Neuromonitoring

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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 early warning of impending brain ischaemia and allow optimization of cerebral haemodynamics, oxygenation and metabolism. Developments in multimodality monitoring have enabled a move away from rigid physiological target setting to an individually tailored, patient-specific approach. 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 brain injury.

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

Learning objectives

After reading this article, you should be able to:

- identify the key intracranial variables that can be monitored at the bedside
- list the advantages and limitations of different monitoring techniques
- understand the role of multimodality monitoring in guiding patient-specific therapy

Besides 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 that provide early warning of impending brain ischaemia and guide therapeutic interventions in brain-injured patients.

Intracranial pressure

Intracranial pressure (ICP) cannot be reliably estimated from any specific clinical feature or head computed tomography (CT) finding. There are two main methods of monitoring ICP.[1] The gold standard is a ventricular catheter. The catheter can be connected to standard pressure transducer which is 'zeroed' at the level of the external auditory meatus. Alternatively, catheters incorporating a solid-state microtransducer are available. Ventricular catheters measure global ICP and have the additional advantages of allowing periodic external calibration and therapeutic drainage of cerebrospinal fluid (CSF). Ventricular catheters are associated with significant complications, including haemorrhage, seizures and CSF infection (ventriculitis). Antibiotic-impregnated or silver-coated catheters are associated with lower infection rates. Fibreoptic and microtransducer (strain gauge) ICP monitoring devices can be sited in the brain parenchyma or subdural space via a cranial access device at the bedside or during neurosurgery. They cannot be recalibrated *in situ* but the zero and sensitivity drift over time is relatively small. Microtransducer-tipped ICP monitoring systems have minimal complication rates but measure localized pressure which may not represent true CSF pressure because of the presence of intraparenchymal pressure gradients in the injured brain.

Consensus guidance recommends that ICP should be monitored in all salvageable patients with severe TBI and an abnormal head CT scan, and in patients with a normal scan if two or more of the following features are present: age over 40 years, unilateral or bilateral motor posturing, or systolic blood pressure less than 90 mmHg.

ICP is a complex variable that, as well as quantifying ICP, allows calculation of cerebral perfusion pressure (CPP), detection of abnormal ICP waveforms and assessment of cerebrovascular reactivity (see below).

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. A low-frequency (2 MHz) pulsed wave ultrasound probe is used to insonate a basal cerebral vessel through an acoustic cranial window to derive cerebral blood flow velocity (FV) from the Doppler shift caused by red blood cells moving through the field of view. If the angle of insonation and diameter of the insonated vessel remain constant, changes in blood FV reflect changes in CBF. The TCD FV waveform resembles an arterial pulse wave 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 (SAH). FV greater than 120–140 cm/second is considered diagnostic but there is considerable inter-individual variation. In a recent study analysing 1877 TCD examinations, almost 40% of patients with clinical evidence of vasospasm had FVs that never exceeded 120 cm/second.[2] An increase in FV greater than 50 cm/second per 24 hours may be a superior diagnostic trigger for vasospasm than absolute FV. TCD may also be used to test cerebral autoregulatory reserve and identify individual-specific CPP targets after TBI.

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TCD is operator dependent and prone to some variability. Long-term recordings are limited by the need for accurate and immovable probe fixation, realistically restricting it to an intermittent monitoring technique.

Continuous quantitative CBF monitoring

Quantitative measurement of absolute regional CBF (rCBF) is possible using thermal diffusion flowmetry (TDF). 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. Although TDF catheters are available for clinical use there are limited clinical data using this technique. rCBF monitoring might be useful where there is a risk of focal cerebral ischaemia, such as in SAH or TBI.

Cerebrovascular autoregulation

Cerebrovascular autoregulation (CA) is frequently impaired after brain injury. Established methods of testing static and dynamic CA are interventional or intermittent and may be not be possible in critically ill patients.

Pressure reactivity index

Cerebrovascular pressure reactivity is a key component of CA. Monitoring and correlation of spontaneous slow waves in arterial blood pressure and ICP allows calculation of a pressure reactivity index (PRx) as a novel method of measuring CA. PRx can be monitored continuously and may be used to define individual CPP targets after TBI.[3] Oxygen reactivity, measured using brain tissue oxygen monitoring ($PtiO_2$), provides additional information about CA.

