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Self-consciousness in non-communicative patients

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Abstract

The clinical and para-clinical examination of residual self-consciousness in non-communicative severely brain damaged patients (i.e., coma, vegetative state and minimally conscious state) remains exceptionally challenging. Passive presentation of the patient's own name and own face are known to be effective attention-grabbing stimuli when clinically assessing consciousness at the patient's bedside. Event-related potential and functional neuroimaging studies using such self-referential stimuli are currently being used to disentangle the cognitive hierarchy of self-processing. We here review neuropsychological, neuropathological, electrophysiological and neuroimaging studies using the own name and own face paradigm obtained in conscious waking, sleep, pharmacological coma, pathological coma and related disorders of consciousness. Based on these results we discuss what we currently do and do not know about the functional significance of the neural network involved in "automatic" and "conscious" self-referential processing.

Keywords: Consciousness; Self-consciousness; Own name; Own face; Coma; Vegetative state; Minimally conscious state; Locked-in syndrome; Event-related potentials; Functional neuroimaging

1. Introduction

Assessment of self-consciousness in severely brain damaged patients is of vital importance for their appropriate therapy and (end-of life) management. Clinical practice shows that recognizing unambiguous signs of conscious perception of the environment and of the self in patients with disorders of consciousness (DOC) can be very challenging (Laureys, Majerus, & Moonen, 2002b). This difficulty is reflected in the frequent misdiagnoses of the vegetative state (VS) (Andrews, Murphy, Munday, & Littlewood, 1996; Childs, Mercer, & Childs, 1993; Tresch, Sims, Duthie, Goldstein, & Lane, 1991), minimally conscious state (MCS) (Schnakers et al., 2006) and locked-in syndrome (LIS) (Bauby, 1997; Leon-Carrion, van Eeckhout, Dominguez-Morales Mdel,

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& Perez-Santamaria, 2002; Ostrum, 1994; Vigand & Vigand, 2000). Bedside evaluation of residual brain function in DOC is difficult because arousal levels may fluctuate and motor responses may be very limited or inconsistent. In addition, consciousness is not an all-or-none phenomenon (Wade & Johnston, 1999) and above all, its clinical assessment relies on inferences made from observed spontaneous or stimulation-induced motor responses (Bernat, 1992).

Integration of multi-modal para-clinical examinations may eventually improve our ability to assess self-consciousness in non-communicative brain damaged patients. Electrophysiological and functional neuroimaging studies permit objective assessment of cerebral function in DOC (for recent reviews, see Giacino, Hirsch, Schiff, & Laureys, 2006; Laureys, Giacino, Schiff, Schabus, & Owen, 2006; Laureys, Owen, & Schiff, 2004; Laureys et al., 2005). We will here briefly define consciousness of environment and self as it can be assessed at the patient's bedside; review the major clinical entities of DOC following severe brain damage; discuss the use of auto-referential stimuli (that is the own name and the own face) that can be passively presented to patients with DOC and review data obtained in split-brain patients, by means of event-related potential studies and by functional neuroimaging studies using the own name and own face paradigm. Based on results obtained in conscious waking, sleep and DOC we discuss what we currently do and do not know about the functional significance of the different ''self-related'' components in relation to ''automatic'' *vs* ''conscious'' self-perception.

2. Consciousness, awareness and wakefulness

There is at present no satisfactory, universally accepted definition of human consciousness and even less so of self-consciousness. For the purposes of clinical neurosciences, consciousness consists of two basis elements: *arousal* (i.e., wakefulness, vigilance or level of consciousness) and *awareness of environment and of self* (i.e., content of consciousness) (James, 1890; Plum & Posner, 1983). The interpretation of this delineation depends however on the clinical, neuroscientific or philosophical approach of the authors. Hereafter we propose operational definitions that can be employed at the patient's bedside. Consciousness is a multifaceted concept and we admit that the proposed neurological definitions do not necessarily overlap with those used by philosophers or basic neuroscientists. By *arousal* we refer to the behavioral continuum that occurs between sleep and wakefulness. This is not an on-off mechanism as it can show rapid fluctuations in response to external stimulation (e.g., to intense, unexpected or novel stimuli) called orienting reaction or vigilance. We define arousal as the presence of prolonged periods of spontaneous or induced opening of the eyes. *Awareness* refers to the thoughts and feelings of an individual. Our operational definition is limited to an appraisal of the potential to perceive the external world and to voluntary interact with it (also called *perceptual awareness*). In practice this can be done by careful and repeated examination of spontaneous motor behavior and the patient's capacity to formulate reproducible, voluntary, purposeful and sustained behavioral responses to auditory, tactile, visual, or noxious stimuli.

Compared to awareness of the environment, awareness of self (or self-consciousness) is an even more complex and ill-defined concept, requiring a representation of self *vs* other (Berrios & Markova, 2003). Northoff and Bermpohl (2004, 2006) assumes self-referential processing, accounting for distinguishing stimuli related to one's own self from those that are not relevant to one's own concerns, to be at the core of the self. Several other authors investigate minimal forms of self that they coined ''mental or core self'' (Damasio, 1999); ''pre-reflective self'' (Gallagher & Zahavi, 2005; Legrand, 2006); ''minimal self'' (Gallagher & Frith, 2003; Gallagher, 2000) or ''experiential self'' (Lambie & Marcel, 2002; Zahavi, 2003. Zeman (2001, 2003, 2005) differentiates six different kinds of representation of self-consciousness. (i) The colloquial sense of self-consciousness—a proneness to embarrassment in the presence of others—implies the subject's awareness that the awareness of others is directed on her. (ii) Self-consciousness as self-detection, refers to awareness of stimuli which directly impinge on the body; of proprioceptive information about bodily position which contributes substantially to our body image; of information about actions which we are about to perform or are performing, giving rise to a sense of agency; of information about bodily state (hunger, thirst, etc.); and of emotions. (iii) Self-consciousness as self-monitoring—extends self-detection in time into past and future, and in range, to encompass more plainly cognitive abilities. It refers to the ability to recall the actions we have recently performed and to our ability to predict our chances of success in tasks which challenge memory or perception.

(iv) Self-consciousness as self-recognition—alludes to our ability to recognize our own bodies as our own, for example in mirrors. (v) The 'awareness of awareness' sense of self-consciousness permits to understand our own behavior and the behavior of others in terms of desires and beliefs, and for implanting and manipulating these (described as the acquisition of a 'theory of mind'). (vi) Self-consciousness referring to our self-knowledge in its broadest sense—one's knowledge of oneself as the hero of a personal narrative, deeply conditioned by one's circumstances and cultural background. This 'autonoetic awareness' permits to relive our past in a form of 'mental time-travel'.

In the present review, we will focus on Zeman's fourth sense, self-consciousness as self-recognition (i.e., mirror self-recognition or specific reactivity to the own name). We will discuss behavioral, pathological, electrophysiological and neuroimaging studies employing self-referential stimuli in the auditory (hearing the own name) and visual (seeing the own face or the own name) modalities that can be passively presented to patients with DOC.

