Anaesthesia and Intensive Care Medicine 2017; 18: 224-229

Neuromonitoring

Malcolm Smith and Martin Smith

Department of Neuroanaesthesia and Neurocritical Care, The National Hospital for Neurology and Neurosurgery, University College London Hospitals

Malcolm E Smith MBChB FRCA is a Clinical Fellow in Neuroanaesthesia and Neurocritical Care at the National Hospital for Neurology and Neurosurgery, University College London Hospitals.

Conflicts of interest: none declared

Martin Smith MBBS FRCA FFICM is a Consultant and Honorary Professor in Neurocritical Care at the National Hospital for Neurology and Neurosurgery, University College London Hospitals.

Conflicts of interest: none declared.

MS is part funded by the National Institute for Health Research via the UCLH/UCL Comprehensive Biomedical Research Centre.

Corresponding author:
Dr Martin Smith
Box 30
The National Hospital for Neurology and Neurosurgery
University College London Hospitals
Queen Square
London
WC1N 3BG

Email: martin.smith@ucl.ac.uk

Abstract

Management of acute brain injury is based on a central concept that prevention of secondary hypoxic/ischaemic injury is associated with improved outcomes. While clinical assessment of neurological state remains fundamental to neuromonitoring, several techniques are 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 an individually tailored approach to patient management in which treatment decisions are guided by monitored changes in physiological variables rather than pre-defined, generic thresholds. Any impact of monitor-guided therapy on outcomes is entirely dependent on the threshold to initiative intervention and subsequent management in response to change in a particular monitored variable, and these remain undefined in many circumstances. This review describes current neuromonitoring techniques used during the critical care management of acute brain injury.

Keywords: Cerebral autoregulation; cerebral microdialysis; cerebral oxygenation; electroencephalography; intracranial pressure; multimodal neuromonitoring; near infrared spectroscopy; neurointensive care

Royal College of Anaesthetists CPD matrix: 2A04, 2F01, 3C00, 3F00

Learning objectives

After reading this article, you should be able to:

- identify the key intracranial physiological variables that can be monitored at the bedside
- understand the advantages and limitations of different neuromonitoring techniques
- understand the use of multimodality monitoring to guide individualised management in a critically ill brain injured patient

Acute brain injury (ABI) management is based on the central concept that prevention of secondary hypoxic/ischaemic injury is associated with improved outcomes. Optimisation of cerebral perfusion, oxygenation and metabolic status is therefore fundamental to the critical care management of ABI. Neuromonitoring allows assessment of multiple aspects of cerebral physiology, early detection of abnormalities and assessment of response to treatment, and can be used to guide individualised treatment strategies to minimise the risk of secondary hypoxic/ischaemic injury [1;2]. Several neuromonitoring techniques may be applied in clinical practice; some are widely available and well-established, whereas others are more novel and less well developed (table 1). The Neurocritical Care Society and European Society of Intensive Care Medicine have published consensus guidelines for the use of multimodality neuromonitoring [3].

Clinical examination

Clinical neurological assessment remains the cornerstone of neuromonitoring. The Glasgow coma scale (GCS) is an easy to use instrument for evaluating neurological status by recording best eye opening and verbal and motor responses to standardized verbal and physical stimuli (table 2) [4]. It provides a global assessment of consciousness, and identifies changes in neurological state by means of serial recording. Sedation and mechanical ventilation, while a mainstay of treatment in ABI, confound the assessment of GCS, and reduced intracranial compliance precludes sedation holds for neurological assessment. The main limitations of the GCS are that verbal responses are not assessable in intubated patients, brainstem function is not directly considered, and GCS 3 may cover a spectrum of brain injury severity. To overcome some of the problems, alternative scoring systems such as the Full Outline of UnResponsiveness (FOUR) score have been developed, but experience with them is limited compared with the GCS [3]. GCS is a global measure so it is important also to identify and document focal neurological deficits (limb weakness) and pupil responses. Infrared pupillometry provides an objective assessment of pupillary reactivity and may be superior to clinical assessment [1].

