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Consciousness as a multidimensional phenomenon: implications for the assessment of disorders of consciousness

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Abstract

Disorders of consciousness (DoCs) pose a significant clinical and ethical challenge because they allow for complex forms of conscious experience in patients where intentional behaviour and communication are highly limited or non-existent. There is a pressing need for brain-based assessments that can precisely and accurately characterize the conscious state of individual DoC patients. There has been an ongoing research effort to develop neural measures of consciousness. However, these measures are challenging to validate not only due to our lack of ground truth about consciousness in many DoC patients but also because there is an open ontological question about consciousness. There is a growing, well-supported view that consciousness is a multidimensional phenomenon that cannot be fully described in terms of the theoretical construct of hierarchical, easily ordered conscious levels.

The multidimensional view of consciousness challenges the utility of levels-based neural measures in the context of DoC assessment. To examine how these measures may map onto consciousness as a multidimensional phenomenon, this article will investigate a range of studies where they have been applied in states other than DoC and where more is known about conscious experience. This comparative evidence suggests that measures of conscious level are more sensitive to some dimensions of consciousness than others and cannot be assumed to provide a straightforward hierarchical characterization of conscious states. Elevated levels of brain complexity, for example, are associated with conscious states characterized by a high degree of sensory richness and minimal attentional constraints, but are suboptimal for goal-directed behaviour and external responsiveness. Overall, this comparative analysis indicates that there are currently limitations to the use of these measures as tools to evaluate consciousness as a multidimensional phenomenon and that the relationship between these neural signatures and phenomenology requires closer scrutiny.

Keywords: disorders of consciousness; vegetative state; minimally conscious state; brain injury; multidimensional

Introduction

Disorders of consciousness (DoCs) are a devastating range of clinical conditions caused by severe damage to the brain that results in profound neurological impairment and often leaves individuals with limited or non-existent abilities for communication or intentional motor behaviour. It is well established that sophisticated forms of conscious experience, and potentially a rich mental life, can persist in some patients with DoC even in the absence of intentional behavioural responses (Owen *et al.* 2006; Monti *et al.* 2010; Naci *et al.* 2014). However, we currently lack reliable objective markers of consciousness and have a very limited understanding of what first-person experience is like in these conditions. There is a pressing clinical and ethical need to accurately detect and characterize consciousness in these patients, as this information is central to judging the well-being, best interests and moral status of individuals with DoC, and is likely to facilitate more precise and well-informed medical decisions about prognosis, possible therapeutic interventions, day-to-day

care needs and in some cases whether life-sustaining treatment should be withdrawn. In this article, I will consider the emerging, well-supported view that consciousness is multidimensional and examine the implications of this approach for the clinical use of some proposed neurophysiological assessments of consciousness in DoC.

Establishing the neural basis of consciousness remains an ongoing scientific challenge, although significant progress has been made in recent decades (Koch et al. 2016; Michel et al. 2019). In healthy individuals and most other clinical populations, subjective reports and behaviour can provide insight into conscious experience. In DoCs, understanding consciousness from a scientific, third-person perspective is highly challenging as subjective reports are either impossible to obtain or highly limited. Given also that behavioural data have limitations in assessing the presence of consciousness in DoC, there has been an ongoing effort to develop accurate measures of consciousness based on neural data. Neural measures of consciousness that can be applied in a task-free setting are particularly appealing as they could, in theory, indicate whether consciousness is present or absent regardless of an individual's cognitive and motor functioning.

The theoretical idea that conscious states are properties that can be described in hierarchically ordered levels is central to many efforts to develop neural measures of consciousness (Bayne et al. 2016). The majority of this article will be devoted to discussing unidimensional measures of signal complexity applied to resting-state brain data in a task-free setting. Patients in a minimally conscious state (MCS) are thought to have a higher level of consciousness, as potentially indexed by properties like resting-state brain complexity, than those in a vegetative state (VS), but lower than that of healthy, awake individuals without DoC.

However, the soundness of conscious levels as a theoretical construct has recently been challenged. It has been proposed that consciousness cannot always be described in terms of a single dimension of analysis and is in fact a multidimensional phenomenon with many components that can vary independently, such as various elements of attentional control, sensory processing, executive function and semantic comprehension (Bayne et al. 2016; Fazekas and Overgaard 2016; Bayne and Carter 2018; Birch et al. 2020). There is also growing recognition of the need for greater diagnostic precision in clinical practice for DoC (Provencio et al. 2020; Kondziella et al. 2021). Due to the highly heterogeneous pathophysiology amongst DoC patients and the fluctuating, dynamic nature of conscious experience, the traditional emphasis on diagnosing a patient according to a conscious–unconscious binary or unidimensional conscious level is not sufficient in capturing the clinically significant forms of variance to consciousness that can occur in DoC.

In this article, I will examine the implications of the multidimensional view of consciousness for several proposed neural measures of consciousness, particularly those designed as indexes of conscious level, in the context of their use in DoC diagnosis. In attempting to evaluate neural measures against any framework, we encounter an epistemic challenge in that we lack a ground truth about both the presence and the subjective quality of consciousness in many DoC patients (Peterson 2016). We cannot confirm with certainty that consciousness is absent based on the lack of overt or covert behaviours, which depend on specific mental capacities that may be lost even when consciousness itself persists. It is also very challenging to understand the subjective quality of experience in these patients, where communication is impossible or highly limited. Furthermore, I contend that within a multidimensional approach to consciousness, DoC diagnosis will shift to involve a greater emphasis on the subjective quality as well as the presence or absence of conscious experience.

As we lack a ground truth about consciousness in many DoC patients with which to validate these measures, I propose to explore a range of indirect evidence from studies where similar neural properties have been investigated in other conscious states where more evidence is available about the subjective quality of consciousness. This includes states occurring temporarily within healthy, neurotypical participants (e.g. sleep, anaesthesia and psychedelics) and conscious states resulting from longer-term neuropathology and other factors (e.g. psychiatric, neurodevelopmental and neurodegenerative disorders and normal ageing). I will use this evidence to examine the relationship between these unidimensional neural properties and conscious experience when conceived of as a multidimensional phenomenon.

This comparative, translational approach, as well as allowing us to evaluate the behaviour of unidimensional neural measures in states where much more is known about the subjective quality of consciousness, also allows us to advance our understanding of these measures despite lacking a ground truth with which to directly validate them. Although studying evidence of the behaviour of these measures in other conscious states is limited in that it cannot provide direct evidence about their relationship to consciousness in DoC, this analysis will highlight uncertainties and knowledge gaps about these neural measures that may raise important practical and ethical questions surrounding their use in DoC assessment.

Consciousness as a multidimensional phenomenon

Consciousness is often thought to be made up of two interrelated dimensions: arousal and awareness (Laureys 2005). Arousal, or wakefulness, is often thought of as the extent to which an agent is responsive to the external environment and is physiologically regulated by the reticular activating system in the brainstem and basal forebrain. Awareness, sometimes referred to as the content of conscious experience, is governed by cortical mechanisms and interactions. It is possible for awareness to become dissociated from arousal, producing states like rapid eye movement (REM) dreaming and ketamine anaesthesia, where an individual has a sensorily rich conscious experience despite lacking wakefulness and responsiveness to the external environment.

Although the distinction between arousal and awareness is helpful in the context of DoC, where sophisticated forms of conscious experience may be present in individuals with limited behavioural responsiveness, it seems that there is more than one dimension along which the contents of consciousness can vary. It has recently been proposed that consciousness can be more accurately characterized by a multidimensional model that accounts for a wider range of factors that may structurally modulate the subjective quality of conscious experience (Bayne et al. 2016). Even if some conscious states, and some different DoC patients and diagnostic categories, can be intuitively ordered according to conscious level, the multidimensional model suggests that we may be missing clinically and ethically relevant forms of variance to consciousness in these patients if we primarily focus on evaluating consciousness along a singular or a small number of dimensions.

