent.

2 The Possibility and Meaning of 'Cerebral Communication'

2.1 fMRI

To date, fMRI is the most commonly used and one of the most promising tools to study DOCs, especially for its noninvasive nature, ever-increasing availability, relatively high spatiotemporal resolution, its capacity to demonstrate the entire network of brain areas activated in particular tasks, and its capacity to provide both anatomical and functional information in the scanned subject. Besides functional data, fMRI techniques also provide other clinically relevant physiological information (e.g., regarding biochemical status, cerebral blood compartment, perfusion, water molecular diffusion, and cerebral microstructure and fiber tracking) (Laureys et al. 2009). There are some limitations to the use of fMRI, for instance in the case of patients who have implanted materials (e.g., metallic implants) that are incompatible with the scanner. In general, the main limitation, or maybe one of the most difficult to assess, especially in case of patients with DOCs, relates to motion artifacts and the duration of the procedure. First, the scanning procedure requires an average time between 15 and 120 min. Second, the methodology used in the fMRI detection of the activated cerebral areas requires repeating the procedure several times in the same subject and/or in different subjects. According to the so-called 'subtraction paradigm,' the brain activation measured before the task (i.e., the control state) is confronted with the brain activation during the task (i.e., the task state), and the difference is assumed to represent the specific brain areas for the task. In order to achieve reliable data, it is necessary to repeat the experiment several times in the same person or in different persons and calculate the average of the results. In this way, it is possible to detect changes in neural activity related to mental activity avoiding the risk of confusing them with false changes resulting from noise (Laureys et al. 2002).

The scientific premise of functional neuroimaging is the functional segregation of the brain. Generally speaking, neuroscientists agree that a cortical area can be specialized for some perceptual or sensorimotor processing and that this specialization is anatomically segregated in the cortex (Laureys et al. 2009). More precisely, it is assumed that the cortical infrastructure of a single function or of a complex behavior can involve different specialized areas combining resources by functional integration between them. As a result, a deep correlation between functional integration and functional segregation is necessary for the brain activities. This coexistence of integration and segregation is the cerebral foundation for functional neuroimaging to be informative about the cerebral activity: Complex behavior can be broken down into more simple and elementary mental operations related to specific cerebral areas.

From a methodological point of view, in the case of the application of fMRI to patients with DOCs, it is important to assess the passive stimulations (i.e., when the patient is not asked to perform any task) and the active paradigms (Boly et al. 2007). Regarding the first point, according to Boly and colleagues, lacking a 'full understanding of the neural correlates of consciousness, even a normal activation in response to passive sensory stimulation cannot be considered as proof of the presence of awareness in patients with DOCs. In contrast, predicted activation in response to the instruction to perform a mental imagery task would provide evidence of voluntary task-dependent brain activity, and hence of consciousness, in non-communicative patients' 'Boly et al. 2007:979'.

We will analyze the issues arising from the assumed 'neural evidence' of consciousness with more details below. What is relevant to note here is that the brain activation in response to passive stimulation is currently not necessarily assumed by the neuroscientific community as proof of consciousness (i.e., awareness). From an ethical point of view, this is relevant, especially regarding Informed consent. The problem is that if brain activation is the only way a patient potentially retains for communicating, but this activation cannot be assumed as proof of conscious activity, then the patient cannot be assumed to be either conscious or able to express a valid Informed consent. For this reason, further technical advancement in the detection of residual consciousness in patients with DOCs is essential in order to resolve the ethical issue of their self-determination (i.e., informed consent).

Regarding the paradigm selection, spatial navigation and motor imagery tasks have been detected as useful mental tasks to identify and assess brain activity and consciousness in patients with DOCs. This new paradigm (i.e., imagery tasks for assessing consciousness through fMRI) could be a useful tool to assess willfulness and consciousness, implement a process of communication with patients with DOCs, and overcome the limitation of the behavioral paradigm based on motor responsiveness.

Neuroimaging in general and fMRI in particular have allowed us to objectively differentiate patterns of cerebral activity in patients with DOCs (Boly et al. 2005). Detection of specific areas yielded by particular tasks is clinically relevant because it potentially gives us the possibility to develop an alternative form of communication with patients lacking the ability to speak and to move (Naci et al. 2013). The aforementioned experiment by Laureys and colleagues, for instance, shows the possibility to communicate with patients by detecting through fMRI the willful activation of specific areas in their brains (Monti et al. 2010). This possibility relies on the identification of the different brain regions and the related mental activities, which have been made possible in recent years.