Intracranial Pressure

Two methods of monitoring intracranial pressure (ICP) are commonly used in clinical practice– ventricular catheters or micro-transducer systems (strain gauge or fibreoptic types) [5]. Ventricular

catheters are considered the gold standard as they measure global ICP. Advantages also include the possibility for recalibration during use and drainage of cerebrospinal fluid to treat intracranial hypertension. Ventricular catheters are associated with greater risks compared to micro-transducer devices, including intracranial haemorrhage, seizures and catheter-associated ventriculitis. Microtransducer devices are usually placed into brain parenchyma via a cranial access device, although subdural placement after craniotomy is an option. They measure localised ICP, but this correlates with ventricular pressure in most circumstances. The complication rate of intraparenchymal microtransducer devices, including infection, is very low. Although recalibration is not possible, zero drift is insignificant over the course of their clinical utility.

ICP monitoring guides targeted management to prevent or treat intracranial hypertension and allows monitoring and management of cerebral perfusion pressure (CPP) which is calculated as the difference between mean arterial blood pressure and ICP. For the accurate calculation of CPP, the arterial pressure transducer must be referenced at the same level as ICP (tragus of the ear) [5].

ICP monitoring is recommended in the management of severe traumatic brain injury (TBI) and increasingly used in other brain injury types, particularly poor grade aneurysmal subarachnoid haemorrhage (SAH) [1]. However, its ubiquity is not supported by clear evidence of improved outcomes from monitored-guided treatment strategies. A recent randomised controlled trial did not identify any difference in 6-month outcomes after TBI between patients randomised to management guided by ICP monitoring compared to clinical and radiological assessment in the absence of ICP monitoring. Because both treatment approaches provided satisfactory outcomes despite the absence of ICP monitoring in one, the results of this study challenge the established practice of maintaining ICP below a universal and arbitrary threshold. Individualised interpretation of ICP in association with other monitored variables might identify circumstances in which modestly elevated ICP might be cautiously accepted. One area of uncertainty is what, if any, action should be taken in response to increases in ICP in the context of normal brain oxygenation [5].

Autoregulatory reserve

Cerebral autoregulation is disturbed or abolished by intracranial pathology, leading to derangements in the relationships between regional cerebral blood flow (CBF) and metabolic demand, rendering the brain more susceptible to secondary ischaemic insults. The pressure reactivity index (PRx), calculated as the moving correlation coefficient of time-averaged data points of ICP and arterial blood pressure, provides a bedside assessment of cerebrovascular reactivity [2]. An inverse correlation between blood pressure and ICP, indicated by a negative value for PRx, represents normal cerebrovascular reactivity, whereas an increasingly positive PRx defines a continuum of an increasingly non-reactive cerebrovascular circulation when changes in blood pressure and ICP are in phase. After TBI, cerebrovascular reactivity varies with perfusion pressure and optimizes within a narrow range of CPP specific to an individual. CPP management within this 'optimal' range, guided by PRx monitoring, minimises the risks of excessive CPP on the one hand and of cerebral hypoperfusion and secondary ischaemic injury on the other.

Cerebral oxygenation

ICP/CPP monitoring provides no assessment of the adequacy of cerebral perfusion, and brain hypoxia/ischaemia can occur when ICP and CPP are within established thresholds for normality. Cerebral oxygenation monitoring provides information about the balance between cerebral oxygen delivery and utilisation, and therefore the adequacy of cerebral perfusion.

Jugular venous oxygenation saturation

Cannulation of the jugular bulb allows intermittent sampling of cerebral venous blood or continuous oxygen saturation measurement using a fibreoptic catheter. The normal range of $SjvO_2$ is 55% to 75%. $SjvO_2$ monitoring relies on the principle that oxygen delivery and supply mismatch will lead to a change in oxygen extraction and therefore in $SjvO_2$. Jugular venous desaturation can be related to low CPP, cerebral vasoconstriction secondary to hypocapnea, or increased oxygen consumption. $SjvO_2 \leq 50\%$ has been associated with worse outcome after TBI, but no interventional trials have confirmed a direct benefit of $SjvO_2$-directed therapy on outcome. $SjvO_2$ monitoring is a global, flow-weighted measure that may miss important regional ischaemia. Furthermore, falsely reassuring high values may be present in scenarios associated with hyperaemia or brain death when tissues are not metabolically active. $SjvO_2$ monitoring is dependent on technical aspects such as correct catheter

placement to exclude the extracranial circulation. It was the first bedside monitor of cerebral oxygenation and is of considerable historic interest but is being superseded by other methods of monitoring.