There is not yet an accepted taxonomy of the dimensions that are optimal for describing human consciousness. It is likely that

Table 1. Possible dimensions of consciousness. One possible taxonomy of a multidimensional model of conscious experience, divided into two families of dimensions (content-related and functional; Bayne *et al.* 2016)

Possible dimensions of consciousness	
Content-related dimensions	Sensory richness
	High-order object representation
	Semantic comprehension
Functional dimensions	Executive functioning
	Memory consolidation
	Intentional agency
	Reasoning
	Attentional control
	Vigilance
	Meta-awareness

we do not currently know enough about consciousness to establish such a taxonomy, which may also depend on which conscious state is being characterized. Bayne *et al.* (2016) have suggested that content-related and functional dimensions may be two broad families of dimensions that describe consciousness (Table 1). Conscious states may differ from each other in terms of which kinds of contents are present in conscious awareness—e.g. the extent to which there is gating of sensory stimuli, and awareness of higher-order objects and semantic representation versus merely lower-level perceptual features. Conscious states may also differ in terms of how and the extent to which different contents of consciousness are available to the organism for different functional purposes. For example, they may vary depending on which and whether certain contents are encoded in working and short-term memory and available for reasoning and other executive and cognitive functions and whether the organism has attentional agency and meta-awareness. As Bayne *et al.* (2016) point out, we can conceive of consciousness coming apart along a range of these dimensions in conscious patients with DoC, and due to the heterogeneity of these conditions, conscious experience may vary considerably between individuals with DoC. However, if this is the case, it is unclear which dimensions of consciousness an increase or decrease in our proposed unidimensional neural measures will reflect, and deepening our understanding of this relationship may have important implications for the use of these measures in diagnostic assessments for consciousness in DoC.

How is consciousness assessed in DoC patients?

Standard forms of DoC assessment typically focus on establishing whether a patient retains the capacity for consciousness. Patients thought to be unconscious based on clinical evaluation are diagnosed as being in a VS (Jennett and Plum 1972), while those found to retain the capacity for consciousness are diagnosed as being in a MCS (Giacino *et al.* 2002). The dominant method for evaluating the presence of consciousness is bedside behavioural testing using instruments such as the Coma Recovery Scale-Revised (CRS-R; Giacino *et al.* 2004). These instruments consider overt behaviours including reproducible responses to command, visual fixation and functional object use. VS patients may display periods of eye opening and wakefulness, as well as reflexive responses to stimuli, but no signs of intentional behaviours (Jennett and Plum 1972). MCS patients intermittently display these intentional behaviours inconsistently but clearly discernibly (Giacino *et al.* 2002).

Although behavioural assessments can sometimes provide strong evidence for the presence of consciousness, they have been shown to misdiagnose up to 40% of conscious patients as unconscious (Schnakers *et al.* 2009; Kondziella *et al.* 2016). The motor behaviours measured by the CRS-R can be absent even when consciousness is present, a phenomenon labelled cognitive motor dissociation (CMD; Schiff 2015). It has been shown that some patients initially diagnosed as VS and thought to be completely unconscious are capable of displaying intentional mental behaviours that are detectable with functional magentic resonance imaging (fMRI), such as wilfully modulating their mental activity in response to command (Owen *et al.* 2006; Coleman *et al.* 2009b; Monti *et al.* 2010; Naci and Owen 2013). These active paradigms requiring volitional agency allow for the detection of consciousness in a further subset of DoC patients with CMD and often for a range of other information about consciousness and mental functioning to be inferred in the patient. However, as with active behavioural tests, the fMRI mental imagery test and other neural task-based assessment paradigms for DoC do not provide evidence for the absence of consciousness and risk missing conscious DoC patients.

To address the limitations of active paradigms, there have been efforts to develop task-free neural measures of consciousness. Some proposed measures evaluate properties in resting-state neural data thought to be related to conscious 'level', in theory irrespective of the presence of any particular cognitive capacities (Casali *et al.* 2013). Other measures aim to elicit event-related potentials (ERPs) in response to certain sensory stimuli that may indicate conscious processing; some of these do not require the individual to intentionally attend to the stimulus (Bekinschtein *et al.* 2009).

As we have no ground truth about consciousness in unresponsive DoC patients with which to directly validate these measures, I propose to examine evidence from studies where these measures were applied in other conscious states, which will allow for an initial, comparative approach to understanding their relationship with conscious experience in a multidimensional sense. I will discuss this evidence and use it to explore the utility of these neural measures in clinically evaluating individuals with DoC when consciousness is conceived of as a multidimensional property.

The remainder of this article will examine evidence for the relationship between conscious experience and the following three electroencephalogram (EEG)-based neural measures, drawn from a range of studies outside of DoC science: measures of resting-state neural complexity (Wu *et al.* 2011), the perturbational complexity index (PCI), a transcranial magnetic stimulation (TMS)–EEG-based complexity measure (Casali *et al.* 2013) and the local global paradigm (LGP; Bekinschtein *et al.* 2009), an ERP-based EEG measure. Many EEG-based measures in particular tend to be informed by the idea of conscious level. As fMRI has higher spatial resolution than EEG, fMRI-based measures tend to be applied less frequently than EEG as measures of global conscious level, although would perhaps lend themselves to differentiating more precise dimensions of conscious experience that are associated with particular spatial regions in the brain.

There are some key limitations to the approach I am taking. Firstly, for resting-state complexity measures, it relies largely on qualitative comparison between studies (in terms of how these measures vary relative to a baseline level), as a direct quantitative comparison is often not possible due to methodological differences between studies. Furthermore, this discussion is largely restricted to results that are comparable in terms of unimodal

Table 2. Resting-state complexity in healthy individuals and clinical populations. Neural complexity in a range of conscious states related to both long- and short-term brain changes. For states in the left and right columns, studies typically draw comparisons against healthy wakeful controls without further discrimination between different standard wake states, although complexity can in fact vary for these as well (middle column). Due to methodological differences between studies, it is not yet possible to draw quantitative comparisons between the states and conditions within each column

Resting-state complexity				
Lower complexity ←		← Normal waking → complexity		→ Higher complexity
Vegetative state	Minimally conscious state	Task focus	Mind wandering	Psychedelics
NREM sleep	REM sleep	Meditation	Viewing movie	Ketamine
Anaesthesia		Viewing visual noise		Depression[a]
Traumatic brain injury (non-DoC)		Hearing speech = hearing random noise		Schizophrenia[a]
Dementia		Peak at age 60 years		
ADHD				
Autism				
Anorexia nervosa				

[a]Mixed results have been obtained for schizophrenia and depression, but in the majority of studies, resting-state complexity has been found to be higher in patients than in healthy controls.

levels and does not consider the varied spatial patterns these measures may display across the brain. These spatial patterns, as has been noted elsewhere, may be an important target for further investigation of the relationship between brain activity and phenomenological dimensions of consciousness (Boly *et al.* 2017; Andrillon *et al.* 2021), but are beyond the scope of this article.

