

EDITORIALS

Is consciousness fragile?

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It is not surprising if anaesthetists think that eliminating consciousness is easy. After all, we put patients to 'sleep' every day, many times a day, and we do so reliably with any of a number of agents. Anaesthetic unresponsiveness can be induced by increasing γ -aminobutyric acid type A transmission (etomidate, propofol, and benzodiazepines), decreasing N-methyl-D-aspartate transmission (ketamine), augmenting α_2 -adrenergic signalling (dexmedetomidine), or combining effects on multiple neurotransmitters and receptors (volatile anaesthetics).¹ Unresponsiveness can even be induced by injection of tiny doses of anaesthetics into certain regions of the brain.² No wonder, then, that consciousness has come to be seen as fragile. This notion is only reinforced when we consider that we can become mildly unresponsive when falling asleep spontaneously or that a mere blow to the head, a faint, or a reduction of a few degrees in core body temperature can induce a coma-like state.

This common notion can be summarized as follows: it is easy to induce unresponsiveness; hence, consciousness must be fragile. The problem with this notion is that unresponsiveness is often an inadequate proxy for unconsciousness.³ Properly defined, consciousness is synonymous with subjective experience (seeing sights, hearing sounds, feeling pain, and having thoughts) whether or not these conscious contents relate to the environment.⁴ Thus, one is vividly conscious not only when awake and interacting with the environment, but also when dreaming, daydreaming, or during hallucinations in delirium. Therefore, it is possible that, at least in some instances, one may be surgically unresponsive yet still conscious,^{3 5 6} a situation that is exacerbated by neuromuscular block,^{7 8} which necessarily dissociates responsiveness from consciousness.

Is consciousness fragile during anaesthesia?

Indeed, studies adopting the isolated forearm test (IFT) have shown that, if patients are allowed to communicate in a limited manner by squeezing the unparalysed hand, they can give direct report of intraoperative events. In our review of IFT studies, the median response rate across IFT studies with clinically relevant stimuli (including laryngoscopy) was 37%.³ An estimate for the real-world response rate after laryngoscopy will be established in the ongoing CONSCIOUS study (NCT02248623). Of course, even if one obtains a meaningful response to simple commands, a patient's cognitive abilities may be far from fully intact. On the contrary, some IFT non-responders may be conscious but incapacitated enough so that they are not able to respond.

A simpler way to determine whether patients are conscious during anaesthesia unresponsiveness is to rely on retrospective reports. Indeed, in recent studies in which unresponsiveness was experimentally induced in young, healthy subjects anaesthetized with sevoflurane, propofol, or dexmedetomidine, the majority of subjects reported having had 'anaesthesia dreams' upon awakening.⁹ In clinical anaesthesia, dreams are reported by around a third of patients.¹⁰ In this context, conscious experience is disconnected from the sensory world, so patients are unaware of surgery. In contrast, if a patient can report intraoperative events after awakening, one must assume that he was conscious and connected to the environment. In the real world, reports of anaesthesia awareness are rare.^{3 6 11} This could suggest that consciousness is usually eliminated by anaesthesia, and when it is not, this is likely to be because of inadequate dosing of anaesthetics.¹² However, explicit recall of experiences can occur after seemingly appropriate drug doses.⁵ Moreover, most anaesthetics typically have powerful amnesic effects at doses much lower than those required for inducing unresponsiveness.¹¹ Thus, the

low report rates of anaesthesia awareness with explicit recall may be because of amnesia rather than unconsciousness.

While some may argue that absence of unpleasant memories is all that matters behaviourally, few patients or caregivers would agree that experiencing agony is acceptable as long as one does not remember it. To wit, a combination of benzodiazepine, β -blocker, and neuromuscular block is rarely used as an anaesthetic. Indeed, patient expectation is that anaesthesia means unconsciousness, not amnesia.

In sum, when we consider that loss of responsiveness or loss of memory is not necessarily synonymous with loss of experience, the evidence is beginning to suggest that consciousness, after all, may not be fragile under anaesthesia. Furthermore, upon reflection, there is a lack of evidence for the fragility of consciousness across various physiological and pathological states.

Is consciousness fragile in other conditions?

When we are awake we are virtually always conscious, whether attending to the environment or daydreaming.¹³ It is still frequently stated that when we fall asleep we lose consciousness. However, when being conscious is properly defined as having an experience, it is now evident that consciousness is present throughout much of the night.¹³ Rapid eye movement (REM) sleep has long been associated with vivid dreaming [82 (sd 19)% of the time in a recent serial awakening paradigm],¹³ but reports of conscious experiences are also obtained in the majority of awakenings from non-REM sleep. Even awakenings from the deepest non-REM sleep (stage N3) yield reports of dream-like experiences 23 (sd 15)% of the time, although these are rare during periods rich in slow-wave activity early in the night. In stage N2, where α -spindles occur in the EEG, the percentage reaches 42 (sd 15)%.¹³ When including retrospective reports of having been conscious but unable to recall the content, the percentages grow even further.

