



Opinion Paper

Alpha oscillations and consciousness in completely locked-in state

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1. Brain computer interface-based communication in completely locked-in state

The completely locked-in state (CLIS) describes an overarching loss of motor functions, including breathing and eye movements, with at the same time preserved cognitive functions (Murguialday et al., 2011). Due to this loss of motor functions, CLIS patients are not any longer able to communicate, and relatives, partners, and caregivers stay uninformed about the CLIS patients' inner world and their needs. Attempts for establishing a brain computer interface (BCI)-based communication by EEG recordings were to some extent successful in patients with minimal residual motor functions, but were repeatedly unsuccessful in CLIS patients (for review Kübler and Birbaumer, 2008). More recently, the research group of Niels Birbaumer reported that they had succeeded in implementing some rudimentary BCI-based communication in CLIS patients, by recording near-infrared spectroscopy (NIRS) responses to yes and no questions (Gallegos-Ayala et al., 2014; Chaudhary et al., 2017). However, these findings have been heavily questioned by Spüler (2019), who could not replicate the previous results when re-analyzing some of the original data. The reasons for the non-replicability have yet to be identified.

2. Alpha oscillations and consciousness

The debate also touched on another topic: Spüler (2019) argued that the down-slowning of EEG alpha activity of CLIS patients, as observed by Chaudhary et al. (2017), could suggest that the patients were either cognitively impaired or in an altered state of consciousness when the recordings took place, which would provide a tentative explanation why, according to his analysis, the BCI-based communication had failed. In their response, Chaudhary et al. (2019) strongly argued against the assumption that alpha oscillations can be considered as a proxy for consciousness, also correctly lining out that alpha oscillations are not a unitary phenomenon. However, the debate about the relation between alpha oscillations and consciousness is somewhat hampered by the fact that it is not always clear to what aspects of alpha oscillations the authors refer. Here, I will go more into detail and will differentiate between the presence/amplitude of alpha activity, the reac-

tivity of alpha oscillations, and the individual alpha peak frequency (IAPF) as potential markers of consciousness and cognitive functioning.

Presence/amplitude of alpha activity: Alpha activity at rest was reported to be diminished in minimally conscious patients, as compared to healthy controls (Lechinger et al., 2013; Chennu et al., 2014). However, aside from reasons outlined by Chaudhary et al. (2019), the presence or the magnitude of alpha oscillations cannot and should not be considered as proxy for consciousness. On the one hand, some deeply comatose patients exhibit very pronounced, widespread alpha oscillations (the so-called "alpha coma", Westmoreland et al., 1975). On the other hand, some individuals with normal brain function do not exhibit any alpha activity in their resting EEG (Chiang et al., 2011). These exceptional cases do not pose a problem for group statistics (as they might be identified as outliers), but for individual assessments. Yet, one should keep in mind that only one out of 35 healthy individuals does not exhibit alpha activity (Chiang et al., 2011).

Alpha reactivity: Alpha reactivity usually refers to the suppression of alpha activity by having the eyes open vs having the eyes closed, but alpha activity might also be suppressed by other forms of stimulation. In early reports, alpha reactivity was considered as a cardinal feature for distinguishing locked-in state (LIS) patients from patients with alpha-coma (Hawkes and Bryan-Smyth, 1974; Markand, 1976). However, alpha reactivity was reported to be absent in some LIS patients, leading to the conclusion that alpha reactivity does not equate to consciousness (Jacome and Morilla-Pastor, 1990). The presence of alpha reactivity is commonly considered as one indicator for normal brain functioning but the absence of alpha reactivity should not be overrated, especially when observed at a single occasion.

Individual alpha peak frequency (IAPF): Spüler (2019) referred to the case report of Hohmann et al. (2018), when arguing that the "alpha rhythm is often used as a neurophysiological marker for consciousness or cognitive abilities" (p. 3). Hohmann et al. (2018) observed a shift of the IAPF towards the lower end of the EEG spectrum in CLIS patients with amyotrophic lateral sclerosis (ALS). Similar to Spüler (2019), these authors argued that the alpha down-slowning could indicate some impairment of cognitive processes, such as inhibition/disinhibition processes (Klimesch et al., 2007) or information-flow gating (Jensen and Mazaheri, 2010). The IAPF has been regarded as marker for impairments in consciousness, with reduced IAPF in minimally conscious patients (Lechinger et al., 2013).