Resting-state neural complexity and dimensions of consciousness

Resting-state complexity in healthy adults

Measures of signal complexity have been widely applied to human brain activity in a range of conscious states and clinical conditions (Table 2) and to data from a range of neuroimaging modalities including EEG, fMRI and magnetoencephalography (MEG). Complexity has no precise definition and a range of methods are thought to capture dimensions of the complexity of a signal, including Lempel–Ziv complexity (Lempel and Ziv 1976) permutation entropy (Liang *et al.* 2015), multiscale entropy (Li *et al.* 2010) and fractal dimension (Varley *et al.* 2020b). While there are differences between methods for quantifying complexity, I will consider them together for the purpose of this article. There is some evidence suggesting that different complexity measures are convergent for neural data (Varley *et al.* 2020c). Overall, resting-state complexity is typically found to be lower during states where consciousness is thought to be largely absent, including non-rapid eye movement (NREM) sleep and anaesthesia, and is lower on an average for patients behaviourally diagnosed as VS than those with an MCS diagnosis (Gosseries *et al.* 2011; Wu *et al.* 2011; Sitt *et al.* 2014; Thul *et al.* 2016; Engemann *et al.* 2018; Varley *et al.* 2020b).

There have been several theoretical links drawn between neural complexity and consciousness. Based on the arousal-awareness model, it has been suggested that complexity corresponds more to the awareness dimension and could be thought to index some element of conscious contents, whereas other unidimensional measures like spectral power may be more closely linked to arousal (Schartner *et al.* 2017b; Scott and Carhart-Harris 2019). One further suggestion is that measures of resting-state neural complexity, which may often indicate the diversity and variability of possible neuronal configurations in a given brain state, may be linked to the possible repertoire of conscious

Table 3. PCI values for a range of conscious states (Casali *et al.* 2013; Sarasso *et al.* 2015; Casarotto *et al.* 2016). PCI value of 0.31 has been proposed as an empirically supported threshold for distinguishing between conscious and unconscious individuals with DoC

State	PCI
Healthy awake volunteers	0.44–0.67
Minimally conscious state	0.37–0.52
Vegetative state	0.19–0.31
Deep anaesthesia (propofol, xenon and midazolam)	0.08–0.31
REM sleep	0.35–0.56
NREM sleep	0.12–0.31
Ketamine	0.35–0.55

contents (Tagliazucchi *et al.* 2014; Schartner *et al.* 2017b; Schwartzman *et al.* 2019). Kolmogorov theory also posits that the complexity and compressibility of brain data are related to conscious level and the extent to which conscious experience is structured and that states with higher conscious levels are characterized by the brain's ability to form more complex, less compressible models of the world (Ruffini 2017). These suggestions are speculative but seem to posit a link between neural complexity and dimensions of consciousness related to sensory richness, the presence of high-level perceptual content and the variability of mental content.

In this section, I will examine the characteristics of a range of states within healthy individuals where complexity has been found to be either higher or lower than the restful waking state often used in a baseline in such studies (summarized in Table 2), including the extent to which certain key dimensions of consciousness such as sensory richness, attentional control, arousal, executive function, memory and meta-awareness may be affected.

Sleep

Human sleep can be differentiated into two physiologically distinct components: REM sleep and NREM sleep (Loomis *et al.* 1935). REM sleep is associated with low muscle tone, wake-like EEG activity and REMs (Matarazzo *et al.* 2011). NREM sleep, which is commonly divided into three substages, is characterized by the deactivation of many brain areas relative to wake and REM,

synchronized EEG activity and slow waves and higher muscle tone than REM sleep.

REM sleep has been associated with levels of resting-state complexity that are similar to the early sleep onset period but higher than other stages of NREM sleep (Pereda *et al.* 1998; Schartner *et al.* 2017a). Conscious experience is reported for the majority of REM awakenings (Nielsen 2000; Siclari *et al.* 2013). REM dreams tend to be immersive and bizarre with a complex narrative and perceptual structure that is mainly instantiated in audio-visual modalities and often involves emotions and movement sensations (Carr and Solomonova 2019). REM dreaming is also reported to be characterized by a relatively high level of sensory richness, especially high levels of visual detail (Fazekas *et al.* 2019). REM dreaming has been described as a form of spontaneous thought that involves the weakening of a range of dimensions that can serve to constrain the contents and flow of conscious experience over time (Christoff *et al.* 2016; Girn *et al.* 2020). This includes a reduction in various dimensions of consciousness that modulate attention and the flow of thought, including 'deliberate' constraints on thought (those under cognitive control, such as executive function, volition and typically meta-awareness), as well as 'automatic' constraints on thought (those operating outside of cognitive control, such as mechanisms of affective and sensory salience; Christoff *et al.* 2016).

NREM sleep, especially deep slow-wave sleep, is associated with substantially lower levels of resting-state complexity compared to both wake and REM sleep (Pereda *et al.* 1998; Andrillon *et al.* 2016; Schartner *et al.* 2017a). In studies of brain complexity, NREM is sometimes used as a proxy for unconsciousness or highly diminished conscious level (for discussion and critique of this view, see Windt *et al.* 2016). Although NREM sleep involves a significant decrease in cortical excitability, it is now widely accepted that conscious experience can occur in any stage of NREM sleep, although waking reports indicate that it occurs less frequently in NREM sleep than in REM sleep (Nielsen 2000; Noreika *et al.* 2009; Siclari *et al.* 2013; Windt 2020). There is also evidence that a broad range of cognitive processes are conserved in NREM sleep, including the processing of auditory, visual or somatosensory stimuli and the preparation of motor responses (Andrillon and Kouider 2020). Reports upon awakening indicate that NREM sleep experiences, when compared to REM dreams, have lower sensory richness and are more likely to be described as feeling like thoughts rather than perceptual experiences (Nielsen 2000; Noreika *et al.* 2009; Siclari *et al.* 2013). They tend to be more fragmented and mundane in content and have a shorter subjective duration (Carr and Solomonova 2019). When awoken during NREM sleep, it is also common to report no experience or to report having had a conscious experience without being able to remember any specific content (white dream), which could be a result of reduced or absent perceptual imagery and thought contents (Windt 2015; Windt *et al.* 2016; Fazekas *et al.* 2019) and suggests that memory loss may be a confounding factor for lower recall rates during NREM sleep. As complexity has been studied over extended periods of NREM sleep without awakening subjects to collect subjective reports, it is possible that intermittently occurring periods of consciousness are associated with higher complexity than non-conscious periods of NREM sleep.

Anaesthesia

Anaesthesia is another state associated with low levels of neural complexity (Ferenets *et al.* 2006, 2007; Li *et al.* 2010; Liang *et al.* 2015; Schartner *et al.* 2015; Varley *et al.* 2020c; Zhang *et al.* 2001). Like deep NREM sleep, general anaesthesia is often used as a proxy for unconsciousness in studies attempting to validate neural measures of consciousness. Yet consciousness may in fact occur in up to 31% of patients even at surgical levels of anaesthetic dosage (Linassi *et al.* 2018), a phenomenon called anaesthesia awareness (AA). Detailed subjective reports about AA are typically delayed and affected by the amnesic effects of hypnotic drugs. The subjective quality of consciousness in AA seems to vary based on anaesthetic agent and dosage (Noreika *et al.* 2011). Like NREM sleep, it is typically perceptually decoupled from external stimuli, fragmented, simple, and mundane in content (Noreika *et al.* 2011; Radek *et al.* 2018; Sleigh *et al.* 2018). However, there is some evidence that aspects of executive functioning (Mashour *et al.* 2021) and meta-awareness (Sleigh *et al.* 2018) are more resistant to anaesthesia than they are to natural sleep (Goupil and Bekinschtein 2012). Some of these cognitive or executive functions may persist to a greater extent at low levels of cortical brain complexity during AA. However, we know little about which dimensions of consciousness are most prominent in AA because both impaired memory and false recall may impact subjective reports (Pryor and Root 2013) and, although the presence and subjective quality of conscious experience may fluctuate significantly during anaesthesia, we are largely reliant on delayed reports.