Just as consciousness can persist throughout periods of slow-wave sleep, it can also persist in other conditions with EEG slowing, such as delirium¹⁴ and post-ictal states.^{15 16} While in these states consciousness appears altered or disturbed, it is certainly not abolished; a relevant example is that subjects may experience pain. This suggests that in anaesthesia, too, the occurrence of EEG slowing will not necessarily imply unconsciousness.

Dissociations between behavioural responsiveness and consciousness also occur in several neurological conditions. Many patients with severe brain damage, who were often considered unresponsive and whose clinical conditions often fluctuated, are now considered to be 'minimally' conscious, as long as a careful, repeated examination uncovers signs of eye tracking or purposeful movements.^{17 18} This type of examination would be difficult under anaesthesia, but is approximated by IFT.¹⁸ Locked-in patients and catatonic subjects are also unresponsive, but the former, and perhaps the latter, are conscious.^{3 18} Even patients deemed in a 'vegetative' state (implying permanent unconsciousness) are now more correctly classified under the 'unresponsive wakefulness syndrome'. This relabelling was triggered by the demonstration with functional MRI that, when asked to imagine either playing tennis or navigating their room, about 20% of behaviourally unresponsive, 'vegetative' patients activate the same cortical areas as control subjects.¹⁹ Such experiments have not been attempted under anaesthesia (but see Davis and colleagues²⁰), but we cannot assume that the results would be uniformly negative. In summary, evidence from anaesthesia, sleep, delirium, and severe brain damage supports the concept that consciousness, far from being fragile, can often be

found if one searches hard enough without trusting exclusively behavioural responsiveness and memory.

Why is consciousness not fragile? Does consciousness shrink and bend before it shatters?

It is often thought that consciousness is lost in an all-or-none manner. Indeed, during induction of anaesthesia with a bolus of propofol, patients cease responding abruptly; the subjective impression of the patient, too, is one of experience vanishing swiftly; one moment one is there and the next moment one is gone. However, there are both theoretical^{4 21} and empirical reasons to think that the level of consciousness and its contents may be graded. Reports from studies of serial awakening from sleep range from full lucidity to perceptual vividness to thought-like mentation to confused, dim (shrunk and bent) experiences.¹³ Delirium and (post)-ictal states also qualify as states of diminished consciousness.^{16 22 23} Minimally conscious patients are likely to lack some conscious content and have reduced levels of consciousness, as also suggested by transcranial magnetic stimulation-EEG studies showing a reduction of information integration in their brains.²⁴ In many of these instances, a narrowing of the 'field' of consciousness could occur if some of the brain areas that normally support consciousness 'drop out'. In fact, during non-REM sleep the overall EEG may show diffuse slow waves, but high-density EEG can reveal local areas of activation, such as in parieto-occipital regions, and when this happens, subjects report dreams with specific content.²⁵ It will be important to determine whether localized EEG activation may also occur with certain anaesthetics, especially at lower doses, and whether it is correlated with dreaming under anaesthesia. At high doses, anaesthetics are more likely to produce a global decrease in the level of consciousness rather than the ablation of particular contents. Even if consciousness is graded in principle, in practice it may 'shatter' in a non-linear manner. Computer simulations indicate that when the overall activation of corticothalamic networks decreases below a certain level, there is a sudden reduction in the functional connectivity between distant parts of the cortex.^{26 27} At present, the EEG correlates of the shatter point of consciousness are unknown, although mere slowing of the frontal EEG is unlikely to be a sufficient measure.

Implications for the future

If consciousness is neither a fragile nor an all-or-none phenomenon, it becomes important to detect its presence with criteria that go beyond behavioural responsiveness and memory. Unfortunately, what is currently available in the operating room, such as the bispectral index, is not adequate to detect awareness in the individual patient^{3 5 28} even in the absence of anaesthetic drugs.⁷ A promising new approach is the use of transcranial magnetic stimulation-EEG to assess the brain's ability to integrate information, which has been applied successfully in non-communicative subjects whether asleep, under anaesthesia, or after brain damage.^{24 29} The spontaneous EEG, if properly interpreted, can also offer useful clinical information,³⁰ and it is hoped that on-line analysis tools can be developed to extract indices of local activation. Such tools should make it possible to reduce the rate of anaesthesia awareness with recall further, and above all, to reduce the high rates of intraoperative awareness without recall suggested by the IFT. Finally, they may facilitate the acceptance that patients under anaesthesia need not necessarily be unconscious (see Eger and Sonner¹¹), as long as the necessary unpleasantness of surgery can be eliminated. Anaesthetic effects on

neural substrates of the fear response may be one approach.³ Perhaps more effective would be to recognize that unconsciousness is not guaranteed during anaesthesia; hence, to develop strategies for sensory disconnection,³ analogous to dreaming while preventing awareness of surgery.

Declaration of interest

R.D.S. has consulted for Air Liquide on the development of medical gases, which is unrelated to this article. R.D.S. is also a Board Member of the BJA. G.T. has consulted for Philips Respiration and has been involved in a research study in humans supported by Philips Respiration; also, he is a consultant for the Allen Institute for Brain Research. The article submitted is not related to any of these relationships.

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