# Neuromonitoring

Martin Smith


## Abstract

The monitoring of critically ill brain injured patients has become increasingly complex. Several techniques are now available for global and regional brain monitoring that provide assessment of cerebral perfusion, oxygenation and metabolic status, and early warning of impending brain hypoxia/ischaemia. Developments in multimodality monitoring have enabled a move away from rigid physiological target setting to an individually tailored, patient-specific approach to the management of acute brain injury. Multimodal monitoring generates large and complex datasets, and systems that analyse and present information in a user-friendly format at the bedside are essential to maximize its clinical relevance. This review describes current neuromonitoring techniques used during the intensive care management of acute brain injury.


**Keywords** Cerebral microdialysis; cerebral oxygenation; intracranial pressure; multimodal monitoring; near infrared spectroscopy; neurointensive care

**Royal College of Anaesthetists CPD matrix:** 2F01, 3C00, 3F00

## Learning objectives

After reading this article you should be able to:

- identify the key intracranial variables that can be monitored at the bedside
- understand the advantages and limitations of different monitoring techniques
- understand the role of multimodality monitoring to guide individualised patient management.

In addition to the continuous monitoring and assessment of cardiorespiratory functions common to all critically ill patients, several techniques are now available for global and regional brain monitoring. These provide assessment of cerebral perfusion, oxygenation and metabolic status and early warning of impending brain hypoxia/ischaemia, and guide targeted treatment after acute brain injury (ABI).[1] Some monitoring modalities are well established whereas others are relatively new to the clinical arena, and their indications are still being evaluated (Table 1).

## Intracranial pressure

There are two main methods of monitoring intracranial pressure (ICP).[2] The gold standard is a ventricular catheter connected to a pressure transducer 'zeroed' at the level of the external auditory meatus. Ventricular catheters measure global ICP and have the additional advantages of allowing periodic external calibration and therapeutic drainage of cerebrospinal fluid (CSF). However, they are associated with significant complications, including haemorrhage, seizures and CSF infection (ventriculitis). Alternatively, fibreoptic and microtransducer (strain gauge) ICP monitoring devices are easy to insert and have minimal complication rates. They are placed in the brain parenchyma via a cranial access device at the bedside or during neurosurgery and, although they cannot be recalibrated *in vivo*, their zero and sensitivity drift over time is relatively small. Microtransducer devices measure localized pressure and this may not represent true CSF pressure because of the presence of intraparenchymal pressure gradients in the injured brain.

ICP monitoring is supported by international consensus guidance for many ABI types, and particularly for traumatic brain injury (TBI). A 2010 meta-analysis suggested that ICP monitoring and management is associated with improved outcome after severe TBI,[3] but a recent randomized controlled trial found no difference in 3- or 6-month outcomes when treatment after severe TBI was guided by ICP monitoring compared to care based on imaging and clinical examination in the absence of ICP monitoring. Whether the findings of this study, conducted in Bolivia and Ecuador, are applicable to wealthier nations with superior pre-hospital care and rehabilitation services remains to be seen. Furthermore, the composite primary endpoint in this study was weighted towards neuropyschological outcomes, and a more conventional measure, the extended Glasgow Outcome Scale, showed a (non-significant) 5% lower mortality and improved outcome in the ICP monitoring/management group.

ICP monitoring does not provide a comprehensive picture of cerebral physiology and pathophysiology, and is best viewed as a key component of a multimodal monitoring technique rather than as a monitoring modality in isolation.

## Cerebral oxygenation

Cerebral oxygenation monitoring assesses the balance between cerebral oxygen delivery and utilization, and the adequacy of cerebral perfusion. Several bedside methods of monitoring global and regional cerebral oxygenation are available.

### Jugular venous oxygen saturation

Measurement of jugular venous oxygen saturation ($SjvO_2$) was the first bedside measure of cerebral oxygenation. As well as having considerable historical relevance, $SvjO_2$ monitoring formed the basis of our understanding of cerebral oxygenation changes after ABI. $SjvO_2$ is a flow-weighted measure that reflects global cerebral oxygenation only if the dominant jugular bulb is cannulated, although in practice the right side is usually chosen. The jugular catheter must be correctly sited to avoid contamination from the extracranial circulation, which is minimal when the catheter tip lies level above the lower border of the first cervical vertebra on a lateral cervical spine radiograph. Because it is a global measure, $SjvO_2$ monitoring is unable to detect regional ischaemia.

