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Assessing the level of consciousness for individual patients using complex, statistical stimuli

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EXTENDED ABSTRACT

One of the most challenging clinical issues in patients with prolonged disorders of consciousness (PDOC) is to reliably estimate their residual, conscious perception of the environment. Vegetative state (VS; recently termed unresponsive wakefulness syndrome, UWS; (Laureys et al., 2010)) patients are believed to retain basic reflexes or sleep-wake cycles while remaining entirely unaware of self and environment (Monti et al., 2010). On the contrary, minimally conscious state (MCS) patients seem to preserve residual cortical functioning together with displaying clear but inconsistent signs of awareness (Giacino and Schiff, 2009). Upon emergence from a minimally conscious state (EMCS) patients recover functional communication, although they often remain cognitively impaired (Di Perri et al., 2016). Several active (e.g. Cruse et al., 2011) and passive (e.g. King et al., 2013) neuroimaging paradigms have recently suggested that some patients clinically classified as UWS can reveal signs of awareness and volitional control which argue that these patients should actually be classified as MCS, EMCS or locked-in syndrome (LIS). Considering that selection and administration of the appropriate rehabilitation programs necessarily require determination of the consciousness state, objective quantitative classification methods will facilitate PDOC treatment.

Following severe brain lesions that lead to PDOC states, it was suggested that the auditory system is less likely to be damaged in comparison with other parts of the brain (Kotchoubey et al., 2015). Moreover, audition was recently suggested to be particularly sensitive to fluctuations in the level of consciousness (Boly et al., 2004; Demertzi et al., 2014; Schiff et al., 2005). The results of a number of auditory studies that attempted to assess conscious processing in PDOC patients, using simple sounds (e.g. Binder et al., 2017), complex sound sequences (e.g. Faugeras et al., 2012; but criticized by Tzovara et al., 2015), familiar sounds (Heine et al., 2015; Perrin et al., 2015), or speech (e.g. Steppacher et al., 2013, but contrary to Rohaut and Naccache, 2017) are still incomplete and partially inconsistent.

In the present study, we build on previous studies by (1) investigating multiple subject groups in the same paradigm, from healthy responding subjects to unconscious patients, and (2) presenting common naturalistic auditory textures i.e. complex sounds whose stimulus

statistics change at a random time during stimulus presentation. Detecting these changes is a challenging, real-world task: in natural sounds, changes may occur unexpectedly, signaling potential dangers, consider for example listening to a busy street and discerning a car that turns towards you. Detecting these changes requires listeners to be aware of the recent acoustic statistics (McDermott et al. 2011, Boubenec et al. 2017).

Analysis of the ERP at the onset of the stimulus could distinguish some groups, but not the supposedly conscious (Responding, Passive, MCS), from the supposedly unconscious groups (Asleep, UWS). Further, we find that a well-known parietal signal (CPP, Centroparietal Positivity, O'Connell et al. 2012), that has been described previously to indicate the integration of evidence, is absent for both deep NREM sleep (first cycles during the night) as well as for the UWS and MCS patient groups.

Turning to an alternative analysis, we assessed dynamical complexity of the neural response at the transitions of stimulus statistics using the Lempel-Ziv (LZ) algorithm. The LZ algorithm can simultaneously quantify integration and differentiation in the nervous system (Casali et al., 2013; Schartner et al., 2015; Wu et al., 2011) and thus has been proposed to estimate the state of consciousness irrespective of other related processes (Tononi et al., 2016). The results showed that LZ complexity distinguished conscious (Responding, NonResponding, MCS) from unconscious (NREM sleep, UWS) subjects, achieving high, cross-validated accuracy even on a single subject basis (~92%, $r=0.8$, $p<<0.001$).

In summary, EEG signal complexity during onset and changes of complex acoustic stimuli provides an objective criterion for distinguishing states of consciousness in clinical patients. These results suggest a path toward a cost-effective tool to choose appropriate treatments for non-responsive PDOC patients.

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