On the basis of such findings, neuroscientists have defined consciousness as the emergent property of the collective behavior of widespread thalamocortical frontoparietal network connectivity (Laureys 2005a). Moreover, it has been possible to identify the different networks elicited by subjective internal self-related thoughts (self-awareness: midline cortical structures) and by external sensory perceptions (external awareness: lateral frontoparietal structures) (Vanhaudenhuyse et al. 2011). On the basis of this knowledge, an experimental paradigm has been developed in which the brain's response to self-related stimuli such as the patient's own name (Qin et al. 2010), and not to external stimuli, has been measured.

However, as stated above, the activation of a brain area as such is not enough to conclude that the patient is aware, since it could be a case of, for example, passive stimulation reaction or implicit learning (Laureys 2005b). The assumed condition to interpret the neuroimaging data as evidence of consciousness is a time-related condition: The activation of the cerebral area in response to a specific task has to last at least 30 s. In this way, it is possible to disentangle the cerebral activation related to a voluntary (re)action from unconscious reactions that are fleeting (Boly et al. 2005; Greenwald et al. 1996; Naccache et al. 2005). Furthermore, as emerging from the aforementioned experiment by Laureys and colleagues, correct yes–no answers to simple questions such as 'Is your mother's name Yolande?" confirm voluntary origin of the fMRI signal (Monti et al. 2010). Discrimination between voluntary and involuntary brain activity is ethically relevant in regard to the prospective use of neuroimaging for communicating with patients with DOCs and particularly for asking them to give an informed consent.

Research for implementing an fMRI-based communication with patients with DOCs is currently in progress. For instance, a new, noninvasive, relatively fast to apply, and reliable fMRI-based spelling device has recently been proposed as a communication tool, which is potentially promising also for patients with DOCs (Sorger et al. 2012). Yet to date, all these attempts are still at the stage of proofs of concept rather than being practical means to really ensure long-term communication. There are some technical problems in the use of fMRI-based technology to communicate with patients with DOCs. For instance, because of the severe brain damage, the coupling of hemodynamics and neuronal signal, which is at the basis of the fMRI assessment of consciousness, could be very different in patients with DOCs compared to that in healthy people. Moreover, given the plasticity of the brain, the anatomy and functional neuroanatomy could have undergone a functional remapping in patient with DOCs, so that a specific cerebral area could have been functionally replaced by another one.

For the abovementioned difficulties, EEG-based communication devices, the so-called brain–computer interfaces (BCI), are being developed as a potentially more practical, transportable, and cheaper alternative to fMRI for communicating with patients with DOCs (Bruno et al. 2011a; Sorger et al. 2003; Naci et al. 2012; Sellers 2013; Lulé et al. 2013). Other relevant results emerged from a clinical case of complete locked-in syndrome (LIS) showing consciousness via ERP (Schnakers et al. 2009a) and from the measurement of pupil size by a bedside camera to communicate with patients with locked-in syndrome (Stoll et al. 2013).

Another possibility emerging from contemporary neurotechnology is the use of TMS-EEG as a tool to probe consciousness in patients with DOCs (Casali et al. 2013; Jacobo et al. 2013). Furthermore, TMS-EEG potentially gives researchers a tool for developing a communication paradigm with patients with DOCs.

2.2 Brain–Computer Interface

BCI is a direct connection between living neuronal tissue and artificial devices that establishes a non-muscular communication pathway between a computer and a brain (Wolpaw et al. 2002). Through BCI, it is possible to detect changes in neuroelectrical activity or brain activity in response to sensory stimulation. The user is then trained to use these changes to select items, words, or letters in communication software or to make choices for neuroprosthesis control (Kübler 2009).

BCI is grounded in a continuous, real-time interaction between living brain and artificial effectors. In this way, a functional hybridization between brain and technology is realized. The operation scheme of a BCI is quite simple: The input is the user's intent coded in the neural activity of her/his brain detected through BOLD response. The output is the device controlled by the user's brain activity.