Attentional shifts

There has also been some investigation of neural complexity during different wake states with varying attentional constraints. A ubiquitous form of attentional shift in the general population is that from task-focused or externally engaged attention to task-unrelated thought or internally directed attention, often termed 'mind wandering' (Seli *et al.* 2016). Mind wandering is estimated to comprise 30–50% of waking consciousness (Smallwood and Schooler 2015), and the periods of restful wakefulness where mind wandering tends to occur more frequently have been associated with higher complexity than task-focused states in several studies (Aftanas and Golocheikine 2002; Li *et al.* 2008; Escrichs *et al.* 2019; Iglesias-Parro *et al.* 2020). Like dreaming, it has been described as a form of spontaneous thought that is subject to weakened mechanisms of attentional and executive control, perhaps allowing for more frequent transitions between a wider and more associative range of conscious contents (Christoff *et al.* 2016; Girn *et al.* 2020). Experience sampling studies have shown that mind wandering is most often described as being thought-like and stimulus independent, or having content that is unrelated to the immediate environment (Laurens *et al.* 2017). A smaller proportion of mind wandering experiences were described as perceptual experiences, involving a range of different sensory modalities (Laurens *et al.* 2017).

Other forms of waking consciousness, like focused attentional states, have stronger deliberate and/or automatic constraints and often involve high executive functioning, attentional control and meta-awareness (Windt 2020). Complexity has been found to be lower during tasks demanding a strong attentional focus, such as arithmetic tasks (Li *et al.* 2008) and meditation [Sahaja Yoga (Aftanas and Golocheikine 2002) and anapanasati (Escrichs *et al.* 2019)], compared to during periods of restful wakefulness. Reports are rarely taken during resting periods in these task-based studies, so the precise quality of conscious experience captured at rest is unclear and may fluctuate (Callard and Margulies 2014). Yet, due to limited demands on attention, these rest periods are likely to involve a higher frequency of mind wandering.

Psychedelics and ketamine

During psychedelic experiences, resting-state complexity increases relative to normal wakefulness (Schartner *et al.* 2017b; Timmermann *et al.* 2019; Varley *et al.* 2020a). Although psychedelic experiences can vary qualitatively based on dosage and drug type (Fortier-Davy and Millière 2020), conscious experience under psychoactive doses of lysergic acid diethylamide and psilocybin is significantly altered compared to normal wake and is commonly reported to involve increased sensory (especially visual) vividness, increased richness of experience and of autobiographical memory, hyper-associative thinking and changes in sense of self and meaning attribution (Bayne and Carter 2018; Girn *et al.* 2020). Several complexity measures have also been found to increase for ketamine-induced states compared to normal waking consciousness (Schartner *et al.* 2017b; Farnes *et al.* 2019). Ketamine is a drug used as a dissociative anaesthetic that produces a disconnected but highly vivid hallucinatory state with many similarities to a psychedelic state, although they are not phenomenologically or physiologically identical (Schartner *et al.* 2017b). Similarities between psychedelic and ketamine states and REM dreaming have long been recognized, but greater meta-awareness is present in psychedelic states (Girn *et al.* 2020).

Psychedelics also seem to impair many functional and cognitive dimensions of consciousness (Bayne and Carter 2018), although not all dimensions (Fortier-Davy and Raphaël 2020). Although declarative and working memory seem to remain unimpaired (Silverstein and Klee 1958), psychedelics lead to impairments on tasks involving mental manipulation or attentional control and are commonly reported to reduce capacity for concentration (Jackson *et al.* 1952), sustained attentional focus (Quednow *et al.* 2012) and speech production (Jackson *et al.* 1952). Psychedelic states are also reported to lead to greater feelings of insight and creativity, which may be the result of increased capacity for more remote and wide-ranging associations. Overall, the capacity for abstract and evaluative thought, including the ability to identify which thoughts are truly insightful, appear to be diminished (Bayne and Carter 2018).

There has also been some exploration of the relationship between complexity measures and the subjectively rated intensity of phenomenological dimensions during psychedelic experiences. (Schartner *et al.* (2017a) conducted a questionnaire after the peak effects of the drug had subsided, which revealed that aggregate self-reported scores for the subjective intensity of the psychedelic experience across all phenomenological dimensions (including ego dissolution, muddled thinking, seeing geometric patterns, unusual imagery, distorted time and space perception, vivid imagination, a sense of inner peace and spiritual experience) were correlated with a range of complexity measures applied to MEG data collected during the peak of the psychedelic experience. This correlation was strongest for ketamine-induced states, where the dimensions the most highly correlated with high brain complexity were ego dissolution and a vivid imagination. Although these results rely on the use of subjective scales about conscious experience, for which individual participants may have very different yardsticks, they suggest that the subjective intensity of many of the phenomenological dimensions associated with psychedelic experiences may have a quantitative relationship with neural complexity (Schartner *et al.* 2017b).

Stimulus information content

The relationship between brain complexity and the meaningfulness of a perceived stimulus has also been studied in fMRI (Boly *et al.* 2015). When healthy participants were shown a movie, complexity was higher than when they were shown a scrambled version of a movie or TV noise. In the TV noise and scrambled movie conditions, each frame essentially carried the same informational content in terms of its high-level meaning to the participants, so the overall informational content was low. The condition involving a coherent short movie, on the other hand, was experienced as containing a greater amount of meaningful, high-level content. This was despite the fact that in all three conditions (movie, TV noise and scrambled movie), each stimulus was equally as differentiated in terms of low-level perceptual content. A similar study conducted in the auditory domain in EEG data, using normal speech at two different speeds and backwards speech, did not find a difference between these conditions (Bola *et al.* 2018), although the difference in meaningful information content between these two conditions, which was assumed to be higher for the coherent speech than for the incomprehensible backwards speech, may not be sufficient to differentiate them in neural data.

Dimensions of consciousness and neural complexity in healthy adults

Measures of resting-state neural complexity are probably sensitive to multiple dimensions of consciousness to varying degrees and are likely to display different spatial patterns during different conscious states. However, this initial analysis, which primarily involves considering how complexity behaves at the whole-brain level and reflects its proposed use as a unidimensional measure of conscious 'level', can nonetheless highlight potential hypotheses about their relationship with specific features of consciousness.

Multiple states that result in relatively high levels of resting-state complexity involve reduced constraints on mental activity (both deliberate and automatic). These constraints can be thought to be related to a range of possible dimensions governing attention that operate both inside and outside of an agent's cognitive control. This includes REM sleep relative to other sleep states, as well as psychedelics and ketamine relative to the normal range of wake states (Girn *et al.* 2020). States where greater attentional resources are engaged or deployed, such as certain kinds of meditation [Sahaja yoga (Aftanas and Golocheikine 2002) and anapanasati (Escrichs *et al.* 2019)] and arithmetic tasks (Li *et al.* 2008), involve reduced complexity. It is possible that the weakening of constraints on the flow and content of thoughts allows a richer, more diverse, dynamic and associative repertoire of conscious contents to emerge, as is reported to various extents during REM dreams, mind wandering, and psychedelic and ketamine states. The weakening of attentional and cognitive constraints and increase in sensory richness and variability of contents in these states also seems to be accompanied by a range of functional dimensions being diminished to various degrees, such that less attentional, executive and cognitive control is available to the agent. Furthermore, these high-complexity states, despite rich contents and increased cortical activation, do not seem to be optimal for vigilance and responsiveness to one's surroundings (Mittner *et al.* 2016) and for engaging in a range of goal-directed behaviours that may require greater executive and cognitive functioning.