Fig. 1 shows that in normal physiological states (underlined); level of arousal and content of consciousness (environmental and self) are positively correlated. You need to be awake in order to be aware (rapid eye movement or REM sleep being a notorious exception) (Hobson, Stickgold, & Pace-Schott, 1998). Patients in pathological or pharmacological coma (that is, general anesthesia) are unconscious because they cannot be awakened. VS is a dissociated state of consciousness (i.e., patients being seemingly awake but lacking any behavioral evidence of 'voluntary' or 'willed' behavior) (The Multi-Society Task Force on PVS, 1994). Patients in MCS will show more than the mere reflex behavior observed in VS survivors, but they are unable to effectively communicate (Giacino et al., 2002). Even for experts, the VS is a very disturbing condition. It illustrates how the two main components of consciousness can get completely dissociated—wakefulness—which remains intact and awareness of environment and self—which is abolished. In addition to its clinical and ethical importance, studying VS patients offers a still largely underestimated means to the study of human consciousness. In contrast to other unconscious states such as general anesthesia and deep sleep, where impairment in arousal cannot be disentangled from impairment in awareness, we are here offered a unique lesional

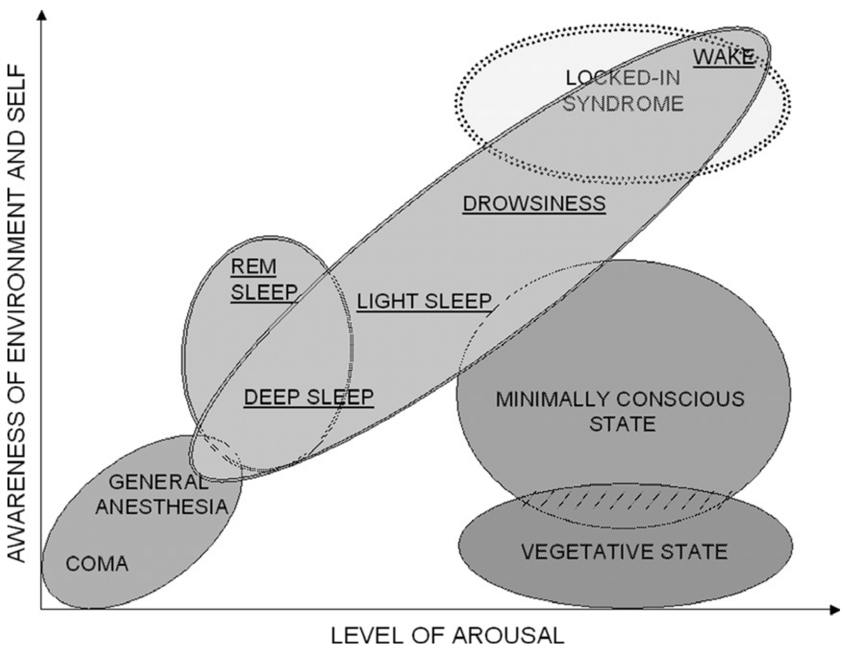

Fig. 1. Arousal positively correlates with awareness of environment and self. Graphical illustration of the two major components of consciousness: wakefulness or arousal (i.e., the level of consciousness) and awareness of environment and self (i.e., the content of consciousness). In normal physiological states (underlined) arousal and awareness are positively correlated (with the exception of the oneiric activity during REM sleep). Patients in pathological or pharmacological coma (that is, general anesthesia) are unconscious because they cannot be awakened. The vegetative state illustrates the dissociation between arousal and awareness (i.e., patients being seemingly awake but lacking any behavioral evidence of awareness of the environment and hence, it is assumed, of self).

approach enabling us to identify the neural correlates of (un)awareness (Laureys, 2005a). The current clinical challenge is to unambiguously disentangle patients residing in the clinical 'gray zone' between VS and MCS (Giacino & Whyte, 2005). The LIS is a rare but horrifying situation where patients awaken from their coma being fully aware of environment and self but remaining mute and immobile (Laureys, Perrin, Schnakers, Boly, & Majerus, 2005).

Unfortunately, for the time being, consciousness or self-consciousness cannot be measured objectively by any machine. In non-communicative patients with DOC, its estimation requires the interpretation of motor responsiveness (Fig. 2). The perception of self we are interested in is a conscious experience: the wakeful unconsciousness of vegetative patients, by definition, precludes this experience. There is of course a theoretical problem to evaluate the subjective experience of self-consciousness (and any other conscious perception or thought) in another person (Bernat, 1992). As stated above, we can only infer the presence or absence of conscious experience in another person and VS and MCS patients, by definition, cannot communicate their thoughts and feelings. At the bedside we are limited to the observation of spontaneous behavior and to evaluate the patient's behavioral responsiveness to external stimuli. If patients never show any sign of voluntary movement it will be concluded they do not experience awareness of environment and hence it is assumed of self. Many scoring systems have been developed for a standardized assessment of consciousness in severely brain damaged patients (for review, see Majerus, Gill-Thwaites, Andrews, and Laureys, 2005). Worldwide, the most used "consciousness-scale" is the Glasgow Coma Scale (GCS). Teasdale and Jennett (1974) developed the GCS as an aid in the clinical assessment of post-traumatic unconsciousness (its advantages and shortcomings are discussed in Laureys et al., 2002a). The GCS has three components: eye (E), verbal (V) and motor (M) response to external stimuli. The best or highest responses are recorded and the maximum score consists of 15 points. It was devised as a formal scheme to overcome the ambiguities that arose when information about comatose patients was presented and groups of patients compared. Self-consciousness is rarely assessed in the clinical evaluation of coma and related conditions. To the best of our knowledge, the only clinical consciousness scale possibly referring to self-consciousness in DOC is the Coma Recovery Scale-Revised (CRS-R, Giacino, Kalmar, & Whyte, 2004). The CRS-R indeed explicitly tests patient's visual fixation and tracking using a moving mirror. We will next briefly define the clinical entities that may be encountered following coma.

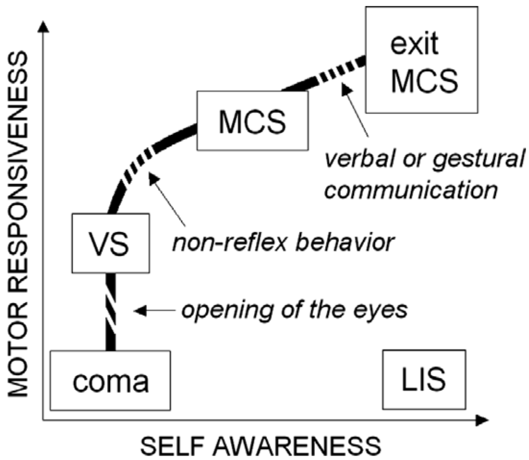

Fig. 2. Evaluation of self-awareness is biased by evaluation of motor responsiveness. Different clinical entities encountered on the gradual recovery from coma, illustrated as a function of self-awareness and motor capacities. Clinicians depend on the interpretation of motor responsiveness when assessing potential self-awareness. Restoration of spontaneous or elicited eye-opening (bilateral ptosis should be ruled out as a complicating factor), in the absence of voluntary motor activity, marks the transition from coma to vegetative state (VS). The transition from VS to the minimally conscious state (MCS) is marked by reproducible evidence of "voluntary" non-reflexive behavior. Emergence from MCS is signaled by the return of functional communication or object use. The locked-in syndrome (LIS) is the extreme example of intact cognition and self-awareness with nearly complete motor deficit (only permitting eye-coded communication).