Normal $SjvO_2$ is 55–75% and interpretation of changes is relatively straightforward (Table 2). Prolonged or multiple

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## Advantages and disadvantages of bedside neuromonitoring techniques

| Technique | Advantages | Disadvantages |
|---|---|---|
| Intracranial pressure (ventricular catheter) | Gold standard<br>Measures global pressure<br>Therapeutic drainage of CSF<br>*In vivo* calibration | Placement technically difficult<br>Risk of haemorrhage<br>Risk of infection |
| Intracranial pressure (microsensor) | Intraparenchymal/subdural placement<br>Easy to place with low procedural complication rate<br>Low infection risk | *In vivo* calibration not possible<br>Measures localized pressure |
| Transcranial Doppler | Non-invasive<br>Assesses regional blood flow velocity<br>Real time with good temporal resolution | Measures relative cerebral blood flow<br>Operator dependent<br>Failure rate of 5—10% (absent acoustic window) |
| Jugular venous oximetry | Assesses balance between flow and metabolism<br>Easy to perform | Global and insensitive to regional changes<br>Risk of vein thrombosis, haematoma, carotid puncture |
| Brain tissue $pO_2$ | Bedside gold standard for brain oxygenation monitoring<br>Represents balance between flow and metabolism<br>Continuous | Invasive<br>Measures regional oxygen tension<br>Utility dependent on probe location |
| Near infrared spectroscopy | Non-invasive<br>Real time<br>Assessment of regional cerebral oxygenation over several regions of interest | Dependent on manufacturers algorithms<br>Lack of standardization between commercial oximeters<br>Signals affected by extracerebral structures |
| Microdialysis | Measurement of local brain tissue biochemistry<br>Early detection of hypoxic/ischaemic injury<br>Monitor of cellular bioenergetic distress | Focal measure<br>Thresholds for abnormality uncertain |
| Electroencephalography | Non-invasive<br>Real time<br>Correlates with ischaemic and metabolic changes | Skilled interpretation required<br>Affected by anaesthetic/sedative agents |

**Table 1**

## Interpretation of changes in jugular venous oxygen saturation

| $SjvO_2$ | Relative blood flow & metabolic changes | Causes |
|---|---|---|
| Normal (55—75%) | CBF and $CMRO_2$ balanced | |
| Low (<50%) | ↓ CBF or ↑ $CMRO_2$ | ↓ Blood pressure<br>↓ $PaCO_2$<br>↓ $PaO_2$<br>↑ ICP or ↓ CPP<br>Seizures |
| High (>80%) | ↑ CBF or ↓ $CMRO_2$ | Cerebral hyperaemia<br>Failure of oxygen utilization (mitochondrial failure)<br>Arteriovenous shunting<br>Brainstem death |

CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate for oxygen; CPP, cerebral perfusion pressure; ICP, intracranial pressure; $PaCO_2$, arterial carbon dioxide tension; $PaO_2$, arterial oxygen tension; $SjvO_2$, jugular venous oxygen saturation.

**Table 2**

desaturation <50% have been associated with poor neurological outcome after TBI. Although widely used for decades, $SjvO_2$ monitoring is being superseded by newer modalities.

### Brain tissue oxygen tension

Continuous measurement of brain tissue $pO_2$ ($PtiO_2$) is now the 'gold standard' bedside measure of cerebral oxygenation.[4] A commercially available $PtiO_2$ catheter (Licox, Integra Neuroscience Ltd., Andover, UK) incorporates a Clark-type cell. Oxygen diffusing from brain tissue crosses a semi-permeable membrane and is reduced by a gold polarographic cathode producing a flow of electrical current that is directly proportional to the tissue oxygen tension (Figure 1).

$PtiO_2$ is a complex and highly dynamic variable that represents the interaction between cerebral oxygen delivery and demand, as well as tissue oxygen diffusion gradients. Although strongly influenced by systemic blood pressure and cerebral perfusion pressure (CPP), $PtiO_2$ is also affected by several other factors including $PaO_2$, $PaCO_2$, and haemoglobin concentration. Which intervention (or combination of interventions) to reverse brain hypoxia is most effective in improving outcome remains unclear. In fact it appears that it is the responsiveness of the hypoxic brain to a given intervention that is the prognostic factor, with reversal of hypoxia being associated with reduced mortality. Positron emission tomography studies suggest that the $PtiO_2$-defined ischaemic threshold lies below 1.8 kPa, but $PtiO_2$ values are best considered within a range rather than as a precise threshold, and ischaemia defined by both duration and depth of hypoxia.