BCI uses a representation of the subject's mentation as the essential component. The psychological task or the intention of the subject is detected and recorded through invasive or noninvasive methods, mostly EEG using surface or implanted electrodes, but also MEG, fMRI, or functional near infrared spectroscopy (fNIRS). There is a significant difference between these methods regarding the ease of use. For instance, while MEG and fMRI are more demanding, require quite sophisticated instruments, and are quite expensive, EEG, NIRS, and invasive systems are portable and thus suitable for use in daily life (Kübler 2009).

In the particular case of patients with DOCs, EEG offers significant comparative advantages on the aforementioned points. Furthermore, it can be useful to develop EEG-BCI systems that can be used at the bedside to detect volitional brain activity and to enable basic communication.

Thus, to date, EEG-based techniques are the most suitable BCIs for clinical application to patients with DOCs even if other technologies, such as fMRI, allow a more detailed spatial resolution and a more precise allocation of neuronal activity than EEG. Whatever technology is used, the detected and recorded cerebral signals are digitized and differently processed by filtering, amplitude measurement, and spectral analysis (Wolpaw et al. 2002). Specific algorithms then translate the processed signals into commands expressing the users' will. In particular, the subject may communicate choosing the words on a screen moving a cursor through his own mind. In this way, BCI provides subjects with a virtual keyboard where the user can press the keys through the brain activity's modulation.

Importantly, BCI provides the user with real-time feedback on their performance, giving her/him the possibility to improve the use of the BCI over time. BCI thus enables a cerebral communication without motor response. This cerebral communication could give to some behaviorally non-responsive patients, such as patients with DOCs, a new opportunity to communicate.

There are several prerequisites to use BCI for communicating with patients with DOCs. The patient should be able to properly understand verbal commands. The patient should also be able to react to external stimulation and express her/his answers through a minimal form of communication (e.g., a binary yes/no communication) while remaining sufficient cognitive capacities enabling the formulation of a reliable informed decision (Lulé et al. 2013). It is possible that patients retain the ability to partially understand commands, to understand but not to follow commands, or to understand and to follow commands but not well enough to make BCI feasible. In order to use a BCI with patients with DOCs, the understanding of the provided information should be matched with their ability to attend to stimuli, to selectively process the salient ones, and to retain information in working memory (Chatelle et al. 2012).

The results emerging from the aforementioned studies by Laureys, Owen, Schiff and others are relevant and promising also in the direction to use BCI with patients with DOCs. A possible communication protocol through BCI emerges from the experiments by Cruse and colleagues (Cruse et al. 2011). They investigated the capacity of patients with DOCs to perform mental motor tasks that are possible to differentiate in their EEG at the single-trial level. Sixteen patients in VS/UWS were asked to imagine squeezing their right hand or moving all their toes, and in 19 % of the patients a support vector machine predicted the task being executed with an accuracy of between 61–78 %. The same test was performed with MCS patients, where 22 % of them were able to follow commands using motor imagery (Cruse et al. 2012). Starting from these results, it could be possible to implement a binary communication by assuming imagination of right hand as ‘yes’ and the imagination of toe movement as ‘no’ (Chatelle et al. 2012).

Another relevant study has been conducted by Lulé and colleagues who tested an EEG-BCI paradigm on 16 healthy subjects and 18 patients in a VS/UWS, in a MCS, and in LIS (Lulé et al. 2013). The results of the study showed that 13 healthy subjects and 1 LIS patient were able to communicate through BCI, and 1 patient in MCS who was unresponsive at the bedside showed command following with the BCI, while all other patients did not show any response to command and could not communicate through BCI. Even if no patients with DOCs were able to functionally communicate through BCI, this study is relevant and promising in showing command following in one patient in MCS.

Further research is needed in order to assess relevant issues limiting the feasibility of BCI with patients with DOCs. Particularly, it is necessary to investigate potential limitations and benefits of multimodal visual–audio–tactile stimulation (Chatelle et al. 2012; Lulé et al. 2013). For instance, a visual-based BCI is sometimes more accurate than an auditory-based BCI (Blankertz et al. 2010). Moreover, auditory stimuli cannot be presented simultaneously and require a longer time to present than visual stimuli (Sellers 2013). Another factor that potentially raises problems for the application of auditory-based BCI to patients with DOCs is that auditory stimulation requires more training (Kübler 2009).

Further studies should investigate the possible long-term mental capabilities potentially retained in patients with DOCs. On the basis of these capabilities, it could be possible to implement a communication that is more complex than a binary yes/no communication (Chatelle et al. 2012).