3. Death, coma, vegetative, minimally conscious and locked-in

The concept of brain death as defining the death of a person is largely accepted (Bernat, 2005) and based on the loss of all brainstem reflexes and the demonstration of continuing cessation of respiration in a persistently comatose patient (Wijdicks, 2001). It should be noted that some authors have proposed that death be defined by the permanent cessation of ‘‘those higher functions of the nervous system that demarcate man from the lower primates’’ (Brierley, Graham, Adams, & Simpsom, 1971). This neocortical or higher brain death definition has been mainly developed by philosophers (Gervais, 1986; Veatch, 1975) and its conceptual basis rests on the premise that consciousness, cognition and social interaction, not the bodily physiological integrity, are the essential characteristics of human life. Based on this definition patients in VS following an acute injury or chronic degenerative disease and anencephalic infants are considered dead. The neocortical definition of death has never convinced medical associations nor courts (for recent review, see Laureys, 2005b).

Coma is characterized by the absence of arousal and thus also of awareness. It is a state of unarousable unresponsiveness in which the patient lies with the eyes closed and has no awareness of self and surroundings (Plum & Posner, 1983). In general, comatose patients who survive begin to awaken and recover gradually within 2–4 weeks. This recovery may go no further than VS or MCS, or these may be stages (brief or prolonged) on the way to more complete recovery of consciousness.

Patients in a VS are awake but are unaware of self or of the environment (Jennett, 2002; Jennett & Plum, 1972). Jennett and Plum cited the Oxford English Dictionary to clarify their choice of the term ‘‘vegetative’’: to vegetate is to ‘‘live merely a physical life devoid of intellectual activity or social intercourse’’ and vegetative describes ‘‘an organic body capable of growth and development but devoid of sensation and thought’’. ‘‘*Persistent* VS’’ has been arbitrarily defined as a vegetative state still present one month after acute traumatic or non-traumatic brain damage but does not imply irreversibility (The Multi-Society Task Force on PVS, 1994). ‘‘*Permanent* VS’’ denotes irreversibility. The Task Force concluded that three months following a non-traumatic brain damage and twelve months after traumatic injury, the condition of VS patients may be regarded as ‘permanent’ and therefore irreversible. It is very important to stress the difference between persistent and permanent vegetative state which are, unfortunately, too often abbreviated identically as PVS, causing unnecessary confusion (Laureys, Faymonville, & Berre, 2000a). When there is no recovery after a specified period (depending on etiology three to twelve months) the state can be declared permanent and only then do the ethical and legal issues around withdrawal of treatment arise (American Congress of Rehabilitation Medicine, 1995; Jennett, 2005). The vegetative state can also be observed in the end-stages of some chronic neurodegenerative diseases, such as Alzheimer’s, and in anencephalic infants.

The criteria for MCS were recently proposed by the Aspen group to subcategorize patients above VS but unable to communicate consistently. To be considered as minimally conscious, patients have to show limited but clearly discernible evidence of consciousness of self or environment, on a reproducible or sustained basis, by at least one of the following behaviors: (1) following simple commands, (2) gestural or verbal yes/no response (regardless of accuracy), (3) intelligible verbalization, (4) purposeful behavior (including movements or affective behavior that occur in contingent relation to relevant environment stimuli and are not due to reflexive activity; e.g., visual tracking of the mirror image or orientation to the own name and not to other names). The emergence of MCS is defined by the ability to use functional interactive communication or functional use of objects (Giacino et al., 2002). Further improvement is more likely than in VS patients (Giacino, 1997). However, some remain permanently in MCS. ‘‘Akinetic mutism’’ is an outdated term that should better be avoided (ANA Committee on Ethical Affairs, 1993) and is now considered to be a subcategory of the minimally conscious syndrome (American Congress of Rehabilitation Medicine, 1995; Giacino et al., 2002). It was first introduced by Cairns in 1941 to describe a condition characterized by severe poverty of movement, speech and thought without associated arousal disorder or descending motor tract impairment. Typical for akinetic mutism is the complete or near-complete loss of spontaneity and initiation so that action, ideation, speech and emotion are uniformly reduced. The absence of internally guided behavior allows attention to be passively drawn to any environmental stimulus that the patient is exposed to (Giacino, 1997). The preservation of spontaneous visual tracking and occasional, albeit infrequent, speech and movement to command, help differentiate akinetic mutsim from VS.

The term "locked-in" syndrome was introduced by Plum and Posner in 1966 to reflect the quadriplegia and anarthria brought about by the disruption of corticospinal and corticobulbar pathways, respectively, (Plum & Posner, 1983). It is defined by (i) the presence of sustained eye-opening (bilateral ptosis should be ruled out as a complicating factor); (ii) preserved awareness of the environment; (iii) aphonia or hypophonia; (iv) quadriplegia or quadriparesis; (v) a primary mode of communication that uses vertical or lateral eye movement or blinking of the upper eyelid to signal yes/no responses (American Congress of Rehabilitation Medicine, 1995).

4. Self-referential stimuli

Clinical practice shows that self-referential stimuli such as the use of the patient's own name or the patient's own face (using a mirror) are more effective stimuli to explore patients' responsiveness as compared to non-self related stimuli. Often, specific behavioral responses to self related stimuli are amidst the first signs heralding further recovery of consciousness as witnessed by some well-documented case-reports (Laureys et al., 2004; Owen et al., 2006). In everyday social interactions, hearing our own first name captures our attention and gives rise to a sense of self-awareness, since it is one of the most socially self related stimuli. Our own first name is intrinsically meaningful for each of us because of its personal significance, its emotional content and repetition along life. Beyond our day-to-day experience, the extreme salience of being presented one's own name or face was highlighted in various experimental and clinical studies. Some of these suggest that self-referential stimuli are so potent that they can "capture attention and subsequently bring the stimulus into awareness" (Mack, Pappas, Silverman, & Gay, 2002). We will next discuss what might make our own name or face "special" or not (see also Gillihan & Farah, 2005).

4.1. Own name

Does one's name capture attention? It seemingly does. For instance, people sometimes notice when their own name was mentioned in a conversation that they were not consciously attending to (i.e., the cocktail party phenomenon). This commonplace observation has been investigated in an experimental setting by Moray (1959). Participants, involved in a dichotic listening task, shadowed spoken messages played in one ear, ignoring the message played in the other ear. When the unattended message consisted of ordinary words, participants did not notice these words. However, participants were able to notice the occurrence of their own names when presented to the unattended ear in approximately one third of trials. These results were replicated later (Wood & Cowan, 1995). In order to study the attention-grabbing properties of one's own name in the visual modality, a visual analogue of Moray's auditory selective attention paradigm has been proposed by Wolford and Morrison (1980). In this study participants were presented two target digits flanking a word to be ignored and were instructed to indicate whether the two digits had the same parity (odd or even). When the irrelevant word was the participant's name, judgments of parity were slowed. Further studies using rapid serial visual presentation of stimuli indicated that the participants did not experience an attentional blink (detection of an initial target impairs detection of additional targets coming next during a short period of time) for their own names although they experienced it for other names (Shapiro, Caldwell, & Sorensen, 1997).The presentation of the participant's name as the target yielded a particularly strong impairment of the detection of following probes (Kawahara & Yamada, 2004). Moreover, the repetition blindness effect (undercounting of identical targets) was attenuated when the target was the participant's own name (Arnell, Shapiro, & Sorensen, 1999) and inattentional blindness was reduced (Mack & Rock, 1998).