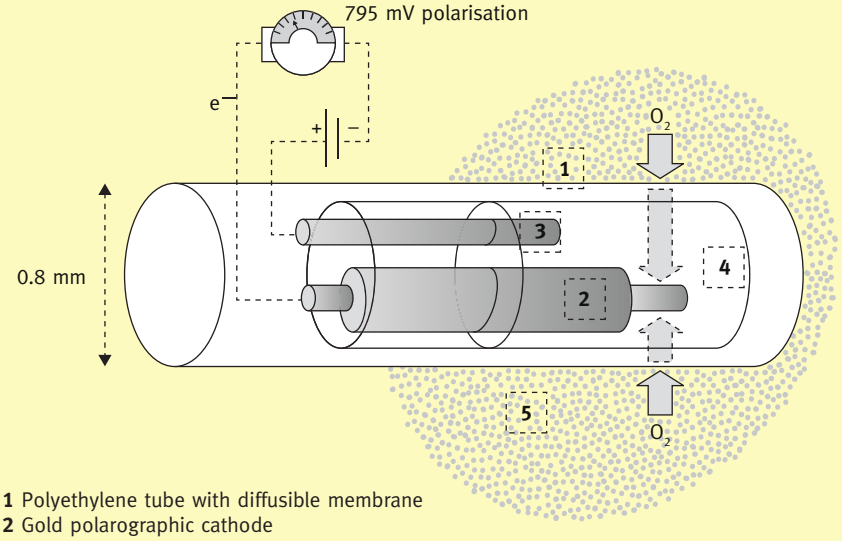
$PtiO_2$ monitoring allows rapid detection of cerebral ischaemia and therefore the possibility to initiate therapy before irreversible neuronal damage occurs. Brain hypoxia can occur despite ICP and CPP being within accepted thresholds for normality, arguing for the monitoring of $PtiO_2$ in addition to ICP/CPP. There is preliminary evidence that $PtiO_2$-directed therapy is associated with improved outcome compared to ICP/CPP-guided therapy alone,[5] and this is currently being investigated in a large multicentre study. Many neurocritical care units incorporate $PtiO_2$-directed therapy into ABI treatment algorithms (Figure 2).

## Near infrared spectroscopy

Near infrared spectroscopy (NIRS) is a non-invasive technique based on the transmission and absorption of near infrared (NIR) light (700–950 nm) as it passes through tissue. Oxygenated and deoxygenated haemoglobin have characteristic, and different, absorption spectra in the NIR and their relative concentrations in tissue can be determined by their relative absorption of light at these wavelengths. Spatially resolved spectroscopy (SRS) derives a scaled absolute haemoglobin concentration (i.e. the relative proportions of oxyhaemoglobin and deoxyhaemoglobin) from which an absolute cerebral tissue oxygen saturation ($ScO_2$) can be calculated. $ScO_2$ provides a continuous measure of the balance between cerebral oxygen delivery and utilization.[6]

In the last decade there has been a rapid expansion in the clinical use of NIRS-based cerebral oximetry during cardiac surgery following evidence from early retrospective studies that NIRS-guided brain protection protocols might lead to a reduction

**Schematic representation of the tip of the Licox brain tissue oxygen sensor**




**1** Polyethylene tube with diffusible membrane
**2** Gold polarographic cathode
**3** Silver polarographic anode
**4** Electrolyte chamber
**5** Brain parenchyma

(Reproduced with permission from Oxford University Press – Nortje and Gupta, *Brit J Anaesth* 2006; 97: 95–106)