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

Retrograde cannulation of the internal jugular vein (IJV) allows measurement of jugular venous oxygen saturation (SjO_2). The 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. SjO_2 is a flow-weighted measure and reflects global cerebral oxygenation only if the dominant jugular bulb is cannulated, although in practice the right side is usually chosen. Intermittent samples aspirated from the catheter provide a 'snapshot' of cerebral oxygenation whereas fiberoptic catheters allow continuous monitoring and on-line display of SjO_2.

Normal SjO_2 is 55–75% and interpretation of changes is relatively straightforward (Table 1).[4] Jugular venous desaturation may indicate cerebral hypoperfusion secondary to decreased CPP or hypocapnea. However, since SjO_2 is a global measure, it is relatively insensitive to regional ischaemia. $SjvO_2$ >85% indicates relative hyperaemia or aterio-venous shunting and is frequently associated with poor outcome.

Interpretation of changes in jugular venous oxygen saturation

SjO_2	Relative blood flow and metabolic changes	Causes
Normal (55–75%)	CBF and $CMRO_2$ balanced	
Low (<50%)	↓ CBF or ↑ $CMRO_2$	↓ Blood pressure ↓ $PaCO_2$ ↓ PaO_2 ↑ ICP or ↓ CPP Seizures
High (>80%)	↑ CBF or ↓ $CMRO_2$	Cerebral hyperaemia Failure of oxygen utilization (mitochondrial failure) Arterio-venous shunting Brainstem death

CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate for oxygen; CPP, cerebral perfusion pressure; ICP, intracranial pressure; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; SjO_2, jugular venous oxygen saturation

Table 1

Brain tissue oxygen tension

Direct measurement of $PtiO_2$ is becoming the gold standard bedside measure of cerebral oxygenation.[5] 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. $PtiO_2$ is a complex and highly dynamic variable affected by several factors including PaO_2, $PaCO_2$, CBF, tissue barriers to diffusion, ICP and CPP.

$PtiO_2$ offers the potential for reliable and selective monitoring of critically perfused brain tissue, although it may miss global oxygenation changes. The normal range is 3.5–5.0 kPa. Absolute thresholds for abnormality are not well established but the ischaemic burden is likely to be related to duration as well as depth of cerebral hypoxia.

$PtiO_2$ >1.0 kPa is associated with critical reductions in rCBF and poor outcome after head injury. There is preliminary evidence to suggest that therapy directed to maintenance of $PtiO_2$ in addition to ICP and CPP is associated with reduced mortality after severe TBI[6] and this is currently being investigated in a large multi-centre study. However, many neurocritical care units already incorporate $PtiO_2$-directed therapy into treatment algorithms (Figure 1).

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. Earlier NIRS monitors were limited to