All these studies suggest that one's own name is a stimulus that automatically grabs attention. Detecting one's name would not require limited-capacity processing resources. However, other studies reported data that do not support this view. In a series of speeded visual search experiments, Harris, Pashler, and Coburn (2004) showed that participants detected their own name more quickly than another individual's name but the effect of the display set size was too pronounced, i.e. search slopes were not flat enough, to reflect "pop-out" parallel search. In addition, the own name was not found to be a more potent distractor than another name. In another study, Harris and Pashler (2004) used the Wolford and Morrison (1980) procedure and evaluated whether the distraction effect due to the participant's name presentation persisted with repeated exposures of that word. They found that a significant slowing on the primary task for the first presentations of the participant's name, but this disruption effect rapidly disappeared with repetition of trials. Moreover, the distraction effect occurring on the first presentations of the participant's name was even eliminated when this name did not appear alone but was embedded in a large display of irrelevant words.

Therefore a first group of studies using Moray (1959) procedure (Wood & Cowan, 1995) and its visual analogue (Wolford & Morrison, 1980) or evaluating reduction of inattentional blindness (Mack & Rock, 1998) suggest that one's own name is a stimulus that automatically captures attention and provokes distraction. A second group of studies leads to strongly moderate such a conclusion. From these experiments, one's name does not seem to grab attention without the same usual attentional capacity limitations found for comparable other words even if one's name is easier to detect than other words (Bundesen, Kyllingsbaek, Houmann, & Jensen, 1997; Harris & Pashler, 2004; Harris et al., 2004). In studies that reported automatic capture of attention the disruption effect was estimated from a small number of presentations of the participant's name (one to four presentations) and small display loads were used. By contrast, in studies that did not find special attention grabbing for one's name, the display loads were more substantial and the distraction effect was evaluated from many presentations of the participant's name. The size of the display load and repetition of trials appear to be crucial factors (Harris & Pashler, 2004).

Taken together, the set of available results suggest that the first occurrences of one's own name, in a context where they are unexpected, provoke an involuntarily shift of attention when the perceptual load of the person's current activity is low and enough capacity is available for the one's name to be perceived. Otherwise, one's name seems not a more potent distracter than other words. In sum, the distraction caused by the presentation of one's name looks like a response of surprise that habituates very rapidly rather than an enduring ability of one's own name to attract attention.

Although one's name is no more potent than other names as a distracter, most studies reported that it is more readily detected as a target than other comparable stimuli (Arnell et al., 1999; Bundesen et al., 1997; Harris & Pashler, 2004; Harris et al., 2004; Shapiro et al., 1997). This particularly easy detection in usual laboratory experiments with healthy participants is consistent with research that showed powerful detection of the own name in situations of reduced consciousness. Auditory presentation of the participant's name during sleep may awaken her or him (Oswald, Taylor, & Treisman, 1960). Robust responses were also found in demented patients whose perception of their own name deteriorated well after perception of time, place and recognition (Fishback, 1977). In addition, after general anesthesia, the patient's reactivity to her or his name occurs first, before reactivity to pain and noise (Kurtz et al., 1977). How can this easier detection of one's own name be interpreted? One's own name has particular properties: it is a very familiar stimulus and it is presumably an emotionally charged stimulus. However, it remains to be shown whether each of these two properties may explain the ease of detection of one's name in the environment. One's own name is a piece of information that we use to process in the auditory modality from infancy: 4–5 month-old infants are able to recognize the sound pattern of their own names (Mandel, Jusczyck, & Pisoni, 1995) (but see Newman, 2005). Later in childhood, one's own name is also one of the first lexical items that we usually learn to write and read (Levin, Both-De Vries, Aram, & Bus, 2005; Villaune & Wilson, 1989). Although it has been shown that word frequency has no pronounced effect on visual search (Rayner & Raney, 1996) it would be premature to exclude the effect of extreme personal familiarity on the ease of detection of words such as one's name in the environment. We think that the extreme familiarity of one's name remains a plausible factor to explain its easier detection.

One's name is usually considered as a positively charged word (e.g., Zajonc, 1998). This emotional property might also be a factor that plays a role in the ease of detection of one's name or in the momentary shift of attention that one's name may produce. However, Harris et al. (2004) showed no advantage of the detection of emotionally charged words in visual search tasks. More generally, evidence as to whether emotional words draw attention is inconclusive outside the psychopathological populations (Harris & Pashler, 2004; Mackintosh & Mathews, 2003; Williams, Mathews, & MacLeod, 1996). Therefore, it is not clear whether the emotional charge of one's name is, even in part, responsible for the facilitated detection of one's name. Recently, Schimmack & Derryberry (2005) suggested that the key variable that makes a stimulus able to attract attention is not its level of emotional valence (positive *vs* negative) but its level of emotional arousal level (provoking a tense or excited state *vs* a relaxed or bored state). It is possible that one's name possesses a very high arousal level making it easy to detect and making it prone to catch attention when enough resources are available for perceiving it. Although such a hypothesis is to be considered seriously, to date the arousal level of the own name remains to be elucidated.

In summary, one's own name does not seem to provoke a solely automatic capture of attention, i.e. it does not grab attention independently of the perceptual load of the ongoing cognitive activity. However the occurrence of one's name in the environment is particularly prone to momentarily trigger an involuntary shift of attention when enough capacity is available. In addition, the own name is especially easy to detect in perceptual search situations. Future research should test whether the high familiarity of one's name and its potentially high arousal level can explain one's name special capacities.

4.2. Own face

Response to another self-referential stimulus such as one' own face could also be useful for the study of residual self-awareness in patients insofar as one's face is not commonly used by other people as an alerting stimulus. Therefore the presentation of one's face is not likely to have been associated with alert or orienting toward another person in the past. The presentation of this stimulus might be more appropriate for tapping explicit self-processing than the presentation of one's name.

Several recent studies demonstrated that faces constitute a class of stimuli that are especially prone to capture attention (Bindemann, Burton, Hooge, Jenkins, & de Haan, 2005; Bindemann, Burton, & Jenkins, 2005; Lavie, Ro, & Russell, 2003; Theeuwes & Van der Stichgel, 2006). However, few studies evaluated whether one's own face, because of its self-significance, is more likely to draw attention than other faces. Tong and Nakayama (1999) showed that, similarly to one's name, one's own face is easier to detect than other faces in visual search tasks but it does not ''pop out'' within a set of faces and is no more distractive than other faces in such tasks (see also Laarni et al., 2000). However, one's face has been shown to disrupt a person classification task from names more strongly than another personally familiar face (Brédart, Delchambre, & Laureys, 2006). Even if, obviously more research is needed to understand attentional properties of one's face, the use of the patient's face as stimulus seems particularly promising for the study of residual self-awareness in non-communicative patients. Indeed, the name (in particular the first name) is a property that we usually share with other people. By contrast, the face is really a unique characteristic (with the exception of identical twins).