**Figure 1**

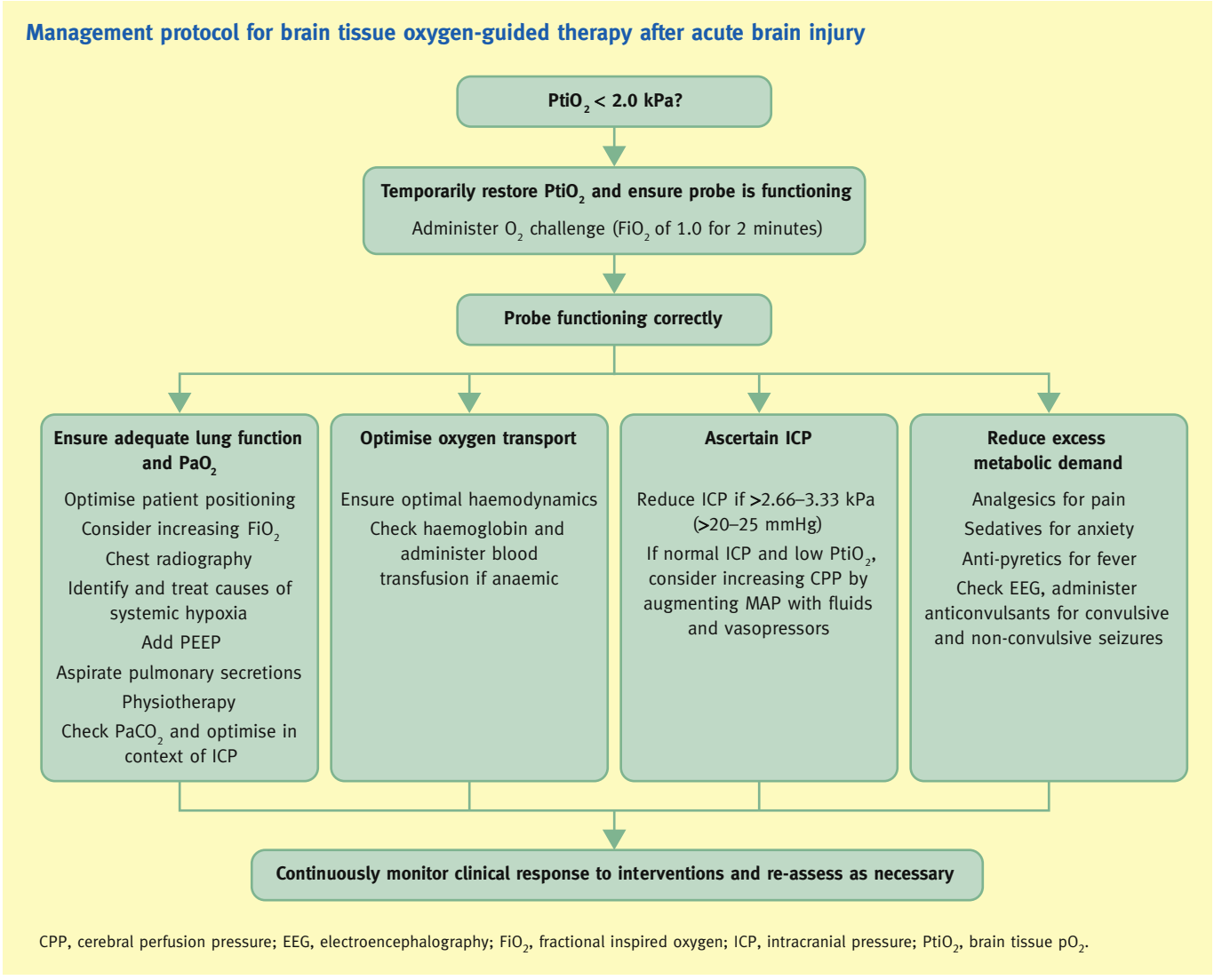



**Figure 2**

in perioperative stroke and postoperative cognitive dysfunction. Although subsequent prospective, randomised controlled trials failed to replicate these outcome benefits, there is evidence of an association between intraoperative cerebral desaturation and an increased risk of perioperative cognitive decline after cardiac surgery.

NIRS is also used to monitor the adequacy of cerebral oxygenation during carotid surgery, where it has similar accuracy and reproducibility in the detection of cerebral ischaemia compared to other monitoring modalities, and some advantages in terms of simplicity and temporal resolution. However, it is impossible to specify an $rScO_2$ threshold that can be widely applied to guide shunt placement and other neuroprotective interventions.