Because of their critical neurological condition, on the basis of the aforementioned studies, it is reasonable to expect that patients with DOCs will eventually be able to partially understand and execute external requests for mental tasks. The question then arises at what level of accuracy the communication can be considered effective.

Other variables to take into account in the evaluation of the results emerging from experiments with BCI involving patients with DOCs are the possibility of questions too difficult to answer or asked when the patients were sleeping, and the fact that movement, ocular, and respiration artifacts are involuntary and can interfere with the instrumental assessment with false-positive results (Boly et al. 2005). These possibilities are ethically relevant because an inadequate assessment of BCI communication may lead to inappropriate clinical decisions.

In short, three main difficulties emerge from the use of BCI for communicating with patients with DOCs (Chatelle et al. 2012): Patients with DOCs have sensory dysfunction, aphasia, arousal fluctuation, and limited attention span; the suitability of BCI is variable for different patients with DOCs.

Besides the difficulties related to the critical neurological condition of the patients with DOCs, potential limitations to the use of BCI for communication with such patients also arise from the general difficulty to map intended responses to motor imagination, which is a complex task that can be challenging to perform for healthy adults as well (Guger et al. 2003). Given the difficulties summarized above, even though the studies have shown promising results, significant time and effort are needed in order to have a clinical application of BCI with patients with DOCs and to improve their quality of life (Chatelle et al. 2012).

In conclusion, it is clear that further investigations and efforts are essential for developing the communication with patients with DOCs through BCI. However, it is also clear that the clinical application of BCI to detect signs of consciousness in patients with DOCs, particularly in patients with MCS, is already feasible and very promising, especially for solving the major problem of misdiagnosing DOCs and for improving clinical care (Lulé et al. 2013). In fact, if repeated reactions to volitional paradigms are detected, it is reasonable to infer that higher cognitive processing and volition are present in these patients. A different question that still remains open is whether and how these responding patients may be able to use their brain responses for controlling a BCI and how much integrity and connectivity of the brain is necessary for a minimal communication through BCI (Kübler 2009).

3 Informed Consent

As a result of these neuroscientific and neurotechnological developments, the ethically and legally relevant question arises: could a reliable and effective 'cerebral' communication justify an assumption of a right to self-determination of these patients? Could it, for example, be justified to ask them for an informed consent to treatment? With current machine learning technology, the answer currently is negative: Giving an informed consent is not yet realistic for these patients. However, while the actual possibility of DOC patients to give informed consent is absent today, the theoretical possibility is present, and with the further development of these technologies, the situation might come to change. Generally speaking, if communication with patients with DOCs through neurotechnology is feasible, it would be ethically warranted to use and improve it by giving the patients new possibilities to exert their autonomy and self-determination.

The formal condition to have self-determination through informed consent in a medical context is the existence of a relationship between the clinician and the patient. Relationship implies a process of communication, that is, the capacity of the involved subjects to express their thoughts and eventually to answer emerging questions on the basis of those thoughts. A cerebrally communicating patient with DOC is formally able to be in relationship with the clinician, which means that the 'formal condition' for an informed consent could be satisfied.

Yet there is also what could be named a ‘substantial condition’ for informed consent: The patients have to retain the capacity properly to understand the information provided and to make a choice on this basis between options and the related consequences. This second condition seems problematic if referred to patients with DOCs: We are not sure that they retain the ability to process the provided information and to properly figure out the related consequences.

More specifically, it is generally accepted that to be valid an informed consent has to respect the following requirements (Faden and Beauchamp 1986):

- Disclosure
- Capacity
- Voluntariness

Disclosure implies two requirements for the clinician/researcher: (1) She/he has to give the patient all the needed information for an autonomous decision and (2) she/he has to check the adequate understanding of the information by the patient. Thus, the clinician/researcher has to describe all the possible clinical or experimental options and all the consequent implications for the patient. Furthermore, she/he has to ensure an adequate understanding of the provided information, both choosing an appropriate tool of communication (e.g., written or oral presentation) and a suitable system of checking the understanding of the information (e.g., through pertinent questions asked at different times).

The second requirement for a valid informed consent is the capacity, which entails the actual ability of the patients not only to understand the information provided, but also to make a reasonable judgment concerning the prospective consequences of her/his decision.

The last requirement, voluntariness, refers to the patient’s right to decide without undue coercion or influence.