Resting-state complexity also seems to be comparatively higher in states with greater sensory richness, such as psychedelics and ketamine states, and may even have a quantitative relationship with perceived perceptual intensity and vividness (Schartner *et al.* 2017b). Sensory gating, the process by which irrelevant or redundant stimuli are normally filtered from conscious awareness, has been shown to be reduced in psychedelic states

(Vollenweider and Geyer 2001; Vollenweider *et al.* 2007), perhaps resulting in greater sensory richness due to more stimuli being concurrently perceived. Relative to other sleep states, increases in resting-state complexity also occur during REM sleep, a state characterized by rich and integrated sensory experiences but high levels of sensory gating (McCormick and Bal 1994). Based on this evidence, a working hypothesis may be that measures of resting-state complexity are sensitive to sensorily rich and variable content repertoires regardless of whether this is caused by external inputs or endogenous activations. It may be the case, as has been theorized (Scott and Carhart-Harris 2019), that complexity measures are less sensitive to dimensions of consciousness that affect vigilance to external stimuli and more sensitive to those that modulate the contents of awareness. This feature is helpful in the context of DoCs where perceptually decoupled experience could arise, involving rich conscious experience despite reduced responsiveness in active paradigms (Bayne *et al.* 2020; Martial *et al.* 2020).

It is currently more challenging to understand which dimensions of consciousness are present in low complexity states like AA and NREM sleep. The quality and dynamics of consciousness in these states could have important parallels with DoC, where complexity is also lower than in healthy waking controls. There is evidence that a range of qualitatively different states may be possible at low levels of complexity. For example, conscious dimensions like executive function and meta-awareness may in fact be amongst the least impaired during AA. However, a challenging confound for both sleep and anaesthesia experiences, due to our reliance on delayed reports, is the possibility of either impaired or false recall of the occurrence of conscious experience or its subjective quality (Pryor and Root 2013).

Many studies investigating complexity and consciousness have significant methodological limitations in that they do not take reports from subjects while measuring their brain activity. Instead, they rely on assumptions about the general characteristics or the conscious level of the states in question to judge the efficacy of a particular neural measure, even in states that are very heterogeneous or where little is known about consciousness. Because of this limitation, much of the present discussion has involved considering evidence that stems from independent lines of research investigating resting-state complexity and phenomenology. Detailed subjective reports that go beyond probing the conscious–unconscious binary in participants, by using either free reports or more targeted questionnaires, will need to be collected alongside neural data to evaluate the relationship between resting-state complexity and consciousness on a more fine-grained level, as has been done for some studies conducted in healthy, awake volunteers (and even during sleep). This level of precision will be particularly important in low complexity states like anaesthesia and NREM sleep where the presence of consciousness may be more intermittent, and low levels of complexity could be the result of the relative infrequency of higher-complexity conscious periods within the data.

Do changes in resting-state complexity always reflect changes in consciousness?

The neurophysiological processes underlying changes in neural signal complexity remain unclear. Although proposed as potential indexes of consciousness, this family of measures may be sensitive to both conscious and non-conscious forms of neurophysiological processing, both of which occur simultaneously in the brain during conscious experience. Resting-state brain complexity also appears to be impacted by demographic factors and clinical conditions. An individual's baseline level of complexity during task-free wakefulness can vary based on their age, sex and certain medications and due to a range of long-term conditions impacting the brain, which in addition to acquired brain injury include psychiatric, neurodevelopmental and neurodegenerative disorders. It is not clear to which extent (if at all) these factors are directly associated with fundamental differences in conscious experience itself, but further exploration of this question will be important for evaluating the kind of reliable diagnostic information about consciousness these measures could provide for individuals with DoC.

Effect of age and sex on complexity

There is evidence that age has a significant effect on resting-state brain complexity. Complexity has been found to increase until mid-adulthood, peaking between ages 41 and 60 years, before gradually starting to decline (Anokhin *et al.* 1996; Yang *et al.* 2013a; Shumbayawonda *et al.* 2018), which suggests that even healthy ageing has a substantial fingerprint on individual resting-state complexity. This change in background electrophysiology across the lifespan has been suggested to reflect underlying processes of brain maturation, synaptic pruning, changes in axonal volumes and hormonal changes (Shumbayawonda *et al.* 2018).

Biological sex has also been found to have some effect on resting-state complexity levels. The effects have been mixed depending on the modality and complexity measure used: EEG fractal dimension was found to be higher on average in women (Ahmadlou *et al.* 2012), whereas permutation Lempel–Ziv complexity of MEG activity was found to be slightly higher in men (although whole-brain values for men and women overlapped considerably; Shumbayawonda *et al.* 2018). The existence of a sex fingerprint in resting-state complexity may be attributable to a range of factors (such as white matter and grey matter changes between the sexes, the effects of hormones and other unknown or environmental factors; Shumbayawonda *et al.* 2018) and may merit further investigation as a potential confounding factor for complexity measures as signatures of consciousness in DoC.

Complexity in neurological and psychiatric conditions

Although some factors impacting baseline complexity levels during wakefulness, such as those related to sex and healthy ageing, may not be directly associated with changes to conscious experience, some neurological and psychiatric conditions are associated with a decrease in baseline levels of resting-state complexity that may reflect significant and direct changes to the individual's conscious experience in addition to the underlying changes occurring on a neurobiological level as a result of the disorder. For example, the majority of studies have found decreased neural complexity in those with dementia caused by Alzheimer's disease (AD; Jeong 2004; Dauwels *et al.* 2010; Yang *et al.* 2013b; Liu *et al.* 2016), although increases have also been reported in some studies investigating preclinical AD (Gaubert *et al.* 2019). AD is associated with a range of pathological changes in the brain, including amyloid plaque and neurofibrillary tangles, engendering changes in neural connectivity (Braak and Braak 1991; Raskin *et al.* 2015). It also involves a range of progressive impairments to memory, visuospatial function, language, attention, problem-solving, meta-awareness, mood and personality (Salloway and Correia 2009). There is also some evidence that a loss of neural complexity is associated with the extent of cognitive impairment in AD, with complexity being inversely correlated with scores in neuropsychological tests (Yagyu *et al.* 1997). However, measures of resting-state

complexity are normally studied as a signature that is informative relative to a reference point (e.g. healthy controls) rather than as an absolute measure that can facilitate cross-disorder comparisons. Therefore, even if a linear relationship with some aspects of phenomenology exists for this population, we cannot assume that it will translate to other populations, including DoC, where we may encounter different absolute ranges of these complexity values for which the same linear relationships may not apply.

Furthermore, even in dementia, impairments present in a heterogeneous way and are often difficult to evaluate where communication is impaired, so we cannot assume uniform impacts on every dimension of consciousness. For example, high levels of meta-awareness are sometimes reported, if apparently intermittently, even at late stages of disease progression (O'shaughnessy et al. 2020). The abnormal whole-brain complexity values observed in a range of other neurological and psychiatric disorders also suggests that the relationship between complexity, neuropathology and cognitive impairment is complex and many-to-one. Both increases (Li et al. 2008; Ahmadlou et al. 2012; Méndez et al. 2012) and decreases (Nandrino et al. 1994) in complexity have been observed for depression, which has been discussed as involving fundamental shifts in conscious experience (Whiteley 2021) and schizophrenia [increase: Li et al. 2008; Takahashi et al. 2010; Fernández et al. 2011; Ibáñez-Molina et al. 2018; Xiang et al. 2019; decrease: Lee et al. 2001; Yang et al. 2015). This suggests that some forms of psychopathology may be associated with abnormally high complexity. There are several possible reasons for the inconsistent results obtained for these conditions, including the use of different complexity measures and methodological differences between studies. Furthermore, schizophrenia can have a range of both positive symptoms (hallucinations, paranoia and delusions) and negative symptoms (cognitive impairment, flattened affect and disorganized thinking) that can present very differently between individuals and in different phases of the disorder. Other conditions that could be thought to involve abnormalities on the level of conscious experience like autism (Lai et al. 2010; Catarino et al. 2011) and attention deficit hyperactivity disorder (ADHD; Sokunbi et al. 2013) have been more consistently found to be associated with abnormally low levels of complexity. The translatability of results observed in different studies remains unclear, but it is possible that quantitatively equivalent decreases in complexity can be associated with a range of qualitatively different neurological and psychiatric impairments affecting consciousness and cognition and that they sometimes do not reflect changes in consciousness at all. As such it is likely that we will face challenges in drawing inferences about specific dimensions of consciousness, or general inferences about the extent of cognitive impairment, based on whole-brain complexity measures alone.

