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Towards using fNIRS recordings of mental arithmetic for the detection of residual cognitive activity in patients with disorders of consciousness (DOC)

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ABSTRACT

Background: Recently, fNIRS has been proposed as a promising approach for awareness detection, and a possible method to establish basic communication in patients with disorders of consciousness (DOC).
Aim: Using fNIRS, the present study evaluated the applicability of auditory presented mental-arithmetic tasks in this respect.
Methods: We investigated the applicability of active attention to serial subtractions for awareness detection in ten healthy controls (HC, 21–32 y/o), by comparing the measured patterns to patterns induced by self-performance of the same task. Furthermore, we examined the suitability of ignoring the given task as additional control signal to implement a two-class brain-computer interface (BCI) paradigm. Finally, we compared our findings in HC with recordings in one DOC patient (78 y/o).
Results and conclusion: Results of the HC revealed no differences between the self-performance and the attention condition, making the attention task suitable for awareness detection. However, there was no general difference between the ignore and attend condition, making the tasks less suitable for BCI control. Despite inconsistent correlations between the patient data and the HC group, single runs of the patient recordings revealed task-synchronous patterns – however, we cannot conclude whether the measured activation derives from instruction based task performance and thus awareness.

1. Introduction

Several factors can hamper the correct diagnosis of patients with disorders of consciousness (DOC). DOC is a collective term and comprises conditions that differ on the dimensions awareness and arousal (for a review on brain functions in DOC, see: Laureys, Owen, & Schiff, 2004). Apart from coma (no signs of awareness and arousal), it also includes patients in a vegetative state (VS), also known as unresponsive wakefulness syndrome (UWS; Laureys et al., 2010), and patients in a minimal state of consciousness (MCS), both showing signs of arousal. However, unlike patients with VS/UWS, who show no evidence of awareness, patients in MCS show at least partial behavioral evidence of self or environmental awareness (Giacino et al., 2002). As diagnostic errors can severely affect the patient's treatment (Giacino et al., 2002), standardized clinical assessment of the level of awareness is essential. Although behavioral scales (e.g. Coma Recovery Scale-Revised [CRS-R] or Glasgow Coma Scale [GCS]; Giacino, Kalmar, & Whyte, 2004; Teasdale & Jennett, 1974) provide a good tool for the differentiation of patients in different awareness states, only overt behavior can be assessed. For this reason, awareness detection with neuroimaging and electrophysiological methods can provide additional information about the patient's state (Giacino et al., 2009). Several studies using functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) have already investigated the suitability of different methods and paradigms for awareness detection in patients with DOC (e.g. Horki, Bauernfeind, Schippinger, Pichler, & Müller-Putz, 2016; Li et al., 2015; Monti et al., 2010; Owen et al., 2006, 2007; Pokorny et al., 2013; Rohaut et al., 2015). Especially fMRI studies have shown that some

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Table 1
Clinical information of the patients in MCS. Patient 1 reached a total CRS-R score of 11 before the fNIRS measurement. Patient 2 reached a total score of 15 before the first fNIRS measurement and a total score of 9 after the last fNIRS measurement.

Clinical Features	Patient 1	Patient 2
Gender [age]	Male [31]	Female [78]
Etiology	Wernicke-Encephalopathy	Polytrauma
CRS-R total score (max. 23)	11	15|9
Auditory function (0–4)	Localization to sound (2)	Reproducible movement to command* (3)|auditory startle (1)
Visual function (0–5)	Fixation* (2)	Fixation* (2)|visual startle (1)
Motor function (0–6)	Localization to Noxious Stimulation * (3)	Object manipulation* (4)|flexion withdrawal (2)
Oromotor/verbal function (0–3)	Vocalization/oral movement (2)	Vocalization/oral movement (2)|vocalization/oral movement (2)
Communication (0–2)	None (0)	Non-functional: intentional* (1)|non-functional: intentional* (1)
Arousal (0–3)	Eye opening w/o stimulation (2)	Attention (3)|eye opening w/o stimulation (2)

Note. w/o = without. CRS-R assessment took place before fNIRS measurement in patient 1; before the first and after last fNIRS measurement in patient 2.
* Indicates MCS.