5. Split selves

The examination of split-brain patients has demonstrated that both hemispheres independently possess the ability for self-face-recognition (Sperry, Zaidel, & Zaidel, 1979; Uddin, Rayman, & Zaidel, 2005). However, evidence that self-recognition preferentially involves the right hemisphere has been reported. Several studies have indicated a left-hand advantage in self-face-recognition tasks in healthy participants (Keenan, Gallup, & Falk, 2003; Keenan, Ganis, Freund, & Pascual-Leone, 2000; Keenan, McCutcheon, Freund, Gallup, & Sanders, 1999; Platek & Gallup, 2002; Platek, Keenan, Gallup, & Mohamed, 2004; Zhu, Qi, & Zhang, 2004) supporting the view that the right hemisphere is predominant in self-recognition. A right hemispheric advantage for self-face recognition in a callosotomy patient has also been reported (Keenan, Wheeler, Platek, Lardi, & Lassonde, 2003). In addition, patients who were undergoing Wada tests were showed images of themselves morphed with a famous face during right and left hemispheric anaesthetization. After the anesthesia has subsided, patients were asked about the face they were shown. They were more likely to report having seen themselves after the anaesthetization of the left hemisphere than after the anaesthetization of the right hemisphere (Keenan, Nelson, O'Connor, & Pascual-Leone, 2001). Finally, healthy patients showed greater right hemispheric activity, as measured by evoked potentials, while presented with morphed or masked pictures of their own face as opposed to pictures of another person (Keenan et al., 2001; Theoret et al., 2004).

However, there are studies that support the opposite view that the left hemisphere has a dominant role in self-recognition. In one study a split-brain patient was presented with morphed images blending his own face with a familiar person's face (Turk et al., 2002). These images were presented separately to the left and to the right hemispheres. In one condition the patient's task was to determine whether a presented image was himself while in another condition his task was to determine whether the image was the familiar person. The rate of self-detection was higher when the images were presented to the left than to the right hemisphere. On the opposite, detection of the familiar person was better when the images were presented to the right than to the left hemisphere. More recently, healthy participants were asked to choose which of two chimeric faces (one made from the left half and one made from the right half of their face) looked more like themselves (Brady, Campbell, & Flaherty, 2004). They showed a bias for the composite made from the half face that lies in their right visual field when they look at themselves in the mirror. When asked to make the same choice for similar images of a friend, they showed the opposite bias, i.e. they preferentially chose the composite made from the half face that lies in their left visual field when they look at their friend. Such results suggest that the left hemisphere is dominant for self-recognition and the right hemisphere is dominant for the recognition of others.

5.1. Evoked potentials to self-referential stimuli

Event-related potentials (ERPs) are a useful complimentary tool to objectively investigate cerebral mechanisms underlying the processing of self-referential stimuli, notably in non-communicative patients. ERPs show the temporal dynamics of electrico-cerebral processes evoked by sensory stimuli, without the need of any explicit or behavioral response. By calculating the means of EEG epochs, the activity time-locked to the stimulus is preserved, whereas spontaneous brain activity cancels itself out for simple statistical reasons. Evoked potentials correspond to voltage deflections, characterized by their amplitude and latency, the latter indexing the time course of information processing from receptive structures to associative cortices (for review see Deuschl & Eisen, 1999).

One interesting potential is the P300 wave (also called P3 or LPC for late positive component) which is elicited when subjects detect a rare and unpredictable target stimulus in a regular train of standard stimuli, i.e. in the oddball paradigm (Sutton, Braren, Zubin, & John, 1965). The P300 wave peaks near 350 ms and has a parietal maximal topography. Particularly alerting and novel stimuli produce an overlap component, labeled P3a, peaking near 250 ms at frontal maximal topography (Squires, Squires, & Hillyard, 1975). Both P3a and P300 (sometimes labeled P3b) vary in amplitude with stimulus probability, but they are differentially affected by the subject's attention. P3a amplitude is quite similar in active or passive attentional tasks whereas P3b is larger in active oddball task, suggesting that P3a is more sensitive to involuntary attention and P3b to attentional mechanisms. Even if the functional significance of P300 is not yet clear, it is seen as a post-decisional process since it follows the EMG response of the stimulus detection (Goodin & Aminoff, 1984). As suggested by Verleger (1988), it would reflect the closure of the cognitive period following the identification of the stimulus.

5.2. Conscious wakefulness

The P300 wave is decreased with reduced voluntary attention, but it is still elicited in passive paradigms, for example when the subjects are instructed to daydream or when they have to solve a word puzzle (Polich, 1989). Its amplitude is particularly large when the rare or deviant stimulus is a word (Lew, Slimp, Price, Massagli, & Robinson, 1999) and when it is salient for the subject, for instance her or his own first name (e.g., Berlad & Pratt, 1995; Fischler, Jin, Boaz, Perry, & Childers, 1987; Muller & Kutas, 1996), and even more if spoken by a familiar voice (Holeckova, Fischer, Giard, Delpuech, & Morlet, 2006). As the P300 wave depends both on the probability of occurrence of the stimulus and its deviance, it is not possible to know whether this potential reflects the detection of the physical characteristics of the subject's own name stimulus (like its probability) or its intrinsic significance. Thus, it was proposed to present the key stimulus (the first name) against a number of other first names in strict equiprobable fashion, to get rid of possible ambiguities linked to semantic category, habituation or physical novelty phenomena, and therefore obtain responses specifically linked to the processing of stimulus significance (Perrin, García-Larrea, Mauguiere, & Bastuji, 1999; Perrin et al., 2005). By this procedure, it was possible to record an electrophysiological response to the subject's own name which signs its identification, i.e. some kind of self-processing, and which is independent of its probability of occurrence. The characteristics of this potential are very consistent with those of the classical P300 wave to tones stimuli. Only the latency of the P300 to first names (500 ms) was much longer than that usually obtained in response to pure tones (300 ms), this being probably the consequence of the difference in the length of the stimulus (see discussion in Perrin et al., 1999)—see Fig. 3(a and b).