While some clinical conditions that affect baseline complexity, like dementia, clearly also have profound impacts on consciousness, it is possible that resting-state complexity levels are also affected in some conditions where a fundamental shift in conscious experience does not appear to be amongst the core symptoms. For example, individuals with anorexia nervosa (AN) have lower resting-state complexity than healthy controls (Tóth et al. 2004; Collantoni et al. 2020), but changes to conscious experience do not seem to be directly implicated in the psychopathology of AN. Lowered complexity may be due rather to the fact that affected individuals have neurobiological damage caused by starvation and prolonged malnutrition (Collantoni et al. 2020). A range of neurobiological changes unrelated to the neural mechanisms of consciousness may also impact values of brain complexity in other disorders affecting the brain, including DoC, where severe brain injury is present. The impact of such neurobiological factors may pose challenges for operationalizing resting-state complexity as a reliable measure of consciousness and in determining the extent to which inferences about their relationship with phenomenology can be translated across clinical populations.

Perturbational complexity index

The following section will review a range of evidence for the PCI (Casali et al. 2013; Table 3), another proposed task-free, unidimensional neural measure of consciousness. PCI is a more recently developed measure that involves locally applying TMS to the brain and then calculating the complexity of the resulting EEG signal. PCI was inspired by theoretical approaches in consciousness science postulating that the emergence of consciousness requires an optimal balance of integration and differentiation in functional neuronal circuitry (Tononi and Edelman 1998; Tononi 2004; Seth et al. 2006). PCI is a method designed to capture these two properties in a single unidimensional index: the extent to which the TMS pulse propagates in the brain is a function of the level of integration of widespread neuronal populations and the complexity of the resulting EEG activity reflects the extent to which this neural response is differentiated (Casali et al. 2013). As such it has been suggested that PCI may be a more sensitive quantitative measure of the fundamental brain activity linked to consciousness than resting-state complexity (Casarotto et al. 2016). PCI has been less widely applied than measures of resting-state complexity (TMS equipment is more costly and less widely available than EEG in clinical settings), so less evidence is available. Yet this brief discussion of the available PCI results from a range of states will serve as a useful comparison point, particularly for highlighting how different passive neural measures of consciousness may correlate with different features of consciousness and reflect different underlying neural mechanisms.

PCI has been designed as a measure that is quantitatively comparable across individuals and conscious states. A PCI value of 0.31 has been proposed as an approximate threshold for distinguishing conscious and unconscious individuals, based on empirical data collected in both DoC and sleeping and anaesthetized healthy volunteers. In healthy, awake volunteers, PCI values have been found to range from 0.44 to 0.67 (Casali et al. 2013).

During NREM sleep, a deeper state of sleep where conscious experience is thought to be less frequent and vivid, PCI values range from 0.12 to 0.31, whereas in REM sleep, where vivid conscious experience occurs more frequently, PCI values were within the range of healthy awake individuals (0.35–0.56). Across several studies examining anaesthetized individuals who were deeply sedated and had lost responsiveness, PCI values were also significantly reduced (between 0.008 and 0.31; Casali et al. 2013; Sarasso et al. 2015). However, during ketamine anaesthesia, which unlike other anaesthetic agents like xenon and propofol does not aim to eliminate consciousness but rather produces a disconnected but vivid conscious state, PCI values were comparable to those obtained for healthy, awake volunteers (0.35–0.55). This is a key point of contrast so far between PCI and resting-state measures of EEG complexity, where ketamine has been found to lead to significantly higher values than during normal waking consciousness.

This point of difference may indicate that PCI, as theorized, reflects different underlying neural mechanisms to resting-state complexity, and so may have a different relationship with the mechanisms underlying consciousness. A possible interpretation is that very 'high entropy' states like those induced by ketamine

and psychedelic drugs involve high neural complexity in terms of maximal randomness or unpredictability, but not necessarily high levels of causal integration. Because PCI is also sensitive to cortical integration, ketamine states, which like psychedelics involve significant impairments to cognitive and executive functioning, do not cause PCI to increase relative to normal wakefulness. Although the relationship between PCI and conscious states is many-to-one, high PCI values may have a stronger association with states characterized by normal levels of cognitive and executive functioning compared to resting-state complexity.

For DoC, PCI has been found to have very high sensitivity and specificity for discriminating behaviourally diagnosed MCS and VS patients at the individual level (over 94% accuracy; Casali *et al.* 2013; Casarotto *et al.* 2016), much higher than reported for measures of resting-state complexity. However, the validity of these results remains unclear because we cannot assume that the VS patients in this study were unconscious just because they were behaviourally unresponsive. VS patients had PCI values ranging from 0.19 to 0.31, within the range of healthy subjects during deep anaesthesia and NREM sleep (Casali *et al.* 2013). MCS patients had PCI values ranging from 0.32 to 0.49, above the values observed in NREM sleep and deep sedation in anaesthesia. PCI values very close to the 0.31 threshold were reported for some patients in both groups.

There has not been any explicit discussion so far about the extent to which factors such as age, sex, medication use, brain damage and other neuropsychiatric conditions may affect PCI, although such factors will be important targets for investigation if PCI is to be operationalized as a reliable, disorder-agnostic tool in the context of DoC assessment.

Local global paradigm

ERPs are another potentially useful way of detecting consciousness in the brain (Kotchoubey 2005). They represent a different but important approach to consciousness assessment that focuses on detecting specific brain functions that may require consciousness. For example, the conscious detection of an oddball tone in a sequence of auditory stimuli is known to be associated with several EEG events. Characteristic neural responses to tone changes that are local in time, mismatch negativity (MMN; Ulanovsky *et al.* 2003) and P3a (Squires *et al.* 1975), are thought to be automatic responses associated with preattentive and preconscious processes. The later P3b ERP component (Squires *et al.* 1975) has been associated with the conscious processes involved in the detection of a global pattern violation occurring over several seconds, although whether this response is in fact a signature of conscious processes in the brain remains a point of contention (Koch *et al.* 2016; Silverstein *et al.* 2015; Naccache *et al.* 2016).

Here, I will discuss the data available for the LGP, a method closely related to the oddball paradigm that separates analysis based on the sensory events expected to produce either a local or a global effect response rather than looking for specific MMN, P3a and P3b ERP components, which can be difficult to disentangle. This paradigm can be applied both passively and actively, either by presenting stimuli with no instruction or by asking participants to pay attention to the sounds. Eliciting a neural response to global pattern violations seems to require conscious attention, although experiments can be designed such that attention can be exogenously attracted, e.g. by using highly engaging audiovisual stimuli, as was done for 3-month-old infants (Kouider *et al.* 2013).

