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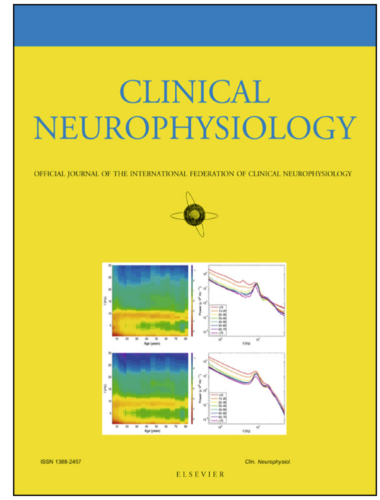

Editorial

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The complexity of disorders of consciousness

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Individuals with disorders of consciousness - such as the vegetative and minimally conscious states - are considered to have preserved wakefulness but absent or limited awareness of themselves and of their environments. A diagnosis of vegetative state (also called unresponsive wakefulness syndrome (Laureys et al. 2010)) is made when there is no motor evidence of awareness - i.e. visual pursuit, command-following - while a diagnosis of minimally conscious state is made when a patient exhibits only a limited response repertoire (Multi-Society Task Force on PVS 1994; Giacino et al. 2002). This apparent dissociation between wakefulness and awareness has made the disorders of consciousness a fruitful model in which to characterise the neural mechanisms that are associated with, and which support, awareness.

In this issue of Clinical Neurophysiology, Thul and colleagues investigated cortical information processing in 15 patients with chronic disorders of consciousness following a range of aetiologies (Thul et al., 2015). Specifically, they quantified the local information content of the electroencephalogram by means of permutation entropy, and the flow of information between cerebral lobes by means of symbolic transfer entropy. Entropy is a measure from information theory that describes the amount of information contained within a signal - in this case, an electrophysiological time series. The authors report a broad reduction in the information content (i.e. the complexity) of the EEG of patients with disorders of consciousness relative to that of healthy controls, and a reduction in information flow from frontal scalp to posterior scalp. Time-frequency entropy measurements in EEG also correlate with depth of and emergence from anesthesia (Vakkuri et al., 2004), which offers some support to the authors' hypothesis that entropy measurements correlate with at least crude consciousness.

Reduced complexity of the EEG and event-related potentials (ERP) of patients with disorders of consciousness has been observed with a number of other methods (e.g. Casali et al. 2013; King et al. 2013a). For example, the Perturbational Complexity Index quantifies the complexity of the ERP evoked by transcranial magnetic stimulation (TMS), and has been shown to track behavioural signs of awareness (e.g. disorders of consciousness, sleep, sedation; (Ferrarelli et al. 2010; Massimini et al. 2010; Casali et al. 2013)). Furthermore, feed-back connectivity is central to a number of theories of consciousness (Dehaene et al. 2006; Balduzzi and Tononi 2009; Friston 2010), and its impairment has been observed in both altered and disordered states of consciousness (Boly et al. 2011; 2012).

While Thul and colleagues observe differences between patients and healthy control participants, they do not observe reliable differences between the levels of the disorder - i.e. between vegetative state and minimally conscious state. Indeed, the complexity metrics show considerable overlap across these two states. From a clinical perspective, the described method for quantifying EEG data is therefore unlikely to improve the accuracy of differential diagnoses in this group. Nevertheless, Thul and colleagues report that the foci of the complexity decrements were consistent with each patient's specific pathology - i.e. focally reduced information content over left-frontal scalp in one patient with left-frontal subdural hematoma. Therefore, while these complexity measures do not track the behavioural profiles of the patients, they may provide information about underlying cortical damage. A study with a larger cohort may also uncover differences between aetiologies that reflect the known patterns of pathology (Adams et al. 1982; 2000). Furthermore, there is evidence that oddball tasks, such as the own-name paradigm employed by Thul and colleagues, have both diagnostic and prognostic value (Faugeras et al. 2012; King et al. 2013b). Therefore, the combination of classical ERP analyses and complexity metrics of the same data may provide a greater level of clinical utility.

As the described entropy metrics did not reliably differentiate patients in the vegetative state from those in a minimally conscious state, it is also likely that they do not track consciousness per se. Indeed, patients in the vegetative state are ostensibly unconscious, while those in the minimally conscious state have at least some level of consciousness (Giacino et al. 2002). A potential confound that may have obscured differences between conscious and unconscious patients is the known difficulty of diagnosing disorders of consciousness (Childs et al. 1993), such that some conscious patients may have been mistakenly diagnosed as unconscious. However, Thul and colleagues employed the gold standard behavioural assessment tool for these disorders, namely the Coma Recovery Scale - Revised (Kalmar and Giacino 2005), which is known to result in greater diagnostic accuracy (Schnakers et al. 2009).

Nevertheless, a group of patients exist who have been misdiagnosed as vegetative state even by the clinical gold standard assessment tool. Such patients demonstrate abilities indicative of consciousness during assessment with functional neuroimaging, but fail to demonstrate these abilities with their behaviour (Fernandez-Espejo and Owen 2013). If these misdiagnosed patients are fully conscious and only appear to be unconscious due to a primarily motor deficit, it follows that the complexity of their EEG signals should fall within the range of healthy individuals. Indeed, the structure of the EEG networks of a misdiagnosed vegetative state patient have been previously shown to be more similar to healthy individuals (Chennu et al. 2014), suggesting that some misdiagnosed patients possess a level of consciousness similar to that of healthy individuals.