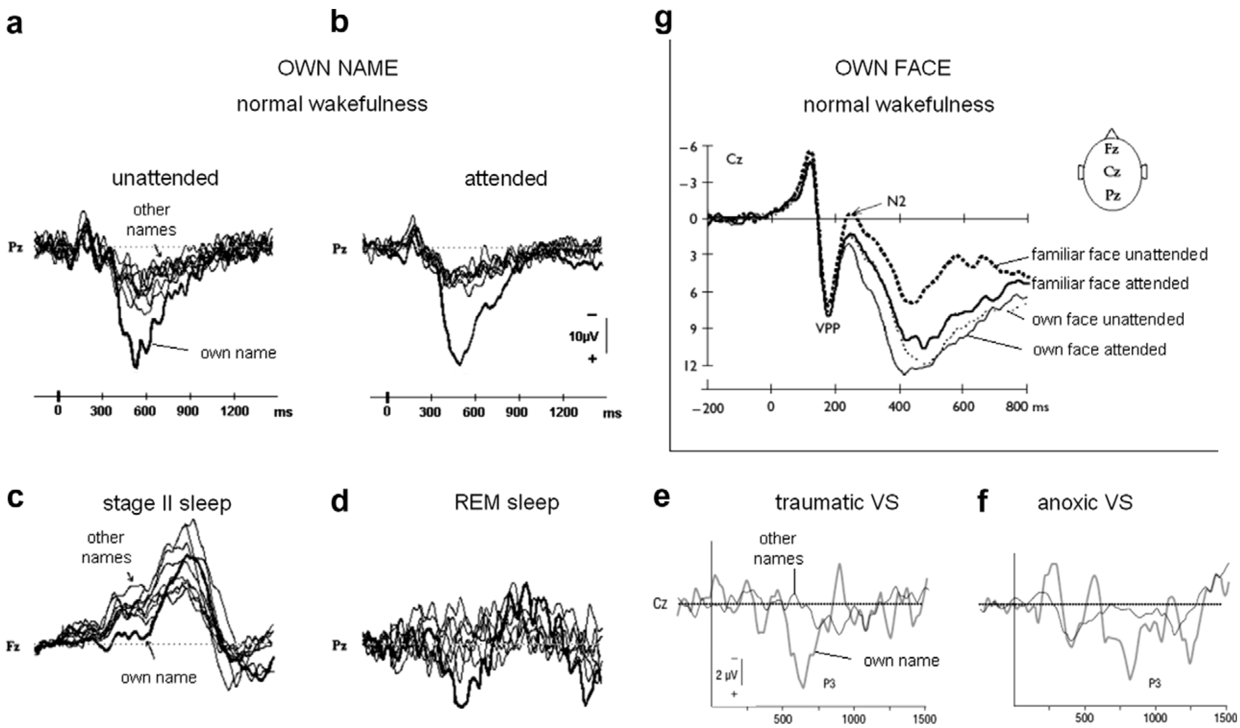

Fig. 3. Event-related potentials to the own name and the own face in normal and altered states of consciousness. P3 response to the subject's own name as compared to each of the 7 other names presented during wakefulness in (a) unattended (i.e., passive presentation) and (b) attended (i.e., asked to count the number of presentations of their own name) conditions. ERP responses persist during (c) stage II sleep and (d) rapid eye movement (REM) sleep. Unpublished figure from data published by Perrin et al. in Clinical Neurophysiology (1999). Preserved P3 response to patient's own name identified in (e) a post-traumatic vegetative state (VS) patient, studied 2 weeks after injury, who failed to recover consciousness at 1 year follow-up; and in (f) a VS patient following cardio-respiratory arrest who died eight months later without ever showing signs of recovery. Reprinted from Perrin et al. in Archives of Neurology—American Medical Association (2006). (g) Grand-average ERPs elicited by attended and unattended self-faces and familiar other faces during normal wakefulness, reprinted from Sui et al. Neuroreport (2006).

Self-processing was also explored by the use the subject's own face, but only in a few studies. Similarly, this stimulus elicits a higher P300 (or LPC) wave than familiar or unfamiliar faces (Ninomiya, Onitsuka, Chen, Sato, & Tashiro, 1998; Sui, Zhu, & Han, 2006), with similar morphology, latency and scalp topography than the response to the subject's own name (Fig. 3g). This effect was not observed in another study (Caharel et al., 2002), probably because of the very high occurrence of the subject's own face, illustrating the major habituation effect of such paradigms.

5.3. Sleep and the vegetative state

The electrophysiological index of self-referential stimuli identification was used in reduced or altered states of consciousness to assess whether some kind of self-processing remains. During sleep, the presentation of the subject's first name evokes a differential brain electrical response, as compared to other first names (Perrin et al., 1999; Perrin et al., 2005; Pratt, Berlad, & Lavie, 1999) suggesting that the identification of self-referential stimuli remains during reduced states of consciousness. Fig. 3c and d illustrates the identification of a P3 wave in stage II and REM sleep. The response appears delayed in stage II sleep, as reflected by the delayed P300 latency, probably because of the decreased transmission of sensory information by the thalamus during slow wave sleep (Steriade, Datta, Pare, Oakson, & Curro Dossi, 1990). During paradoxical or REM sleep, the P300 wave is not delayed but increased in amplitude at the left hemisphere recordings; probably reflecting the activation of partially different intracerebral generators as compared to wakefulness.

Very recently, the integrity of detection of the subject's first name was investigated in patients in a vegetative state, in a minimally conscious state and in a locked-in syndrome (Perrin et al., 2006). A P3 wave was observed in response to the patient's first name, as compared to 7 other first names, in all LIS patients, in all MCS patients and in 3 out of 5 patients in a VS (see Fig. 3e and f). The P300 latency was delayed for MCS and VS patients as compared to healthy volunteers, suggesting a slower top–down processing. Even if only 3 scalp electrodes were recorded during this experiment, it is interesting to note that the P300 response was maximal at parietal sites as was observed for controls. These results suggest that partially preserved self-referential stimuli identification could be observed in non-communicative brain damaged patients. Our group failed to identify a P3 response to the own name during profound general anesthesia using propofol and remifentanil. Some authors, however, using an auditory oddball paradigm (employing sounds not the subjects' own name) demonstrated a P3 response in pharmacological coma (Jessop et al., 1991; Reinsel, Veselis, Wronski, & Marino, 1995; Sneyd et al., 1994; Ypparila, Karhu, Westeren-Punnonen, Musialowicz, & Partanen, 2002)—but others failed to confirm these results (Plourde & Boylan, 1991; van Hooff, de Beer, Brunia, Cluitmans, & Korsten, 1997; Van Hooff et al., 1995). Also in pathological coma a P3 can sometimes be observed and has been proposed by limited series to herald some prognostic value (Gott, Rabinowicz, & DeGiorgio, 1991; Mutschler et al., 1996; Signorino, D'Acunto, Angeleri, & Pietropaoli, 1995). Finally, presentation of the own name in comatose patients was shown to increase the chances of obtaining a differential brain responses associated to information processing (Signorino et al., 1995).

In conclusion, differential electrical brain responses are still observed in different states of reduced (stage II sleep and REM sleep) or altered (VS and MCS) consciousness. However, this response is sometimes delayed (reflecting delayed processing) and/or had a different scalp topography (reflecting the activation of partially different generators), as compared to healthy awaked subjects. In all cases, it shows that a differential cognitive detection is made between the subject's own name and other first names. But what does a preserved P300 to the own name learns us with regard to consciousness?

5.4. What does a P300 mean?

An important clinical question in the study of non-communicative patients is the significance of this differential P300 brain response, and if it could reflect conscious perception. By using an alerting stimulus, one could expect to observe a frontal P3a in response to the subject's own name, because it generally reflects an orienting processing. This could be particularly true in patients in an altered states of consciousness. Surprisingly, a parietal P300 (or P3b) was observed, a component which is thought to be modulated by voluntary attentional processes. This could suggest that top–down attentional mechanisms are partially preserved in some of these patients, i.e. that the dorsal system still modulates the sensory cortex (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000). As suggested by Picton (1992), the P300 potential could reflect access of salient information to conscious processing. However, since the elicitation of a P300 wave is not necessarily concomitant to conscious awareness (it is also evoked during unconscious, subliminal perception, Brazdil, Rektor, Daniel, Dufek, & Jurak, 2001), we would rather limit the current interpretation of our identified P300 response in some of our patients in a VS as an index of partially preserved, albeit restricted, cerebral processing for "automatic" speech comprehension.