In short, an autonomous decision expressed through an informed consent presupposes that the patient retains four essential components: (1) understanding relevant information concerning treatment or research and related risks and benefits, (2) appreciating different therapeutic or research methods and related consequences, (3) reasoning about different options, and (4) communicating a personal choice (Petrini 2010; American Psychiatric Association 1998).

Tools for assessing these standards have been proposed (Grisso and Appelbaum 1998; Appelbaum 2007), but criticisms have been raised regarding the risk of not taking into account the emotional dimension of the informed consent process (Northoff 2006), and their application to patients with DOCs seems problematic. A conceptual foundation of a mechanistic explanation of capacity has been proposed recently in order to develop the proper tools to empirically detect and assess capacity in patients with DOCs who show responsiveness through BCI or fMRI-BCI (Peterson et al. 2013). The starting point of this proposal is that the inner mental life of some patients behaviorally diagnosed as VS may be richer and more active than assumed so far and that this mental activity could be used to implement a BCI communication in exceptional cases. Even so, to communicate through BCI with patients with DOCs does not guarantee the possibility to involve these patients in medical decision making. The question arises whether or not these BCI-communicating patients retain the ability to make an informed decision regarding their ordinary or experimental treatment. Peterson and colleagues suggest a reductionist approach in order to detect this capacity in patients with DOCs: They start from the MacCAT-T criteria (i.e., understanding, reasoning, justification, appreciation) and try to decompose them in sub-components that can be assessed even in patients with DOCs. This is a robust empirical approach, with prospective relevant clinical implications in the direction of translating BCI-mediated communication from laboratory to clinics. Yet this approach focuses only on cognitive functions without taking into account the emotional dimensions of the informed consent process (Northoff 2006). Autonomy is a complex capacity, which relies not only on cognition, but also on emotion, morality, and sociality (Jox 2013).

It is usually not so easy to implement the communicative process of informed consent described above and particularly tricky to assess the emotional components and the extra-scientific variables that come into play, for example, the sociological and psychological background of the patient that affect and potentially bias his/her understanding of the information (Northoff 2006). These difficulties seem even more relevant in the case of patients with DOCs, even if they are able to cerebrally communicate. It would be very complicated to properly communicate relevant and complex and often specialized information regarding therapy and/or research to these patients. Furthermore, it is reasonably difficult to assess their ability to process this information, to properly understand it, to develop a reasonable judgment regarding the consequences of the prospective choices, and to freely take the better decision for themselves. Thus, even if the experimentally developed system of cerebral communication with patients with DOCs will in due course be translated into clinical practice, its prospective use for a direct consent from the patient remains ethically challenging.

The use of neurotechnology for obtaining informed consent from patients with DOCs is challenging also at the legal level. At present, the role of the legal guardian is not questioned, as this legal instrument is necessary for these patients. Several issues arise concerning the role of guardians, especially concerning the biases they (and clinicians as well) may have regarding quality of life and end-of-life decisions. Empirical results suggest that the personal well-being of chronically ill people is often higher than expected (Albrecht and Devlieger 1999; Bruno et al. 2011b). Even if we have no direct evidence, it is reasonable to assume that a further developed neurotechnology-mediated direct communication can be expected to increase their quality of life, a consideration that strengthens the ethical imperative to support this development. In addition, novel technologies should be further used to better disentangle the different DOCs, whose diagnoses have been shown to have an astonishingly high rate of error estimated between 30 and 40 % (Schnakers et al. 2009b). A better diagnosis would allow a better therapeutic strategy for the patient, for example, by detecting the patient's perception of pain and/or suffering (Demertzi et al. 2013) or her/his inclusion in an appropriate clinical trial. Importantly, even if cerebrally communicative, patients with DOCs remain highly vulnerable and this vulnerability likely affects his/her capacity of self-determination. Because of the aforementioned reasons, the use of neurotechnology to obtain informed consent from patients with DOCs is ethically problematic. A reasonable position could be to distinguish between different kinds of decisions, namely between therapeutic, experimental, and more drastic decisions such as euthanasia, to give a different weight to the patients' answers in relation to the different contexts.