There has been limited investigation of the utility of NIRS after ABI where its application is confounded by the optical complexity of the injured brain. Modern technology is able to overcome some of these confounding issues, and NIRS-derived haemoglobin variables, including cerebral oxygenation, have recently been investigated as a non-invasive assessment of cerebral autoregulatory status after ABI. In the research setting, NIRS-monitored changes in the oxidation status of oxidized cytochrome *c* oxidase (CCO), the final electron acceptor in the mitochondrial electron transport chain responsible for over 95% of oxygen metabolism, provides additional information about cellular energy status which, in association with haemoglobin-based NIRS variables, may aid in the determination of ischaemic thresholds in the injured brain.[6]

There are several concerns over the clinical application of NIRS and the one most often highlighted is the potential for 'contamination' of the signals by extracranial tissue. Some commercial cerebral oximeters use two detectors and a subtraction-based algorithm which assumes that the detecting optode closest to the emitter receives light that has passed mainly through the scalp whereas that arriving at the farthest detector has mainly passed through brain tissue. Although there is weighting in favour of intracerebral tissue with an inter-optode spacing (distance between light emitter and detector) greater than 4 cm, all current commercially available devices remain prone to some degree of extracerebral contamination. It has recently been demonstrated that the NIRS-derived CCO signal is highly specific for intracerebral changes, potentially making it a superior biomarker to other, haemoglobin-based, NIRS variables.

## Transcranial Doppler

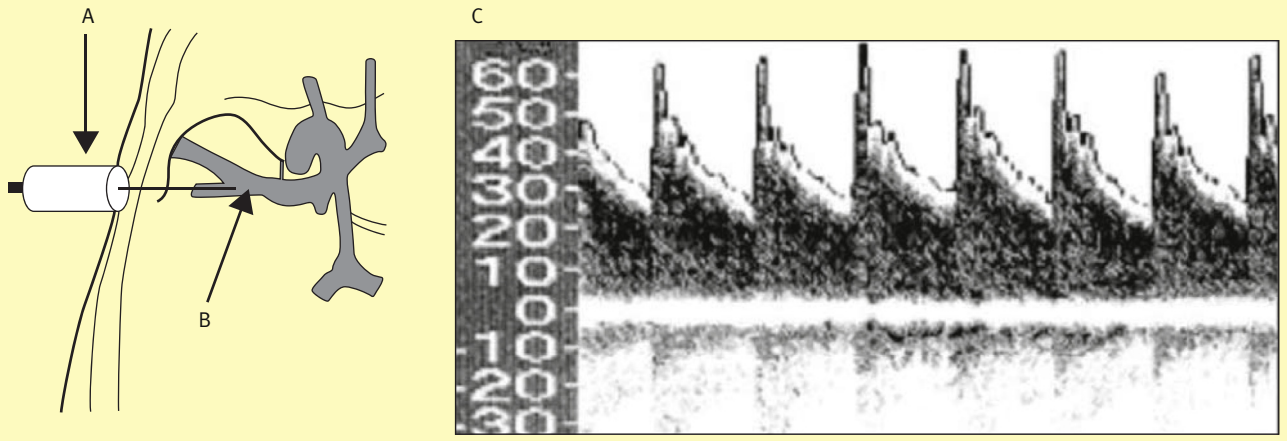



**Figure 3**

## Cerebral blood flow

Two bedside methods for assessing cerebral blood flow (CBF) continuously are available.

### Transcranial Doppler ultrasonography

Transcranial Doppler ultrasonography (TCD) is a non-invasive technique for assessing cerebral haemodynamics in real time.[7] It uses a low-frequency (2 MHz) pulsed-wave ultrasound probe to measure blood flow velocity (FV) through large cerebral vessels from the Doppler shift caused by red blood cells moving through the field of view. It measures relative blood flow changes rather than actual CBF. The TCD FV waveform resembles an arterial pulse wave (Figure 3) and may be quantified into peak systolic, end diastolic and mean FVs, and pulsatility index (PI). PI provides an assessment of distal cerebrovascular resistance.

TCD is most commonly used in the diagnosis and management of cerebral vasospasm after subarachnoid haemorrhage, and also to test cerebral autoregulatory reserve. It is operator dependant, prone to some variability, and long-term recordings are limited by the need for accurate and immovable probe fixation.

### Continuous quantitative CBF monitoring

Quantitative measurement of absolute regional CBF is possible using a thermal diffusion flowmetry (TDF) probe sited in brain parenchyma. The TDF catheter consists of a thermistor heated to a few degrees above tissue temperature and a second, more proximal, temperature probe. The temperature difference between thermistor and temperature probe is a reflection of heat transfer and can be translated into a measurement of CBF. TDF catheters are available for clinical use but there are limited clinical data using this technique.

