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Can self-relevant stimuli help assessing patients with disorders of consciousness?

Renata del Giudice [a,b], Christine Blume [a,b], Malgorzata Wislowska [a,b], Julia Lechinger [a,b], Dominik P.J. Heib [a,b], Gerald Pichler [c], Johann Donis [d], Gabriele Michitsch [d], Maria-Teresa Gnjezda [a], Mauricio Chinchilla [e], Calixto Machado [e], Manuel Schabus [a,b,*]

[a] University of Salzburg, Department of Psychology, Laboratory for Sleep, Cognition and Consciousness Research, Hellbrunner Strasse 34, 5020 Salzburg, Austria
[b] Center for Cognitive Neuroscience Salzburg (CCNS), University of Salzburg, Hellbrunner Strasse 34, 5020 Salzburg, Austria
[c] Apallic Care Unit, Neurological Division, Albert-Schweitzer-Klinik, Graz, Austria
[d] Apallic Care Unit, Neurological Division, Donauspital Wien, Vienna, Austria
[e] Institute of Neurology and Neurosurgery, Department of Clinical Neurophysiology, Havana, Cuba

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ABSTRACT

Emotional and self-relevant stimuli are able to automatically attract attention and their use in patients suffering from disorders of consciousness (DOC) might help detecting otherwise hidden signs of cognition.

We here recorded EEG in three Locked-in syndrome (LIS) and four Vegetative State/Unresponsive Wakefulness Syndrome (VS/UWS) patients while they listened to the voice of a family member or an unfamiliar voice during a passive. Data indicate that, in a passive listening condition, the familiar voice induces stronger alpha desynchronization than the unfamiliar one. In an active condition, the target evoked stronger alpha desynchronization in controls, two LIS patients and one VS/UWS patient. Results suggest that self-relevant familiar voice stimuli can engage additional attentional resources and might allow the detection of otherwise hidden signs of instruction-following and thus residual awareness. Further studies are necessary to find sensitive paradigms that are suited to find subtle signs of cognition and awareness in DOC patients.

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1. Introduction

The gold standard in diagnosing patients with Disorders of Consciousness (DOC), i.e. Minimally Conscious State (MCS) and Vegetative State/Unresponsive Wakefulness Syndrome (VS/UWS) (Laureys et al., 2010), remains the assessment with behavioural scales such as the Coma Recovery Scale - Revised (CRS-R) (Giacino, Kalmar, & Whyte, 2004). However, due to arousal fluctuations, attentional, perceptual and motor deficits, behavioural assessment is extremely challenging in these patients and has repeatedly been linked to a high rate of misdiagnoses (Andrews, Murphy, Munday, & Littlewood, 1996; Schnakers, Vanhaudenhuyse, et al., 2009).

* Corresponding author at: Laboratory for Sleep, Cognition and Consciousness Research, Department of Psychology, University of Salzburg, Hellbrunner Strasse 34, 5020 Salzburg, Austria.

E-mail addresses: Renata.delGiudice@sbg.ac.at (R. del Giudice), christine.blume@sbg.ac.at (C. Blume), malgorzata.wislowska@gmail.com (M. Wislowska), Julia.Lechinger@sbg.ac.at (J. Lechinger), Dominik.Heib@sbg.ac.at (D.P.J. Heib), gerald.pichler@stadt.graz.at (G. Pichler), maria-teresa.gnjezda@stud.sbg.ac.at (M.-T. Gnjezda), braind@infomed.sld.cu (M. Chinchilla), braind@infomed.sld.cu (C. Machado), manuel.schabus@sbg.ac.at (M. Schabus).

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The possibility to be considered as being in a MCS is based on the assumption that if a patient retains consciousness, he or she will be able to give evidence of his/her awareness, for example by purposeful motor responses. In this case, the clinician infers that the patient retains some degree of consciousness of the self and/or the environment and this likely affects the daily care and interaction with the patient.

This rationale, however, is inherently problematic as patients may not be able to "give evidence" of their awareness when suffering from severe motor deficits like quadriplegia or spasticity. When considering patients in a Locked-in Syndrome (LIS), the limitations of behavioural assessment become particularly obvious (Giacino et al., 1995). Although this syndrome is not a disorder of consciousness in a strict sense, these patients can be entirely unable to produce any motor output with even eye movements being impaired ("totally locked-in syndrome"). Therefore, from a behavioural point of view, they seem to be VS/UWS, while in fact they are both awake and aware by definition and the level of information processing and consciousness is comparable with healthy individuals (Laureys, Gosseries, & Tononi, 2015; Laureys, Owen, & Schiff, 2004; Schnakers, Majerus, et al., 2008). It has to be mentioned that, although LIS patients are considered to retain a level of consciousness comparable to that of heathy individuals, due to their clinical condition and brain damages their brain responses can differ from controls and be sometime similar to that of DOC patients (Laureys et al., 2004, 2015).