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The IAPF at rest is relatively stable within individuals (Grandy et al., 2013a). Among others, it was found to be positively correlated with better memory performance (for review Klimesch, 1999) and general intelligence (Grandy et al., 2013b). The IAPF increases during childhood and adolescence and declines with ageing (for review Klimesch, 1999). This decline was found to be accelerated by dementia (Moretti et al., 2004), but LIS patients (after ventral pontine ischemic infarction) showed only a modest IAPF decrease (Babiloni et al., 2010). To some extent, the IAPF also varies with task demands/activation level, with increasing demands leading to increased IAPFs and relaxation leading to decreased IAPFs (for review Mierau et al., 2017).

The interindividual variation of the IAPF by group factors, as well as intraindividual variation by task demands are on average in the range of 1 Hz or less (Moretti et al., 2004; Mierau et al., 2017). Given this, it is noteworthy that the dominant EEG frequencies of the CLIS patients investigated by Chaudhary et al. (2017) were indeed relatively low, with three of four patients exhibiting a dominant frequency of ≤ 7 Hz, which is below the common alpha range (8–12 Hz). This could in principle indicate some impairment of cognitive processes and consciousness in these individuals, as suggested by Spüler (2019). However, the discussion leads back to square one: Spüler (2019) considers the down-slowning of the EEG as evidence for an impairment of cognition or an altered state of consciousness in the investigated CLIS patients and as possible cause why the BCI-based communication had, according to his data analyses, failed. Chaudhary et al. (2019) consider this discussion as widely irrelevant, as based on their data analyses the CLIS patients were able to communicate.

3. Consciousness in CLIS

As stressed by De Massari et al. (2013), there is practically no possibility to comprehend or infer the emotional and cognitive state in CLIS patients. The little we know about this state was often obtained in studies that sought to establish BCI-based communication with these patients, even though some of these studies were unsuccessful in this regard (e.g. Kübler and Birbaumer, 2008; De Massari et al. (2013). Kübler and Birbaumer (2008) proposed that the complete loss of motor control and feedback might lead to the cessation of voluntary cognitive activity and goal directed thinking, which might result in a widely diminished ability for instrumental learning as well (Chaudhary et al., 2017). Murguialday et al. (2011) showed in their single-case study that the transition from LIS to CLIS in this patient included a loss of vision and of vibrotactile information processing. Thus, in CLIS, there is considerable functional loss beyond that of motor control. Moreover, the CLIS transition is accompanied by an increasing slow wave sleep (SWS) fragmentation during day- and nighttime, meaning that CLIS patients might have frequent transitions into SWS, when tested with BCIs (Soekadar et al., 2013). These issues of sleeping and variations of vigilance during BCI investigations of CLIS patients have been discussed by Kübler and Birbaumer (2008), De Massari et al. (2013), and Chaudhary et al. (2017, 2019).

However, ALS might also directly lead to some further deterioration of cognition, even after the transition to CLIS, since ALS patients show progressive grey matter pathology in the course of their disease (Verstraete et al., 2012; Bede and Hardiman, 2018; for review Chipika et al., 2019). To the best of my knowledge, neither the IAPF (Hohmann et al., 2018) nor event-related potential (ERP) recordings (Kotchoubey et al., 2003) have been used to assess neurocognitive functions in ALS patients over the course of illness. Visual inspection of the ERPs presented by Gallegos-Ayala et al. (2014) in their initial report on BCI-based communication in CLIS suggests that both the auditory N100 and the target-related P300

were absent at that time-point. The N100 and P300 have been considered as potential markers for predicting coma and other low responsive patients' outcome (Daltrozzi et al., 2007). Their absence might therefore, in support of the claim made by Spüler (2019), be considered as some additional evidence for cognitive impairments in CLIS patients. But again: the absence of alpha oscillations and alpha reactivity, a reduced IAPF, missing or substantially reduced ERP components are not conclusive evidence for impaired cognition or an altered state of consciousness. A much stronger case could be made if some of these markers systematically changed within the course of the disease (Chipika et al., 2019). Such longitudinal data are urgently needed to evaluate the odds that BCI-based communication in CLIS can succeed.

Declaration of Competing Interest

The author has no potential conflicts of interest to be disclosed.

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