A similar BIS value does not mean a similar depth of anaesthesia

Editor—The recent editorial and accompanying two studies provide more intriguing information as regards the complex nature of general anaesthesia. However, there are two aspects of the terminology used within the papers which I believe have the potential to cause confusion.

First, there is the suggestion that equi-anaesthetic concentrations of a drug can be defined by the same bispectral index (BIS) value. I have no concerns if an author’s methodology describes titrating anaesthetic drugs to a particular BIS value, but authors should not believe that because patients have the same BIS values this indicates a similar depth of anaesthesia. There is abundant evidence to the contrary. The onset of anaesthesia is generally defined as loss of consciousness (LOC) and this is an easily observed endpoint. The available data do not support BIS or any depth of anaesthesia (DoA) monitor as being able to define LOC with a particular BIS number. In the two papers discussed in the editorial, the BIS value at LOC for sevoflurane and propofol were 70 vs 61 and 80 vs 63. These are significantly different BIS values indicating inter-individual variability. To add further confusion, data currently under analysis, which I obtained during a study of BIS-guided anaesthesia back up with the isolated forearm technique not only confirm this inter-individual variability (patients responding to command during surgery with BIS values anywhere between the low 40s up into the 80s), but the same patient may respond at quite different BIS values at different times during the procedure.

Secondly, Mourisse and colleagues state that ‘unconsciousness was assessed with the validated method of BIS reflecting the depression of the cerebral cortex’. To back up this statement, they refer the reader to a paper discussing the validation of ‘DoA’ monitors. Although this is a well-written article, it is essentially descriptive and in the concluding paragraph the authors write: ‘When validated, DoA monitors can be integrated into future anaesthetic advisory and feedback systems’. To me, this suggests that DoA monitors are yet to be validated!

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Editor—We thank Dr Russell for his response to the editorial and his interest in our articles. He expresses concerns about the terminology we have used. We wish to respond in three ways.

First, we did not use the term ‘DoA’ in the papers. ‘DoA’ suggests that anaesthesia is a variable that is somehow measurable. In fact, we first have to define anaesthesia, then as a next step, we can try to measure anaesthesia. If we can measure anaesthesia, we can control it.

We therefore were seeking evidence that general anaesthesia has cortical (amnesia and unconsciousness) and subcortical components (antinociception, immobility, and autonomic stability). LOC and inhibition of movement in response to a noxious stimulus are two separate endpoints of anaesthesia, although mutual influences between components are possible. This concept is not new and was recently discussed in this Journal. We have used BIS as a measure of cortical activity. The blink reflex and the withdrawal reflex were used as measures of subcortical activity. BIS does not test ‘DoA’, but rather the hypnotic component of the state of general anaesthesia.

Secondly, Dr Russell is right that LOC does not correspond to a particular BIS value. We do not agree that LOC is an easily observed endpoint. An exact determination of the time of LOC depends on the frequency of asking, and asking itself can influence the time of LOC. Furthermore, determining LOC is subjective and, around the LOC, the dose–response curve for BIS is at its steepest. All these factors contribute to a large variability. That does not alter the fact that we found a discrepancy between the BIS values at LOC for sevoflurane and propofol. However, we believe we can make a valid comparison between dose–response curves for BIS against sevoflurane or propofol concentrations, as we excluded periods of excitation and burst suppression. We are uncertain about the place of the isolated forearm technique in our concept. Apart from being subjective to the interpretation by the anaesthetist, it is not always clear whether a response is initiated by cortical or subcortical structures. Therefore, it is not a surprise to see responses at low BIS values.

Thirdly, as the BIS monitor can reduce the incidence of awareness, it is validated for this application. That is what we are referring to in our introduction. BIS could not be validated in a straightforward way as a measure of the state of arousal of a patient because there is a lack of an objective gold standard. Therefore, one has to rely on indirect indices, such as anaesthetic drug concentrations or clinical scales. BIS—the most widely evaluated index—is not a perfect measure, if only because of the time that is required for the computation from the raw EEG.

In conclusion, we have abandoned the term ‘DoA’. The increasing evidence for the crucial role of subcortical...
functions, particularly at the level of the spinal cord, suggests that the time has come to stop using the term ‘DoA monitor’ to indicate a device for solely monitoring cortical functions.

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Hypothermia and cerebrovascular reactivity

Editor—Lavinio and colleagues¹ have touched upon an important topic by suggesting that temperatures above 37°C may cause hyperaemic derangement of cerebrovascular reactivity in severely head-injured patients. However, one of the major limitations of their retrospective analysis lies in the fact that the effects of temperature could not be separated from any temporal changes that occurred in the brain after injury. Rewarming took place at a time when inflammatory responses in the brain presumably had evolved significantly compared with when the patients were cooled.² Indeed, the authors acknowledge that the fever and loss of autoregulation observed in their patients may both, in fact, be epiphenomena of inflammation and suggest that prospective studies be performed. In this respect, I would like to draw attention to a study that may provide some additional insight into this matter.

In 2004, we reported on the use of systemic hyperthermia as an experimental therapy for patients with chronic hepatitis C virus infection, who are non-responders to conventional treatment with interferon.³ During 23 experiments at 41.8°C, we continuously measured cerebral oxygen extraction and middle cerebral artery blood flow velocity in patients. At regular temperature intervals, we formally assessed cerebral pressure-flow autoregulation by static tests using phenylephrine infusion, and by measuring the transient hyperaemic response to carotid compression and release. Our data showed that temperatures exceeding 40°C were associated with a marked decrease in cerebral oxygen extraction, a proportional increase in cerebral blood flow velocity, and a transient impairment of pressure-flow autoregulation. These associations remained after multivariate adjustment for variations in arterial partial pressure of carbon dioxide, mean arterial pressure, and propofol blood concentration.

The current findings by Lavinio and colleagues¹ seem to confirm these earlier observations of transient cerebral vasoparalysis and hyperaemia during profound hyperthermia in patients with normal brains. However, their data suggest that similar effects become apparent at much lower temperatures in patients with head trauma, possibly reflecting an increased vulnerability of the injured brain to the deleterious effects of heat.

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Editor—We thank Dr Cremer for his comments. Cremer and colleagues³ previously demonstrated that systemic temperature exceeding 40°C is associated with partial vasoparalysis of cerebral vessels in normal brains. Our findings suggest that a similar scenario may happen in head-injured patients exposed to moderate hypothermia for refractory intracranial hypertension.¹

Cremer highlights that in our series of brain-injured patients, the hyperaemic derangement of cerebrovascular reactivity became apparent as soon as rewarming from moderate hypothermia exceeded the 37°C brain temperature threshold, reflecting a significantly increased vulnerability of cerebrovascular reactivity of the injured brain. We also emphasize that this phenomenon is commonly undetected by plain intracranial pressure (ICP) monitoring, which lacks explicit information about cerebral vasoreactivity. In this regard, a steady ICP after rewarming from moderate hypothermia is often falsely reassuring, inducing suboptimal control of systemic temperature in brain-injured patients.