There is also another question related to the 'big issue' of the relationship between neural activity and consciousness, a question pertaining to the meaning of information rather than the processing of information, particularly to its emotional meaning. Even if we must conclude that the correct activation of a particular area to a specific yes–no question suggests the preservation of awareness in the scanned subject, we do not know what kind of awareness she/he preserves. In accordance with the global neuronal workspace model (Dehaene et al. 2011), awareness is the result of functional integration of different areas of the brain. All we can infer from the neuroimaging assessment is that particular areas are processing information, but their interrelation with other cerebral areas remains problematic, so that the significance of their particular activation for awareness also remains problematic. It is theoretically possible, for instance, that the patient is able to functionally process the information but not to meaningfully process the information, in the sense that she/he is not able to relate a specific emotional meaning to the information or to relate the same meaning compared with a healthy person. In that case, we cannot be sure that the meaning that the words have for us is the same meaning that they have for the patient, and while they appear to understand the questions, this apparent understanding remains uncertain and open for interpretation.

Functional responsiveness of the patient, shown to be able to perform specific mental tasks, like moving through a space or playing a sport (Owen et al. 2006), suggests the preservation of semantic capacity. Yet even in this case, it is possible that the capacity to understand the meaning of the information is limited or different from that in healthy people. Particularly, it could be limited to the functional meaning of external information, and the patient could be unable to really understand the meaning of self-related requests concerning, for instance, caring and end-of-life decisions.

The identified conditions for a reliable and effective communication with patients with DOCs for evidence of awareness are robustness, repeatability and correct responses to simple questions. From an ethical point of view, the ability to communicate does not imply the ability to make informed decisions, since capacity is not competence. As stated above, we agree with Peterson and colleagues that, given the present uncertainty regarding the effective capacity of patients with DOCs to make a valid informed decision, they should be allowed to participate in clinical decision making if the capacity threshold for the decision in question is sufficiently low (e.g., for treatments options instead of end-of-life decisions). Notwithstanding the problems summarized above, the involvement of patients with DOCs, who are unable to express an informed autonomous decision, has been gradually justified in clinical practice and research.

4 Discussion

Recent investigations of residual consciousness in patients with DOCs led to new possibilities for communicating with them, i.e., in a 'cerebral' communication without external behavior. This prospective new form of communication potentially raises new ethical challenges, such as the necessity to assess the residual capacity of self-determination in patients with DOCs, the necessity to clarify whether cerebral communication is valid for informed consent, and the necessity to clarify whether cerebral communication implies new forms of management of patients with DOCs.

In the fMRI assessment of consciousness and in the related implementation of communication (with or without BCI), there is an assumption that deserves particular attention. If the BOLD response in the patient is similar to the response in healthy volunteers, it is reasonable to assume that the patient is conscious. Schematically, the logic is the following: (1) Task *t1* implies some signal change (BOLD, EEG or other) which can be identified by classifier (support vector machine learning or other) without a priori assumptions on neuroanatomy or normal patterns; (2) task *t1* implies the yes–no response of the patient as identified by the classifier; and (3) if the yes–no response is correct, then the patient consciously communicated. In active paradigms, a correct communication can be assumed as final evidence of conscious origin. However, as pointed out above, in passive paradigms, the activation of a particular cerebral area per se need not suggest a conscious activity because it could be an 'automatic' processing. Therefore, it is necessary to develop proper clinical and/or neuroimaging protocols in order to assess this risk of false positive. The question of the relationship between brain activation and consciousness however remains open: When is the activation of a cerebral region equivalent to or evidence of the presence of awareness? In the case of patients with DOCs, this issue is ethically highly relevant, particularly regarding the possible neurotechnology-mediated informed consent. This could be required only if it is reasonable to assume that the detected brain signals are evidence of consciousness.

If neurotechnology-mediated communication with patients with DOCs is feasible, it would be ethically warranted to ask them directly for informed consent to ordinary or experimental treatments. This makes it all the more important to clarify the conditions for an effective and reliable communication with the patients through neuroimaging. The theoretical premise for the use of volitional paradigms in the neuroimaging assessment of awareness and volition is that the patient is able to understand instructions, wants and is able to perform what is required (Kübler 2009). In the execution of the investigation and in the interpretation of the emerging data, it is important to assess the risk of false-positive results. A robust and repeated activation of the brain area of interest in response to external instructions has been suggested as proof of the capacity to understand and obey command. In case of evident and repeated brain activation in response to different kinds of tasks at different times, it is reasonable to conclude that a reliable communication is taking place. In other words, we agree that robustness, repeatability, and correct responses to simple questions for communication are essential requirements for assuming neuroimaging evidence of cerebral activation in patients with DOCs as evidence of awareness (Kübler 2009).