As previously mentioned, studies with healthy participants appear to show that reaction to one's name is not automatic but can be involuntary. Of course, it is accompanied with an explicit recognition of one's name in healthy participants. However, this does not proof that the patients' P300 brain response to their names reveals an explicit recognition. This brain response might be the correlate of a mere implicit response that would not involve self-consciousness or even consciousness at all. A brain response to self-referential stimuli may be, but is not necessarily, a sign of self-consciousness. In everyday life one's name is often used as an alerting external stimulus provoking an orienting response. Hence, the patients' P300 response might merely reflect a conditioned orienting response due to hearing one's name.

It has been reported that the visual presentation of the participant's name as a distractor triggers an orienting response (measured by skin conductance response, SCR) when this stimulus is located inside the focus of attention but not when it is located outside this focus (Gronau, Cohen, & Ben-Shakhar, 2003). This suggests that attention to one's name is needed for the SCR to appear. Therefore the recording of SCR in addition to the ERPs seems interesting. The occurrence of a differential SCR response to the auditory presentation of the own name might indicate that the patient was attending her or his auditory environment. It is possible that the occurrence of SCR will occur in MCS and not in VS. Stimulation-induced SCR changes have been shown to correlate with the level of consciousness in severely brain damaged patients (Wijnen, Heutink, Boxtel, Eilander, & Gelder, 2006). Studies in healthy volunteers, however, have shown enhanced autonomic arousal in response to conscious as well as nonconscious stimuli (Williams et al., 2004). Hence, changes in autonomic arousal play a role in differentiating emotionally salient sensory input, even in the absence of conscious recognition.

6. Functional neuroimaging of self-consciousness

A recent meta-analysis by Northoff et al. (2006) of 27 PET and fMRI studies comparing hemodynamic brain responses obtained during active paradigms comparing processing of stimuli related to the self with those of non-self-referential stimuli identified activation in cortical midline structures in all studies and occurring across all functional domains (e.g., verbal, spatial, emotional, and facial). Cluster and factor analyses indicated functional specialization into ventral, dorsal, and posterior cortical midline areas. The latter encompasses the posterior cingulate cortex and adjacent precuneus and is considered to be involved in self integration—that is linkage of self-referential stimuli to the personal context (Northoff & Bermpohl, 2004). Neuroimaging studies during tasks involving self-processing (i.e. self-reflection, self-perspective and free thoughts) have also reported the activation of the medial prefrontal areas. Gusnard, Akbudak, Shulman, and Raichle (2001) for example showed medial prefrontal activation when subjects had to make two judgments in response to pleasant *vs* unpleasant pictures (i.e. self-referential) as compared to indoors *vs* outdoors pictures (i.e. not self-referential). The same area was also shown to be engaged when subjects had to make self-referential judgments about trait adjectives (i.e. self-referential processing) as compared to when they had to make case judgments (Kelley et al., 2002) and when subjects responded to statements requiring knowledge of, and reflection on, their own abilities, traits and attitudes—i.e. self-reflective thought—(Johnson et al., 2002). Taking a self-perspective (i.e. being the agent of an history) also activated medial prefrontal/anterior cingulate cortices (Vogeley et al., 2001). Finally, activation of the mesiofrontal areas was described in studies dealing with the conscious resting state, i.e. free thought (Mazoyer et al., 2001; Raichle et al., 2001), a brain state which "instantiates functions that are integral to the self".

6.1. Own name

Using an EEG-PET paradigm passively presenting the own name and other names without requiring subjects to attend or respond (and hence applicable to brain damaged patients) we have recently identified a linear regression between the P300 amplitude and right medial prefrontal cortex, right superior temporal sulcus and precuneus activation (Perrin et al., 2005) (Fig. 4). fMRI studies have also shown activation in medial prefrontal and right paracingulate cortex (Kampe, Frith, & Frith, 2003) and in left medial prefrontal cortex (Staffen, Kronbichler, Aichhorn, Mair, & Ladurner, 2006) when comparing brain activation to presentation of the subject's own name to other names using fMRI. These results are in line with the proposed critical role of midline structures in self-referential processing (Lou, Nowak, & Kjaer, 2005; Northoff & Bermpohl, 2004). Previous neuropsychological studies have also shown that impairments of self-awareness or self-reflection, as well as incapacity to reflect on personal knowledge, occur more frequently following medial prefrontal damage than other regions (Ackerly & Benton, 1947; Damasio, Tranel, & Damasio, 1990; Stuss, 1991; Wheeler, Stuss, & Tulving, 1997).

Self-referential stimuli have only sparsely been used in functional neuroimaging studies in patients with DOC. We used EEG-PET in a patient in MCS studied six months after a left frontal hemorrhage and showed that auditory self-referential stimuli (patient's own name) induced a more widespread activation than did non-self-referential emotional stimuli (baby cries) and much more than did meaningless noise (Laureys et al., 2004). At time of PET scanning, the patient showed eye fixation and tracked family members and a moving mirror, made no spontaneous limb movements, sporadically uttered incomprehensible (apparently meaningless) groans and inconsistently obeyed simple commands (e.g., showed his tongue when asked by his wife in 3

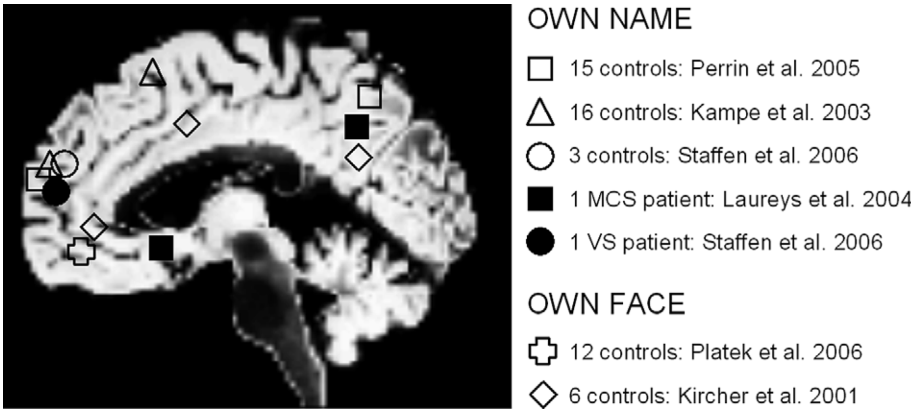

Fig. 4. Activation in cortical midline structures in functional neuroimaging studies during stimulation of self-related auditory (own name) and visual (own face) stimuli in healthy controls and in published case reports of VS and MCS patients.