There have been several studies applying the LGP to DoC patients (Bekinschtein *et al.* 2009; Faugeras *et al.* 2011; King *et al.*

Table 4. Results of the LGP in a range of conscious states. The LGP, a variant of the auditory oddball paradigm, in a range of conscious states. The presence of the global effect has been thought to indicate the presence of consciousness, whereas the local effect is associated with preconscious, preattentive processing of auditory stimuli

State	Finding
Minimally conscious state	Local effect sometimes present, global effect sometimes present (less frequent than local effect; Bekinschtein *et al.* 2009)
Vegetative state	Local effect sometimes present (less frequent than in MCS), global effect uncommon (less frequent than in MCS; Bekinschtein *et al.* 2009)
General anaesthesia	Local effect present in auditory regions only, global effect absent (Nourski *et al.* 2018)
REM sleep	Local effect present but distorted, global effect absent (Strauss *et al.* 2015)
NREM sleep	Local effect present but distorted, global effect absent (Strauss *et al.* 2015)
Attention on task	Local effect present, global effect amplified (Bekinschtein *et al.* 2009)
Attention off task	Local effect present, global effect diminished (Bekinschtein *et al.* 2009)
Infant (3 months)	Local effect present, global effect present but delayed (Kouider *et al.* 2013)

2013). Bekinschtein *et al.* (2009) found that the global effect was absent in all four VS patients and in one of four MCS patients. Faugeras *et al.* (2011) found the global response to be present in 2 of the 22 VS patients studied. King *et al.* (2013) found that 14% of VS patients displayed a significant global effect, compared to 31% of MCS patients and 52% of healthy controls. The global effect has been found to be absent in both NREM and REM sleep (Strauss *et al.* 2015) and in anaesthesia (Nourski *et al.* 2018; Table 4). It is typically present in awake, healthy participants where attention is being paid to the stimulus. In macaques, the global effect has also been found to be absent after ketamine anaesthesia (Uhrig *et al.* 2016). Ketamine and REM sleep both involve vivid conscious experiences that are highly disconnected from the external environment. These findings emphasize that the global effect can be absent where consciousness is present and that we cannot rule out that this is the case in DoC patients where no global effect is detected.

Implications of the multidimensional approach for neural measures of consciousness in DoC

Neural measures of conscious level and the multidimensional framework

An appraisal of neural measures of conscious 'level' within a multidimensional framework of consciousness suggests that these measures may be more sensitive to some specific dimensions of consciousness than others. This may mean that such neural measures do not straightforwardly measure conscious 'level' or provide a generalizable or hierarchical characterization of the conscious state or extent of residual mental functioning in an individual with a DoC.

There are clear limitations to this comparative and translational approach, one of which is that indirect evidence about neural measures cannot provide a direct ground truth with which to validate these measures. Furthermore, it is unclear to what
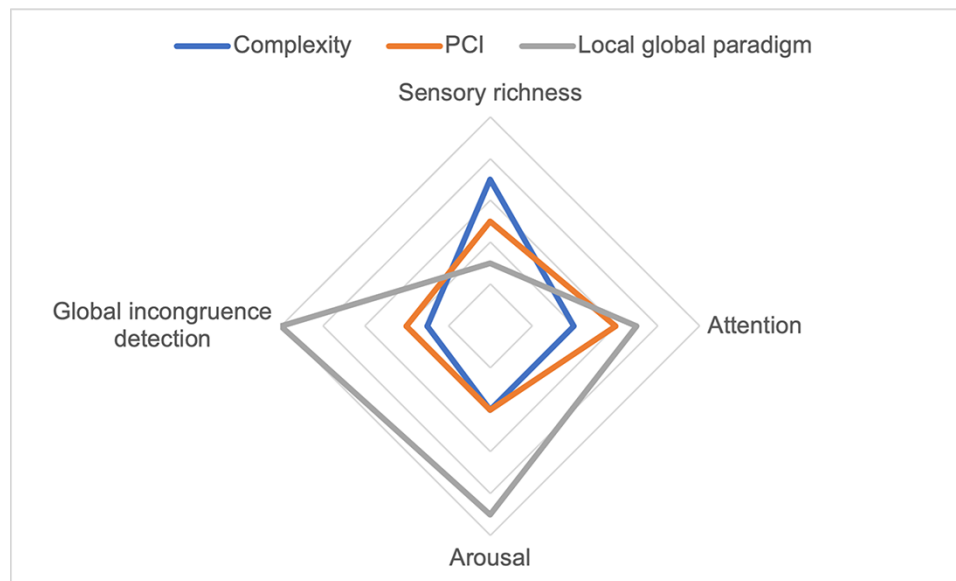
Figure 1. Possible sensitivity of three proposed neural measures of consciousness [resting-state complexity measures (complexity), PCI and the global effect in the LGP] to four dimensions of consciousness (or families of dimensions)

extent insights based on studies conducted in healthy participants and clinical populations outside of DoC can generalize to the relationship between these measures of consciousness in individuals with DoC, who have severe acquired brain damage. Despite these limitations, the qualitative observations that can be drawn from the comparative evidence considered in this article may provide insight into how the three measures considered (resting-state complexity, PCI and LGP) could fit into a multidimensional framework for clinically assessing consciousness in DoC and highlight potential limitations to their use in this context.

A multidimensional appraisal indicates some ways in which these measures, all of which were proposed as measures that can provide generalizable evidence about the presence of consciousness or conscious 'level', can come apart. Figure 1 offers a rough sketch indicating the possible relationship between each of these measures and four of the conscious dimensions discussed in this article. These dimensions have been selected to highlight informative instances of dissociation that we may observe between the three measures, rather than to be broadly representative of the dimensions that it may be important to evaluate in individuals with DoC.

The mechanisms underlying the presence of the global effect in the LGP are relatively well understood, so they can provide clear evidence for some dimensions of neurocognitive processing, such as global incongruence detection (although whether this capacity necessitates consciousness remains a matter of debate). The presence of the global effect also depends on the individual being awake and responsive to the external environment (high arousal) and is more likely to be present when the individual is attending to the stimulus. However, the global effect is absent for sensorily rich internally generated experiences (e.g. REM dreams and ketamine).

As highlighted in Fig. 1, unidimensional measures of resting-state brain complexity seem to have a more general, less precise relationship with the neural mechanisms underlying conscious experience. Evidence suggests that complexity is especially sensitive to states with high levels of sensory richness and a dynamic and variable range of conscious content resulting from minimal attentional constraints (including, to varying extents,

psychedelics, ketamine, REM dreaming and mind wandering). Unlike the global effect in the LGP, it appears to be sensitive to sensory richness irrespective of whether the individual displays high levels of external responsiveness or arousal. Because complexity is lower in states with greater constraints on attention, it may also be inversely correlated with many dimensions of cognitive and executive functioning. However, complexity has a more general relationship with the mechanisms underlying a range of conscious dimensions, so it is unlikely to allow for a more fine-grained dissection of precise conscious and neurocognitive functions such as global incongruence detection.

Like measures of resting-state complexity, PCI was also designed as a unidimensional measure of conscious 'level', so like measures of resting-state complexity, it seems to be associated with a more general range of neural mechanisms and conscious dimensions. However, evidence indicates that PCI may have a more balanced sensitivity to states with high levels of executive and attentional control and those with high levels of sensory richness but minimal attentional constraints. In this sense, PCI values may not have an inverse relationship with attentional control, as may be the case for resting-state complexity measures. PCI values in the same quantitative range can correspond to—e.g. normal wakefulness, REM dreaming and ketamine—states displaying varying levels and forms of attentional control. Further studies examining PCI in a wider range of conscious states and patient groups may help to clarify the ways in which it may dissociate from measures of resting-state complexity, perhaps as a result of having a closer causal relationship with the neural mechanisms of consciousness in the brain.

Limitations of neural measures of conscious level in DoC diagnosis

Scrutinizing unidimensional neural measures of conscious level in terms of their relationship with a wider range of phenomenological dimensions highlights several potential limitations to their use in the diagnosis of consciousness in individuals with DoC. Firstly, comparative evidence suggests that measures of neural complexity tend to have a higher sensitivity to the presence

of certain qualitative forms of conscious experience than others, rather than corresponding to an increase in conscious 'level' *per se*. However, as their relationship with more specific conscious states is broad and appears to be many-to-one, they are unlikely to provide a reliable basis for drawing inferences about the presence of any particular conscious dimension or neurocognitive mechanism (in the way that is possible using ERPs like the LGP).