DOC patients are consciously aware, but issues of expense and accessibility preclude the general use of fMRI assessment. Therefore, recent efforts focused on translating the fMRI paradigms to be also applicable with EEG recordings. For example, Cruse et al. (2011, 2012) investigated bedside detection of awareness with EEG in patients in the VS and compared their findings to healthy controls. Also Goldfine, Victor, Conte, Bardin, and Schiff (2011) investigated the use of EEG to determine awareness in three patients with severe brain injury, ranging from MCS to locked-in-state (LIS). All studies found in some patients evidence for task performance using EEG recordings, which seems to be a suitable tool for identifying awareness in patients. Although these findings and results are very encouraging, further investigations and improvements are necessary. For example, EEG recordings are strongly influenced by movement and muscle artefacts. Furthermore, as also some healthy controls are not able to produce significant task related EEG records (e.g. Cruse et al., 2011) additional recording modalities have to be investigated to allow a more proper and valid assessment of the presence or absence of consciousness. Recently, functional near-infrared spectroscopy (fNIRS, for an overview about the method see Ferrari & Quaresima, 2012; Scholkmann et al., 2014) has been proposed as a very promising approach within this context (Kempny et al., 2016; for a first detailed review see Rupawala, Dehghani, Lucas, Tino, & Cruse, 2018). fNIRS is a non-invasive optical technique for the in vivo assessment of cerebral oxygenation and perfusion (changes of oxygenated [oxy-Hb] and deoxygenated hemoglobin [deoxy-Hb]), which is strongly correlated with the fMRI blood-oxygen-level-dependent (BOLD) signal (Steinbrink et al., 2006; Strangman, Culver, Thompson, & Boas, 2002). Using a motor imagery task, Kempny et al. (2016) were the first to assess brain function in DOC patients using fNIRS. However, studies have shown that even some healthy subjects are not able to produce stable cortical activation patterns using motor-related mental tasks. EEG and fMRI studies that investigated, which type of mental imagery task generates the most robust activation across subjects, showed a clear evidence that mental arithmetic is the most promising task (Friedrich, Neuper, & Scherer, 2013; Friedrich, Scherer, & Neuper, 2012, 2013; Harrison, 2014; Harrison, Noseworthy, Reilly, Guan, & Connolly, 2017).

Therefore, mental arithmetic, which also has a long history in fNIRS studies, (e.g. Bauernfeind, Leeb, Wriessnegger, & Pfurtscheller, 2008; Hoshi & Tamura, 1993; Pfurtscheller, Bauernfeind, Wriessnegger, & Neuper, 2010; Tanida, Sakatani, Takano, & Tagai, 2004; Verner, Herrmann, Troche, Roebers, & Rammsayer, 2013), seems to be a very promising task approach to assess brain function in DOC patients.

The current study aimed to investigate whether an auditory presented mental arithmetic task (serial mental subtraction) is suitable to measure reproducible hemodynamic responses in patients with DOC, and is based on, and will be compared to, our previous investigations onto this task (i.e. Pfurtscheller et al., 2010). The auditory pathway was chosen as it is usually one of the last remaining input channels in DOC patients (Laureys et al., 2000; Perrin et al., 2006). Reproducible changes in oxy- and deoxy-Hb concentration during mental arithmetic as well as to healthy participant's comparable hemodynamic responses might indicate command following and thus awareness in the patient. Furthermore, differentiable responses to selective attention versus ignoring of auditory presented serial subtractions might raise the chance to implement the task in a mental arithmetic based two class Brain-Computer-Interface (BCI; e.g. Bauernfeind, Scherer, Pfurtscheller, & Neuper, 2011; Schudlo & Chau, 2014; Stangl, Bauernfeind, Kurzmann, Scherer, & Neuper, 2013). For a healthy control group we hypothesized an oxy-Hb decrease in medial anterior prefrontal areas (Pfurtscheller et al., 2010) during the self-execution of a serial subtraction task and the attention to the verbal presentation of the execution of a serial subtraction task. Instead of a different task as a control measure, we wanted to explore whether the ignoring of the same task (auditory presented subtractions) elicits differentiable hemodynamic responses. In the context of motor task execution, Hummel et al. (2004) and Wriessnegger et al. (2012) found opposite activation patterns for inhibition vs. execution of the same motor task.

2. Material and methods

2.1. Participants

Ten healthy adult individuals with at least higher education entrance qualification (eight male, aged between 21 and 32, $M = 26.2$, $SD = 3.46$) and two DOC patients (one female, 78 years and one male, 31 years) in MCS took part in this study. All participants were informed about the procedure and objectives of the study and gave informed written consent. For the patients (at the Albert-Schweitzer Hospital in Graz, Austria) their legal authorities gave informed written consent. The study was approved by the local ethics committee (Medical University of Graz, Austria) and is in accordance with the ethical standards of the Declaration of Helsinki. The patients were behaviorally assessed using the CRS-R in order to evaluate their level of awareness (Table 1). The CRS-R, which is used to differentiate patients in VS from those in MCS or emergence from MCS (eMCS), consists of 6 subscales with each hierarchically arranged items. For a VS diagnosis, each subscale rating has to indicate VS, whereas for a diagnosis of MCS or eMCS only one subscale rating has to indicate the according state (different cut-off scores for VS/MCS/eMCS per subscale).

2.2. Mental arithmetic tasks

The healthy controls (HC) performed one measurement session of serial subtraction tasks (three different conditions), based on the work of Bauernfeind et al. (2008) and Pfurtscheller et al. (2010). During the experimental session all subjects were seated in a comfortable armchair in front of a TFT monitor. The distance between the participants and the screen was about 120 cm. The whole recording lasted around 40 min including breaks. To avoid artifacts, the participants were instructed to