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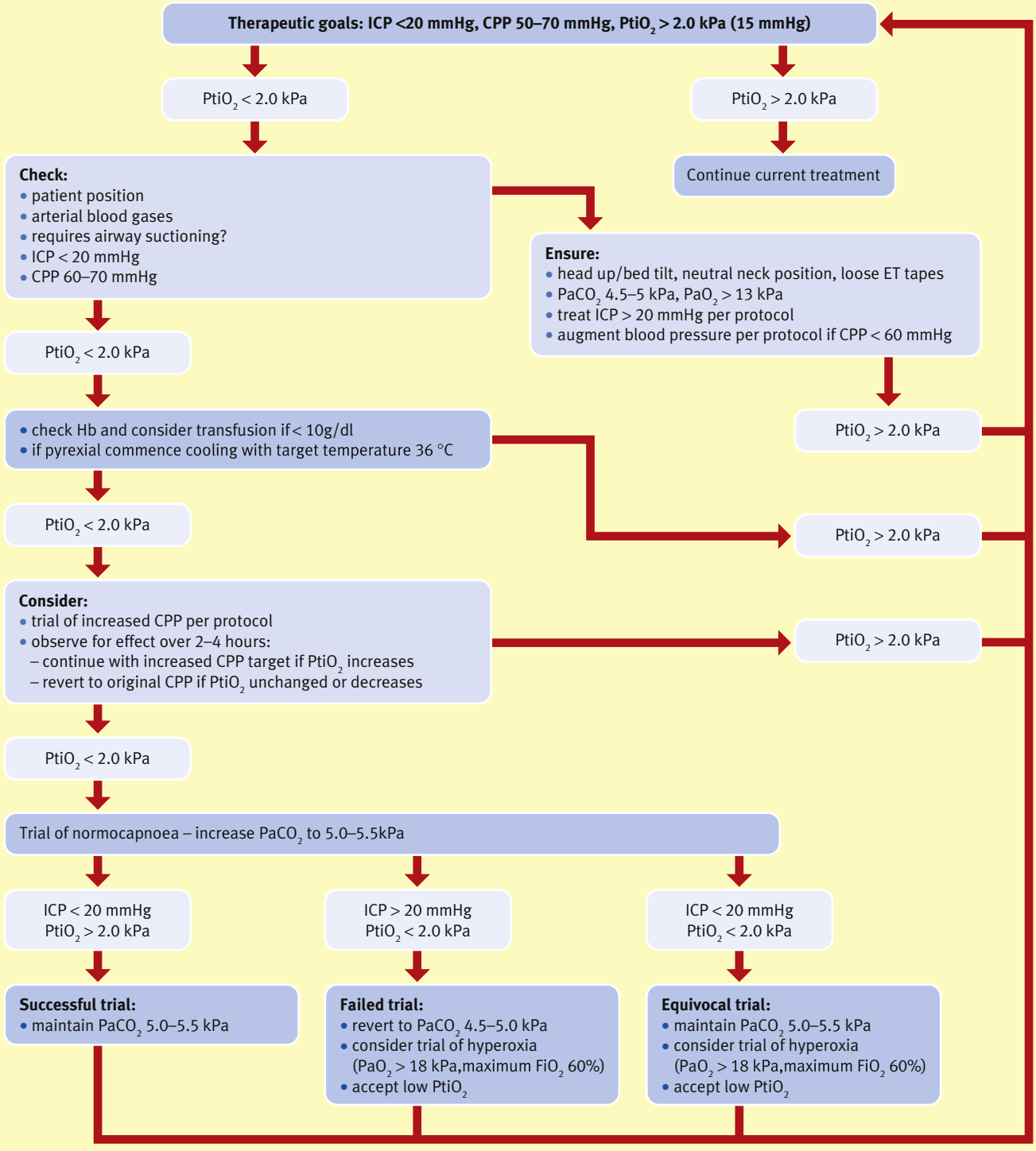
Brain tissue oxygen-guided management of severe head injury



BBB, blood–brain barrier; CBV, cerebral blood volume; CPP, cerebral perfusion pressure; ET, endotracheal tube; Hb, haemoglobin; ICP, intracranial pressure

Figure 1

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measuring changes in the concentrations of oxy- and deoxy-haemoglobin but more recent developments, using spatially resolved spectroscopy (SRS), provide an absolute measure of cerebral tissue oxygen saturation (ScO_2) that is a reliable and continuous measure of the balance between cerebral oxygen delivery and utilization. The utility of ScO_2 is confounded by the optical complexity of the injured brain and changes in systemic physiological variables. Clinical applications in brain-injured patients are limited by these issues which are often not appreciated by clinicians.

It is now possible to measure changes in the concentration of oxidized cytochrome c oxidase (CCO), the terminal complex of the mitochondrial electron transfer chain responsible for over 95% of oxygen metabolism. NIRS-derived CCO therefore offers the potential to assess cerebral cellular energy status, as well as oxygenation and haemodynamics, over multiple regions of interest.[7]

The potential for 'contamination' of the NIRS signal by extracranial tissue has been a major concern but modern SRS systems have high sensitivity and specificity for intracranial changes. There is wide intra- and inter-individual baseline variability in ScO_2. The 'normal' range lies between 60% and 75%, with a coefficient of variation for absolute baseline values of around 10%. This means that NIRS is best used as a trend monitor, and claims that absolute thresholds for cerebral ischaemia/hypoxia can be identified should currently be treated with caution.

There is substantial interest in the clinical application of NIRS bolstered by some recent evidence that NIRS-guided treatment can improve clinical outcome in specific clinical scenarios where the brain is 'at risk,' particularly during cardiopulmonary bypass. However, there is thus far no evidence to support the widespread application of NIRS as a monitor of cerebral well-being during routine surgical procedures or in critically ill patients on the ICU.