Another practical limitation to these unidimensional measures of consciousness is that baseline values for an individual may be impacted by demographic and disorder-specific factors. Resting-state complexity varies based on age and possibly also sex, as well as in a range of brain-based disorders including DoC. Furthermore, some of the factors impacting measures of complexity in these cases may not be directly linked to changes in conscious experience (e.g. in AN). This further complicates the process of drawing inferences about consciousness in DoC based on these measures, as many of these factors may need to be accounted for in diagnosis, and the specific forms of brain damage present in DoC may have their own fingerprint for some measures of resting-state complexity.

The extent to which these factors like age, sex, and neurological and psychiatric conditions impact PCI has not been studied, but as a unidimensional measure, it may face similar limitations to resting-state complexity in the context of DoC assessment. However, unlike measures of resting-state complexity, PCI has the advantage of being designed as an absolute index of consciousness, such that PCI values are intended to be comparable between individuals and between different clinical populations (Casarotto *et al.* 2016). As such, it may eventually be easier to quantify the factors that impact this measure and to operationalize how they should be accounted for in DoC assessment. The fact that PCI is theorized to be mechanistically linked to conscious processing, rather than just detecting side effects of this processing, may also mean that it will be easier to eventually establish clearer associations between PCI and specific dimensions of consciousness, possibly independently of other neural differences between individuals and populations.

Overall, the limitations of unidimensional neural measures in providing information about consciousness within a multidimensional framework raise potential ethical issues for the use of these measures in DoC assessment. Our lack of knowledge about how these measures relate to consciousness both in general and in a translational, DoC-specific context could lead to either an overestimation or underestimation of an individual's general level of neurocognitive impairment or otherwise to a mischaracterization of the qualitative nature of their conscious experience and mental functioning in ways that may impact diagnosis, prognosis and treatment.

By contrast, the precise constraints and limitations of ERP-based paradigms like the LGP as tools for evaluating consciousness are better understood. We know that the absence of a signature like the global effect does not necessarily equal the absence of the underlying neural capacity or mechanism, so with this understanding its risks within DoC assessment are minimal. However, there is still an important open question about whether the global effect necessitates consciousness. Furthermore, one possible advantage of measures of conscious 'level' like resting-state complexity and PCI may be their potential for detecting signatures of perceptually decoupled conscious experiences—something that may be more challenging to achieve with ERP-based paradigms.

How should we evaluate consciousness as a multidimensional phenomenon in DoC assessment?

With increasing awareness of the fact that conscious experience, both in general and in DoC, is dynamic, heterogeneous and multidimensional, there has been wider recognition of the need for greater diagnostic precision in DoC assessment and endophenotypes (Provencio *et al.* 2020; Kondziella *et al.* 2021). There is also wider acknowledgement of the benefits of multimodal and multitechnological (Demertzi *et al.* 2017) approaches to diagnosis in DoC, where multiple neurophysiological and behavioural assessments and modalities are combined to improve diagnostic reliability (Giacino *et al.* 2018; Kondziella *et al.* 2020). Several multimodal paradigms have been proposed and implemented (Coleman *et al.* 2009a; Gibson *et al.* 2014; Sergent *et al.* 2016; Hermann *et al.* 2020; Møller *et al.* 2020). Such paradigms may be used to increase the reliability of a binary diagnostic judgement about the presence of consciousness in a patient, but could also be an important tool for improving the richness and precision of our diagnostic approach to consciousness in DoC.

Within a multimodal diagnostic framework, each neural assessment could be seen to provide different information about consciousness and neurocognitive functioning in a patient, such that combining differently designed paradigms with underlying links to different conscious dimensions may eventually allow for richer insight into the subjective quality of consciousness in individuals with DoC. ERPs such as the LGP fit into this framework in quite a clear way. This ERP and others allow for clear inferences about specific neural mechanisms that may shed light on an individual's capacity for specific forms of perceptual and cognitive functioning (incongruence detection, semantic comprehension, as well as more basic forms of sensory processing) without necessarily being generalizable to all dimensions of consciousness or neurocognitive functioning. Assessment paradigms for DoC that incorporate a range of ERPs have been proposed (Møller *et al.* 2020). Although it is challenging to establish with certainty whether any ERP is a true signature of consciousness (Kotchoubey 2005), the functional neural circuitry highlighted by these measures may nonetheless provide information that can inform prognosis (Sergent *et al.* 2016) and care, treatment and rehabilitation decisions for these patients.

Other forms of neural assessment, such as active, task-based fMRI paradigms, may also be informative within a multidimensional assessment paradigm. Active paradigms have clear limitations, but a patient's ability to participate in such a paradigm by, e.g. generating mental imagery in response to command, can provide strong positive evidence not only for consciousness, but for a range of specific dimensions of consciousness (depending on the exact task, these include semantic comprehension, reasoning, long-term memory, memory consolidation and sustained attention to internal imagery; Naci *et al.* 2017). Passive fMRI paradigms that assess neural activity in a task-free setting, such as that which occurs in response natural speech (Sokoliuk *et al.* 2021) or an engaging short movie (Naci *et al.* 2014), also have the potential to be highly informative with regard to specific dimensions of conscious experience such as speech comprehension; recognition of familiar voices, objects and faces; theory of mind; executive function and experiencing affective states (Naci *et al.* 2017). However, in the absence of volitional mental activity, it remains unclear to what extent evidence about conscious experience itself can be drawn based on the neural responses observed in these passive paradigms.

The diagnostic value of levels-based neural measures of consciousness is less clear within a multimodal, multidimensional framework for DoC assessment. Resting-state complexity and PCI cannot be used to draw general inferences about an individual's level of consciousness or neurocognitive functioning as they are more sensitive to certain dimensions and forms of conscious experience than others. However, these unidimensional measures seem to have only a relatively general association with a range of conscious mechanisms and dimensions that does not allow for fine-grained distinctions or inferences about any single property and that therefore leads to considerable diagnostic ambiguity within a multidimensional framework. The limitations of neural measures of conscious 'level' within a multidimensional understanding of consciousness means that their use in DoC diagnosis will need to be carefully scrutinized. However, investigation of the spatial patterns of properties like neural complexity in the brain using more spatially precise modalities like fMRI or high-density EEG may eventually allow for more precise relationships with phenomenology to be inferred.

Conclusion

There is a pressing clinical and ethical need for reliable, precise methods for characterizing consciousness in individuals with DoC, who are a highly heterogeneous and challenging clinical group. There is also a growing view that consciousness is multidimensional, even though some proposed neural measures of consciousness are centred on the idea that consciousness is a property that can be described in terms of hierarchical 'levels.' Here, I have examined a range of comparative evidence about the relationship between these measures, such as those indexing resting-state neural complexity and the TMS–EEG-based PCI, and conscious experience, suggesting that elevated levels of these measures correlate with an increase in some dimensions of consciousness and not others. Furthermore, these measures may be affected by a range of disorder-specific and demographic factors that are not directly reflective of fundamental changes to consciousness. Analysing such neural measures within a multidimensional framework for consciousness has emphasized the need for closer scrutiny of their relationship to both phenomenology and neurobiological impairment before they can ethically be used to support inferences about conscious experience in individuals with DoC. This analysis also suggests that, based on our current level of knowledge, neural measures with clearer links to more specific elements of phenomenology and/or neurocognitive functioning, such as ERP-based measures like the LGP, may currently be the most informative assessments within a diagnostic paradigm that adequately accounts for the multidimensionality, variability and possible heterogeneity that may characterize conscious experience amongst those with DoC.

Conflict of interest statement

None declared.

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