Neuroimaging methods, such as functional magnetic resonance imagery (fMRI) and electroencephalography (EEG), have thus been used to overcome the limitations of behavioural assessment (Bruno, Gosseries, Ledoux, Hustinx, & Laureys, 2011; Cruse, Monti, & Owen, 2011; Monti et al., 2010; Owen, Schiff, & Laureys, 2009) and to investigate cognitive functioning and awareness in DOC patients. As wilful command-following is a strong indicator of retained awareness and can reliably be detected via EEG recordings. Many studies have adopted designs in which patients are asked to actively perform a task and follow commands, the so-called "active paradigms" (e.g., Cruse et al., 2011, 2012; Monti et al., 2010; Owen et al., 2006; Schnakers, Perrin, et al., 2008). More specifically, these paradigms circumvent the need for voluntary motor behaviour by relying on neurophysiological indicators of awareness. Therefore, if a patient is able to understand and follow task instructions, by performing the active condition we can assume that he/she retains a certain level of consciousness and volition. In previous active studies using EEG and active protocols, healthy participants and patients were often asked to focus their attention on and count their own name, which was presented auditorily among other names. A larger P3 amplitude for attended own names as compared to unattended names was for example observed in controls as well as in a group of MCS and one LIS patient but not in VS/UWS patients (Schnakers, Perrin, et al., 2008, 2009). This was interpreted as an indicator of voluntary behaviour and, thus, conscious top-down control. This straightforward interpretation of the P3 response has, however, recently been challenged by Silverstein, Snodgrass, Shevrin, and Kushwaha (2015). The authors were able to show that the P3 component can be also elicited by entirely subliminal stimulus presentation and, thus, that specific cognitive processes can occur without consciousness. The interpretation of the presence of a P3 component as an index of conscious processing is, therefore, substantially challenged. In another study, stronger theta event-related synchronization (ERS) as well as alpha event-related desynchronization (ERD) was reported when subjects counted the presentation of the subject's own name (SON) as compared to when participants were merely passively listening to it without a specific instruction (Fellinger et al., 2011). Interestingly, this task-induced (de)synchronization was evident only when the SON was to be counted, but not when participants were asked to count other unfamiliar names (UN). These findings support the notion that, due to its intrinsic emotional content and self-relevance, the SON might be easier to process than other names and may even facilitate the engagement of additional top-down attention (Holeckova, Fischer, Giard, Delpuech, & Morlet, 2006; Höller, Kronbichler, et al., 2011; Mack, Pappas, Silverman, & Gay, 2002; Perrin et al., 2005; Ruby et al., 2013). It has been consistently reported that other emotionally and self-relevant stimuli, such as familiar objects, infant cries or the voice of a family member are strongly processed in a bottom-up manner (Bekinschtein et al., 2004; Di et al., 2007; Jones, Hux, Morton-Anderson, & Knepper, 1994; Laureys, Perrin, & Brédart, 2007; Laureys et al., 2004). Therefore, emotionally relevant information may be easier to process, due to the stronger bottom-up strength, and therefore facilitate the deployment of top-down attention. Emotional stimuli may, thus, be particularly useful in paradigms that use instruction-following manipulations, such as in an active task, in DOC patients (de Jong, Willemsen, & Paans, 1997; Di Stefano, Cortesi, Masotti, Simoncini, & Piperno, 2012; Di et al., 2007; Fellinger et al., 2011; Holeckova et al., 2006; Perrin, Castro, Tillmann, & Luauté, 2015). This adaptation might therefore be crucial in preventing false negative results that is in missing wilful behaviour in non-communicative individuals. This is particularly true as active tasks usually involve a high demand on intact higher cognitive processes such as sustained attention, sensory processing, or remembering the instruction (Kondziella, Friberg, Frokjaer, Fabricius, & Møller, 2015).

The current study adopts a paradigm that has already been validated in healthy controls (del Giudice et al., 2014) and investigates the suitability of such a paradigm for the assessment of individual awareness levels in a first sample of DOC and LIS patients. We adopted the classic own name paradigm including a passive and an active condition (e.g. Schnakers, Perrin, et al., 2008) and additionally varied the familiarity of the voice (i.e. the voice of a familiar person vs. the voice of a stranger) and thus the emotional relevance of the stimuli. The introduction of familiar voices in the active condition, aims at confronting patients with emotionally relevant material, which might capture additional attentional resources, maximize patients' responsiveness and facilitate detection of task relevant stimuli. In the passive condition, participants were presented with their own name as well as other unfamiliar names uttered by both a familiar and a stranger's voice. In the active condition, we only presented UN in order to better differentiate top-down attention (i.e. instruction following and counting) from bottom-up attentional processes, which might be initiated automatically by the presentation of the SON (Perrin, García-Larrea, Mauguière, & Bastuji, 1999; Portas et al., 2000; Wood & Cowan, 1995).

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