The same logic can be applied to patients in the minimally conscious state. Indeed, it is unclear to what extent ‘minimally’ conscious implies full consciousness but only some of the time, or a lower/different level of consciousness than that experienced by awake healthy individuals (Kotchoubey et al. 2014). A theoretically-driven index of ‘conscious’ processing that has also been validated in other altered states of consciousness (e.g. sleep, sedation) may speak to this conundrum, and shine a light on these important clinical challenges while simultaneously contributing to our search for the neural underpinnings of consciousness.

Conflict of Interest:

The authors declare no conflict of interest.

References

Adams JH, Graham DI, Jennett B. The neuropathology of the vegetative state after an acute brain insult. Brain. 2000;123:1327–38.

Adams JH, Graham DI, Murray LS, Scott G. Diffuse Axonal Injury Due to Nonmissile Head-Injury in Humans - an Analysis of 45 Cases. Ann Neurol. 1982;12:557–63.

Balduzzi D, Tononi G. Qualia: The Geometry of Integrated Information. PLoS Comput Biol 2009;5:e1000462.

Boly M, Garrido MI, Gosseries O, Bruno M-A, Boveroux P, Schnakers C, et al. Preserved feedforward but impaired top-down processes in the vegetative state. Science. 2011 May 13;332:858–62.

Boly M, Moran R, Murphy M, Boveroux P, Bruno M-A, Noirhomme Q, et al. Connectivity changes underlying spectral EEG changes during propofol-induced loss of consciousness. J Neurosci. 2012;32:7082–90.

Casali AG, Gosseries O, Rosanova M. A Theoretically Based Index of Consciousness Independent of Sensory Processing and Behavior. Sci Transl Med 2013;5:198ra 105.

Chennu S, Finoia P, Kamau E, Allanson J, Williams GB, Monti MM, et al. Spectral Signatures of Reorganised Brain Networks in Disorders of Consciousness. PLoS Comput Biol. 2014;10:e1003887.

Childs NL, Mercer WN, Childs HW. Accuracy of diagnosis of persistent vegetative state. Neurology. 1993;43:1465–7.

Dehaene S, Changeux J-P, Naccache L, Sackur J, Sergent C. Conscious, preconscious, and subliminal processing: a testable taxonomy. Trends Cogn Sci. 2006;10:204–11.

Faugeras F, Rohaut B, Weiss N, Bekinschtein TA, Galanaud D, Puybasset L, et al. Event related potentials elicited by violations of auditory regularities in patients with impaired consciousness. Neuropsychologia 2012;50:403–18.

Fernandez-Espejo D, Owen AM. Detecting awareness after severe brain injury. Nat Rev Neurosci. 2013;14:801–9.

Ferrarelli F, Massimini M, Sarasso S, Casali A, Riedner BA, Angelini G, et al. Breakdown in cortical effective connectivity during midazolam-induced loss of consciousness. Proc Natl Acad Sci U S A. 2010;107:2681–6.

Friston K. The free-energy principle: a unified brain theory? Nat Rev Neurosci 2010;11:127-38.

Giacino JT, Ashwal S, Childs NL, Cranford R, Jennett B, Katz DI, et al. The minimally conscious state: definition and diagnostic criteria. Neurology.

2002;58:349–53.

Kalmar K, Giacino JT. The JFK Coma Recovery Scale--Revised. Neuropsychol Rehabil 2005;15:454–60.

King J-R, Sitt JD, Faugeras F, Rohaut B, Karoui El I, Cohen L, et al. Information sharing in the brain indexes consciousness in noncommunicative patients. Curr Biol 2013a;23:1914–9.

King JR, Faugeras F, Gramfort A, Schurger A, Karoui El I, Sitt JD, et al. Single-trial decoding of auditory novelty responses facilitates the detection of residual consciousness. Neuroimage 2013b;83:726–38.

Kotchoubey B, Vogel D, Lang S, Müller F. What kind of consciousness is minimal? Brain Inj 2014;28:1156–63.

Laureys S, Celesia GG, Cohadon F, Lavrijsen J, Leon-Carrion J, Sannita WG, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med 2010;8:68.

Massimini M, Ferrarelli F, Murphy MJ, Huber R, Riedner BA, Casarotto S, et al. Cortical reactivity and effective connectivity during REM sleep in humans. Cogn Neurosci 2010;1:176–83.

The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (1). N Engl J Med 1994;330:1499–508.

Schnakers C, Vanhaudenhuyse A, Giacino JT, Ventura M, Boly M, Majerus S, et al. Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. BMC Neurol 2009;9:35.

Thul A, Lechinger J, Donis J, Michitsch G, Pichler G, Kochs EF, et al. EEG entropy measures indicate decrease of cortical information processing in Disorders of Consciousness. Clin Neurophysiol 2015, This Issue.

Vakkuri A, Yli-Hankala A, Talja P, Mustola S, Tolvanen-Laakso H, Sampson T, et al. Time-frequency balanced spectral entropy as a measure of anesthetic drug effect in central nervous system during sevoflurane, propofol and thiopental anesthesia. Acta Anaesthesiol Scand 2004;48:145-153.

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