out of 4 trials) but failed to make functional communication. Subsequent to EEG-PET the patient could make intelligible vocalizations and later showed signs of intentional communication. Overall cortical metabolism was 44% of normal control values (3.1 *vs* 7.1 mg/100 g min) and comparable to values previously observed in the vegetative state. Presentation of the patient's own name activated precuneus, anterior cingulate/mesiofrontal, right temporo-parietal, left dorsolateral prefrontal and bilateral angular gyri (midline activation is represented in Fig. 4). As stated above, the precuneus and adjacent posterior cingulate cortex was identified in many neuroimaging studies on self-processing (self-reflection: (Kircher et al., 2002, 2000; Kjaer, Nowak, & Lou, 2002), self-perspective: (Vogeley et al., 2001) and free thoughts: (Mazoyer et al., 2001; Raichle et al., 2001)) and on third-person perspective (see for example Ruby & Decety, 2001). In a broader perspective, this region seems to play a central role in the neural network subserving human consciousness. It is one of the most active cerebral regions in conscious waking (Andreasen et al., 1995) and one of the least active in states of altered consciousness such as REM and deep sleep (for a review see Maquet, 2000), in VS (Laureys et al., 1999), in hypnosis (Maquet et al., 1999) and in general anesthesia (Alkire et al., 1999; Fiset et al., 1999; Kaisti et al., 2002).

Our neuroimaging study permitted to objectively measure context-dependent higher-order auditory processing in a MCS patient which was not assessable at the patient's bedside using clinical evaluation. The described large-scale 'higher-order' cortical activation in MCS and the importance of meaningful stimuli (i.e., with emotional valence) in recruiting the widespread cortical activation has also been observed by others. Schiff et al. (2005) showed selective activation in components of the cortical language networks during presentation of narratives read by a familiar voice and containing personally meaningful content (compared to baseline) in two MCS patients. Presentation of the narratives played backward activated the same networks as forward narratives in the healthy controls, but not in the MCS patients. Similarly, Bekinschtein et al. (2004) showed amygdala activation induced by stimuli with emotional valence (the voice of the patient's mother compared with an unfamiliar voice) in a MCS case five months after trauma.

So far, functional neuroimaging in cohort studies of patients unequivocally meeting the clinical diagnosis of the VS, external stimulation using for example noxious (Laureys et al., 2002a) or auditory (Boly et al., 2004; Laureys et al., 2000a, 2000b) stimuli have classically shown systematic activation of primary sensory cortices disconnected from higher-order associative cortices considered necessary for conscious perception. However, anecdotal but increasing evidence from ERP (Hinterberger, Wilhelm, Mellinger, Kotchoubey, & Birbaumer, 2005; Kotchoubey et al., 2005; Perrin et al., 2006) and functional neuroimaging (de Jong, Willemsen, & Paans, 1997; Giacino et al., 2006; Menon et al., 1998; Owen et al., 2005) have shown 'preserved' evoked potentials or activation patterns in predicted regions of cortex in patients diagnosed as in VS. With regard to self-referential processing a recent fMRI study has reported selective medial prefrontal activation to the patient's own name as compared to other names in a VS case studied 10 months after cardiac arrest (Staffen et al., 2006). The patient died 1 year later without ever showing signs of awareness.

The question that arises is whether the observed brain activation indicates awareness. It is important to emphasize that studies of implicit learning, priming and anesthesia have shown that many brain processes go on in the absence of awareness. How can we disentangle in the previously reported data *automatic* from *conscious* brain activation. Owen et al. (2006) have recently addressed this issue by asking non-communicative patients to actively perform mental imagery tasks. In one exceptional VS patient studied five months after a cerebral trauma, activation was observed in the supplementary motor area after being asked to imagine playing tennis. When asked to imagine visiting the rooms of her house, activation was seen in premotor cortex, parahippocampal gyrus and posterior parietal cortex. Near identical activation was observed in the 34 healthy volunteers studied in Cambridge and Liège. The patient's decision to 'imagine playing tennis' rather than simply 'rest' must here be seen as an act of willed intention and, therefore, clear evidence for awareness. Interestingly, when re-examined six months later the patient showed inconsistent visual tracking—the most frequently encountered clinical sign of recovery from VS. Hence, fMRI results preceded the clinical evolution. Similarly, a study by Di et al. (2007) on 7 VS patients showed higher order cortical activation to the patients' own name in 2 patients who evolved to MCS 3 months after scanning.

6.2. Own face

Results from functional neuroimaging studies of self-recognition using the own face remain inconclusive. In an early PET study by Sugiura et al. (2000) the left fusiform gyrus and right supramarginal gyrus were considered to be involved in the representation of one's own face. More recent fMRI studies concluded that the right prefrontal regions are involved for self-face-recognition (Keenan, Wheeler, & Ewers, 2003; Platek et al., 2004). Uddin, Kaplan, Molnar-Szakacs, Zaidel, and Iacoboni (2005) reported that a neural network in the right hemisphere including the inferior frontal gyrus and the inferior parietal lobule is activated by the recognition of the self-face. Evidence suggesting bilateral involvement in self-face-recognition also exists. Kircher et al. (2000, 2001) reported activation in the right limbic system, left prefrontal cortex and temporal cortex during self-face processing. More recently, Sugiura et al. (2005) observed selective activation of the right occipito-temporo-parietal junction and frontal operculum, as well as in the left fusiform gyrus during self-recognition. Platek et al. (2006) recently argued for a bilateral network for both perceptual and executive aspects of self-face processing, rejecting the hemispheric dominance models. They showed that some regions of the medial frontal and parietal lobes were specifically activated by familiar faces but not unknown or self-faces, possibly signifying that these areas serve as markers of face familiarity and that the differences associated with self and familiar face-recognition are subtle and seem localized in a network encompassing lateral frontal, parietal, and temporal cortices. At present, there seems to be a lack of convergence as to precise anatomical locations underlying self-face-recognition.

So far, the patient's own face has not been employed in functional neuroimaging studies in DOC. A PET study by Menon et al. (1998) visually presented photographs of familiar faces in an upper boundary VS or lower boundary MCS post-encephalitis patient who subsequently recovered consciousness. Compared to meaningless pictures, the visual association areas encompassing the fusiform face area showed significant activation. Behaviorally, there was no evidence of awareness of environment except occasional visual tracking of family members.

7. Conclusion

Assessing self-consciousness in coma survivors who remain unable to verbally or non-verbally express their thoughts and feelings is difficult by means of behavioral observation only. Self-referential stimuli such as the patient's own name and own face are clinically valuable arousing and attention-grabbing emotional stimuli and their use increase the chances to obtain non-reflex ("willed" or "voluntary") motor responsiveness in DOC. Event-related potential and functional neuroimaging studies using such stimuli are currently being validated to help in differentiating unconscious vegetative from fluctuating minimally conscious patients. At present, based on evidence obtained from neuropsychological, neuropathological, electrophysiological and neuroimaging studies in sleep, pharmacological coma, pathological coma and related disorders of consciousness, we must conclude that the neural underpinnings of self-referential "unconscious" *vs* "conscious" processing remain to be further elucidated prior to their use in non-communicative brain damaged patients. However, the recent and increasing interest from the neuroscientific community for the study of self-referential processing, as evidenced by the present volume, will improve our insights into the neural correlates underlying the self, clarifying concepts so far resistant to empirical analysis.

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