Cerebral microdialysis

Cerebral microdialysis (MD) allows bedside analysis of biochemical substances in brain tissue extracellular fluid (ECF) and provides unique information regarding the cellular metabolic environment.[8]

A miniature MD catheter is placed in brain tissue and diffusion of molecules across the semi-permeable dialysis membrane at its tip allows collection of substances from the brain ECF in the microdialysate. Commercial assays for glucose, lactate, pyruvate, glycerol and glutamate are available for use with a bedside analyzer (CMA Microdialysis, Solna, Sweden) and normal values have been established (Table 2). The MD 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 (Figure 2).

Cerebral MD monitors tissue hypoxia/ischaemia and cellular energy failure, and biochemical trends provide information that can be used to guide treatment decisions. MD can be used to evaluate the adequacy of cerebral perfusion and oxygenation, guide CPP management and assess the metabolic response to therapy. Because it measures changes at the cellular level, it has potential to detect cerebral hypoxia/ischaemia before changes can be identified by more conventional monitoring techniques or clinical status. Such predictive value of MD might offer substantial advantages over other monitoring techniques.

Continuous electroencephalography

The electroencephalogram (EEG) can be been used to monitor depth of sedation in brain-injured patients and to diagnose and guide therapy in those suffering from seizures or status epilepticus. Monitoring of continuous EEG (cEEG) is becoming more widespread because of an increasing awareness that non-convulsive seizures are common in patients with acute brain injury.[9] Similarly, cortical spreading depolarization is increasingly recognized as a cause of secondary brain injury and has been identified in up to 50% of patients after TBI. cEEG generates large quantities of data but improvements in data storage capability and the development of 'smart' systems to identify potential abnormalities are increasing user acceptability.

Cerebral microdialysis markers of secondary brain injury

Microdialysis variable	Monitor of	Notes
Glucose <1.5—2.0 mmol/litre	• hypoxia/ischaemia • reduced cerebral glucose supply • cerebral hyperglycolysis	• interpret in relation to serum glucose concentration
Lactate:pyruvate ratio (LPR) >20—25	• hypoxia/ischaemia • cellular redox state • reduced cerebral glucose supply	• most reliable biomarker of ischaemia • tissue hypoxic threshold for raised LPR not established
Glycerol >100 μmol/litre	• hypoxia/ischaemia • cell membrane degradation	• increased glycerol may also occur because of production of glycerol from glucose
Glutamate >15—20 μmol/litre	• hypoxia/ischaemia • excitotoxicty	• large inter- and intra-patient variability

Table 2

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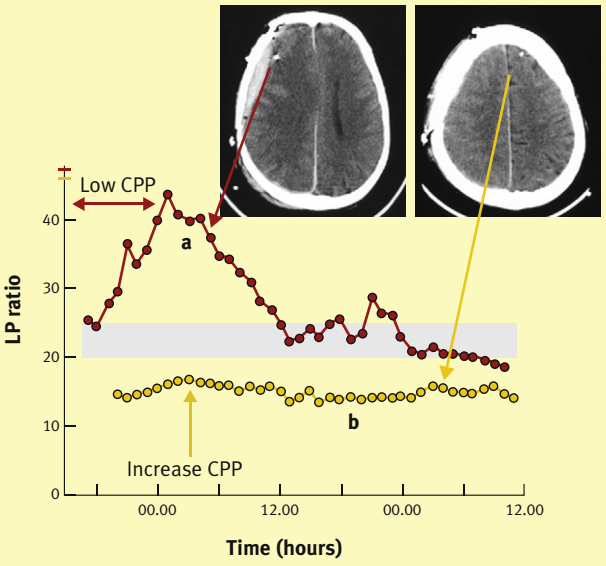
Changes in lactate: pyruvate ratio in 'at risk' (a) and normal (b) brain during a period of low and normal cerebral perfusion pressure



The normal range for lactate:pyruvate ratio is shown by the shaded area
Note the rise in lactate:pyruvate ratio in the 'at risk' tissue during a period of cerebral hypoperfusion
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Figure 2

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.[10] However, multimodal monitoring generates large and complex datasets and there is a need to develop systems that provide improved data presentation and analysis at the bedside. Mathematical models of the cerebral circulation and energy metabolism are being used in the research setting to interpret multimodal monitor-derived data and maximize their clinical usefulness. Such models 'analyse' measured variables and produce new data-streams, allowing the clinician to access simultaneously measured variables as well as model predictions of measured and unmeasured variables. In this way enhanced clinical information can be provided in real-time. ◆

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