## Cerebrovascular autoregulation

Established methods of testing static and dynamic cerebrovascular autoregulation (CA) are interventional or intermittent, and may be not be applicable in critically ill patients.

## Cerebral microdialysis markers of secondary brain injury

| Microdialysis variable | Monitor of | Notes |
|---|---|---|
| Glucose <1.5—2.0 mmol/litre | • Hypoxia/ischaemia<br>• Reduced cerebral glucose supply<br>• Cerebral hyperglycolysis | • Interpret in relation to serum glucose concentration |
| Lactate:pyruvate ratio >20—25 | • Hypoxia/ischaemia<br>• Cellular redox state<br>• Reduced cerebral glucose supply | • Most reliable biomarker of ischaemia<br>• Tissue hypoxic threshold for raised LPR not established |
| Glycerol >100 μmol/litre | • Hypoxia/ischaemia<br>• Cell membrane degradation | • Increased glycerol may also occur because of production of glycerol from glucose |
| Glutamate >15—20 μmol/litre | • Hypoxia/ischaemia<br>• Excitotoxicity | • Large inter- and intra-patient variability |

**Table 3**

Under normal circumstances, increased arterial blood pressure (ABP) leads to cerebral vasoconstriction within 5—15 seconds and a secondary reduction in cerebral blood volume and ICP. When CA is impaired, CBV and ICP increase passively with ABP, with opposite effects occurring during reduced ABP. Monitoring and correlation of spontaneous slow waves in ABP and ICP allows calculation of a pressure reactivity index (PRx) as a continuous assessment of CA. A negative value for PRx, when ABP is inversely correlated with ICP, indicates normal CA, and a positive value a non-reactive cerebrovascular circulation. PRx may be used to guide therapy after TBI and identify optimal CPP.[8]

## Cerebral microdialysis

Cerebral microdialysis (MD) allows bedside analysis of biochemical substances in brain tissue extracellular fluid (ECF).[9] MD is a focal monitoring technique and the catheter is usually placed in 'at risk' tissue (e.g. the region surrounding a mass lesion) so that biochemical changes in the area of brain most vulnerable to secondary insults are monitored. Glucose, lactate, pyruvate, glycerol and glutamate are the most commonly measured substances in the clinical setting. Each is a marker of a particular cellular process associated with glucose metabolism, hypoxia/ischaemia or cellular energy failure (Table 3). Because lactate can be an energy substrate for the brain as well as an indicator of anaerobic metabolism, it is usual to monitor the lactate:pyruvate ratio rather than lactate alone.

One of the main advantages of cerebral MD monitoring is its ability to assess glucose metabolism. Reduced oxygen and glucose supply because of inadequate cerebral perfusion is a major contributor to secondary brain injury but several other factors are also implicated. For example, glucose utilization may increase dramatically even in the presence of adequate supply (cerebral hyperglycolysis), leading to critical reductions in cerebral glucose levels. Cerebral oxidative metabolism of glucose may also be impaired because of mitochondrial dysfunction and cellular energy failure, and MD monitoring offers unique insights into the ensuing metabolic crisis. Because it measures changes at the cellular level, MD has potential to detect cerebral hypoxia/ischaemia before changes can be identified by more conventional monitoring techniques or clinical status.

## Continuous electroencephalography

The electroencephalogram (EEG) is used to diagnose and guide therapy in those suffering from seizures or status epilepticus.[10] Monitoring of continuous EEG (cEEG) is becoming more widespread because of an increased awareness that non-convulsive seizures are common in patients with ABI. cEEG is limited by its attenuation by anaesthetic and sedative agents and is a resource intense technology, requiring skilled personnel for interpretation. Telemedicine may increase the adoption of cEEG by allowing interpretation away from the bedside, as will the development of automated seizure detection software.

## Multimodal monitoring

Combining data from multiple monitoring modalities overcomes many of the limitations of individual techniques. Multimodal monitoring allows cross validation between monitors, artefact rejection and greater confidence to make treatment decisions.[1] However, multimodal monitoring produces large and complex datasets and, in order to maximize clinical relevance, there is a need to develop systems that analyse and present the information in a user-friendly format at the bedside. ◆

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