Brain tissue oxygen tension

Direct and continuous measurement of brain tissue oxygen tension ($PbtO_2$) using implantable catheters that operate analogous to Clark electrodes is becoming established as the gold standard method of cerebral oxygenation monitoring at the bedside [6]. $PbtO_2$ probes are placed in sub-cortical white matter usually in 'at risk' metabolically active tissue, such as specific vascular territories after SAH and peri-lesional locations in patients with intracerebral haematoma, although some experts argue for routine probe placement in normal appearing frontal region with an assumption that $PbtO_2$ changes in uninjured tissue are reflected globally in the brain.

$PbtO_2$ is a complex variable that may be influenced by global determinants of oxygen delivery such as PaO_2, $PaCO_2$, FiO_2, mean arterial pressure, haemoglobin, cardiac and respiratory function, as well as by brain specific factors including ICP, CPP, autoregulation, vasospasm and cerebral tissue oxygen gradients (which are often increased in the injured brain). Normal values for $PbtO_2$ lie between 2.6 and 4.6 kPa, with an ischaemic threshold in experimental conditions of 1.8 kPa. In the clinical setting low $PbtO_2$ is best considered within a range rather than as an absolute critical threshold, and ischaemia defined by both duration and depth of hypoxia [6].

Observational studies suggest outcome benefits of supplementing ICP/CPP-guided management with $PbtO_2$-directed therapy to maintain $PbtO_2 > 2.6$ kPa [7], but which intervention or combination of interventions should be used to normalize $PbtO_2$ is uncertain. The responsiveness of brain tissue hypoxia to a given intervention rather than the nature of the intervention appears to be the prognostic factor, with reversal of hypoxia being associated with reduced mortality. Many neurocritical care units incorporate $PbtO_2$-guided therapy into treatment protocols (figure 1).

Near-infrared spectroscopy

Near infrared spectroscopy (NIRS) is a non-invasive technique based on the transmission and absorption of near infrared light (700-950 nm) as it passes through tissue. Oxygenated and deoxygenated haemoglobin have characteristic and different absorption spectra in the near infrared, and their relative concentrations in tissue can be determined by their relative absorption of light at these wavelengths [8]. NIRS-based cerebral oximeters derive a scaled absolute haemoglobin concentration (i.e. the relative proportions of oxy- and deoxyhaemoglobin) from which an absolute regional cerebral tissue oxygen saturation ($rScO_2$) is calculated and displayed as a simple percentage value. Cerebral oximetry is increasingly used for brain monitoring during cardiac surgery, but a recent systematic review found only low-level evidence linking intraoperative desaturation with postoperative neurologic complications and insufficient evidence to conclude that interventions to prevent or treat reductions in $rScO_2$ are effective in preventing stroke or postoperative cognitive dysfunction. During carotid surgery, $rScO_2$ has similar accuracy for the detection of cerebral ischaemia compared to other monitoring modalities, and advantages in terms of simplicity. However, a precise $rScO_2$ 'threshold' to guide shunt placement or other neuroprotective interventions has not been defined. There are limited data on the use of NIRS in the management of brain injury and no outcome studies investigating NIRS-guided management. Emerging applications include the use of NIRS as a non-invasive monitor of cerebral autoregulation and, in the research setting, of cellular energy metabolism by monitoring changes in the oxidation status of oxidised cytochrome *c* oxidase, the final electron acceptor in the mitochondrial electron transport chain responsible for over 95% of oxygen metabolism [8].

The NIRS technique has several confounders including potential signal contamination from extracranial tissue. The presence of intracranial haematoma, cerebral oedema or subarachnoid blood might also invalidate some of the assumptions upon which NIRS algorithms are based, although this has been used to advantage in the development of a hand-held NIRS device to identify intracranial haematomas in pre-hospital environments.

Cerebral blood flow

Cerebral blood flow is a major determinant of oxygen delivery and can be altered after ABI. In association with impairment of autoregulatory reserves, this may cause or worsen secondary ischaemic injury.

Transcranial Doppler ultrasonography

Transcranial Doppler (TCD) is a technique that utilises ultrasound to assess blood flow velocity (FV) in basal cerebral vessels. The FV waveform is similar to a standard arterial waveform; systolic, diastolic and mean FV can be measured, and the pulsatility index (FVsystolic – Fvdiastolic / FVmean) derived as an assessment of distal cerebrovascular resistance [9].