Even if a form of cerebral communication with patients with DOCs is possible, assessing their capacity to understand the provided information in order to express a valid informed consent is a challenge. A method commonly used to assess the patient's capacity to understand is to ask her/him to describe with her/his own words what previously communicated by the researcher (Leo 1999; Appelbaum PS-Grisso 1988). This is presently not possible in the case of patients with DOCs, who are able only of a yes–no communication through neuroimaging. It is also problematic to assess the ability of patients with DOCs to appreciate the provided information. Appreciating the information means that the patient is aware that such information is applicable to her/him at a specific time (Gert et al. 2006). In other words, it requires the ability to understand the notions of self and time, and the ability to refer to the self as a dynamic entity shaped through time.

Regarding the reasoning as a requirement for an autonomous decision, a yes–no responsive patient could have impairments in executive function, that is, in the ability to organize, plan, and categorize information. She/he could be able to understand specific information, but not to collect and coordinate different information in order to make a complex decision like withholding or withdrawing life-sustaining treatments. Communication of a personal choice is also problematic in patients with DOCs. Besides possible cognitive impairments, they can present volitional impairments that do not allow them to make and express a personal decision. Finally, the abilities required for an autonomous decision and for a proper informed consent (i.e., understanding, appreciation, reasoning, and choice) are gradable abilities. It is possible that a patient with DOCs retains them only partially. This raises the question of what degree of the aforementioned abilities the subject must retain in order to consider her/him as able to give an informed consent.

The abovementioned difficulties to assess the patient's capacity of proper understanding to give a valid informed consent are technically and ethically relevant. While it can currently be questioned whether a positive cerebral activation in response to particular tasks is evidence of consciousness, it is important to note that a negative result does not imply the absence of willful responsiveness. In fact, different factors could impair the ability to react to external stimulation, even if the patient retains awareness (Boly et al. 2007). Some types of brain damage could impair the patient's ability to understand and/or to perform the selected task. These impairments could lead to a relative reorganization of the brain, involving other areas in the execution of a specific task. Evidence of residual awareness could be flickering and fluctuating. In addition, the patient could decide to not execute the command or be sleeping during the execution of the task. The argument that a negative result cannot be assumed as evidence of absence of consciousness is also ethically relevant for the management of patients with DOCs, especially regarding end-of-life decisions.

Notwithstanding the progress in the use of neurotechnology for diagnosing patients with DOCs and for communicating with them, further studies are needed particularly in the following domains: assessing possible obstacles in the use of neuroimaging for communicating; refining technology in order to disentangle voluntary from involuntary brain activity; training patients on using BCI; defining how much cerebral integrity is necessary for communicating through BCI; investigating possible functional brain remapping affecting patients' capacity to process information; and assessing how to ensure and check an adequate understanding of information by patients. At present, we have the technology, but we need new categories to describe patients who are behaviorally unresponsive but cerebrally communicative (Giacino et al. 2014).

5 Conclusion

The prospective development of a neurotechnology-mediated communication with patients potentially offers new way to exercise the right to self-determination. Specifically, neurotechnology can give clinicians the opportunity to detect covert awareness and facilitate a correct diagnosis or to directly communicate with patients, for example, by asking them if they feel pain. The most important impact of these prospective applications concerns ethical considerations of informed consent. It is theoretically possible to ask patients directly for informed consent by communicating through neurotechnology, but the complexity of the decisions to take in clinical context (which affects the rational as well as the emotional subjective dimensions) urges great precaution. It seems as yet premature to assume that a 'cerebral communication' with patients is enough to assess important ethical issues like informed consent since further investigations are scientifically and ethically appropriate.

In conclusion, to date, the use of neurotechnology to communicate with patients is still at the stage of proof of concepts, but the theoretical possibility and empirical results thus far strongly urge a continued reflection about possible clinical implementations. Particularly, cerebral communication with these patients to express an informed consent raises important theoretical as well as practical issues: the patient's effective ability to understand and process the provided information, her/his ability to integrate the provided information to make a coherent personal decision, and her/his ability to feel the relevance of the clinical options. These issues deserve further reflection at the scientific, technical, legal, and ethical levels. And from an ethical perspective, we should note that even scientifically minor advances could yield important improvements from the patient's point of view.

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