TCD can be useful in patients with severe TBI to detect low CBF, for example, during intracranial hypertension, and to assess cerebral autoregulation [9], but is most widely used in the management of SAH in which regular assessments assist in the diagnosis and management of cerebral vasospasm-related delayed cerebral ischaemia [3]. FV values >120cm/s in the middle cerebral artery (MCA), or an increase of $\geq$50cm/s/day from baseline, indicate developing or established vasospasm. High FV may also be related to hyperaemia, and this can be delineated from vasospasm by calculation of the Lindegaard ratio (mean MCA FV/extracranial internal carotid artery FV). A ratio $\geq$ 3 is indicative of vasospasm, and > 6 of severe spasm. Although real-time and non-invasive, TCD requires a level of technical skill and provides only a measurement of relative changes rather than absolute CBF.

Thermal diffusion flowmetry

Thermal diffusion flowmetry (TDF) is an invasive, continuous and quantitative monitor of regional CBF. A commercial TDF catheter is available, but clinical data regarding ischemic thresholds or their correlation with clinical outcomes are lacking.

Cerebral microdialysis

Cerebral microdialysis (MD) allows monitoring of regional brain tissue biochemistry. A miniature MD catheter is placed into brain tissue and diffusion of molecules across a semi-permeable dialysis membrane at its tip allows collection and bedside analysis of the small solutes that pass from the brain extracellular fluid into the perfusate (dialysis fluid). Similar to $PbtO_2$ monitoring, the MD catheter is ideally placed in ‘at risk’ tissue. Glucose, lactate, pyruvate and the lactate:pyruvate (LP) ratio are the variables most commonly measured clinically; each is a marker of a particular cellular process

associated with glucose metabolism, hypoxia/ischaemia and cellular energy failure [10]. One advantage of MD over other bedside neuromonitoring modalities is its ability to differentiate ischaemic and non-ischaemic causes of cellular energy dysfunction. Elevated LP ratio (>40) combined with low brain glucose (<1.0 mmol/L) suggests severe hypoxia/ischaemia and is associated with poor outcomes after TBI. There is currently no evidence that interventions to normalise brain tissue biochemistry improve outcomes.

Electrophysiology

Electroencephalography (EEG) is used for diagnosis and treatment monitoring in patients with seizures and status epilepticus, and to provide dynamic information about brain function, including the presence of ischaemia, when clinical examination is limited [1]. Continuous EEG monitoring should be undertaken in patients with unexplained or persistent altered consciousness to exclude non-convulsive seizures which are common after ABI and associated with poor outcomes.

Spreading cortical depolarisations (SDs) are pathological events characterized by near-complete, sustained depolarization of neurons and astrocytes, and a potent cause of secondary brain injury. SDs can currently only be detected by electrode strips placed directly on the cortical surface (electrocorticography), limiting their applicability. Advances in scalp EEG and NIRS technology are likely to result in the development of non-invasive methods of monitoring SDs.

Multimodal monitoring

The diversity of neuromonitoring techniques partly reflects the fact that no single monitor is able to comprehensively report the breadth of pathophysiological changes after ABI. Despite the insights that individual devices provide, there is a paucity of evidence showing a reliable influence on clinical outcomes of monitor-guided treatment. Incorporating two or more techniques into a multimodal neuromonitoring strategy provides a more comprehensive picture of the (patho) physiology of the injured brain and its response to treatment (figure 2). The utilisation of ICP and $PbtO_2$ is a common and logical approach, aided by the availability of a single probe capable of monitoring both. Given the number of variables monitored and the complex interplay between them, computational analysis and

integration of data is an essential prerequisite for the presentation of user-friendly information at the bedside.

Multimodality neuromonitoring allows an individually tailored approach to patient management in which treatment decisions are guided by monitored changes in physiological variables rather than pre-defined, generic thresholds. Any impact of monitor-guided therapy on outcomes is entirely dependent on the thresholds to initiative intervention and subsequent management in response to changes in particular monitored variables, and these remain undefined in many circumstances. Further, which variables are surrogates of injury severity and which are modifiable targets for treatment remains unclear. High-quality clinical trials are required to establish whether adoption of a multimodal neuromonitoring strategy improves patient outcomes after ABI.

References

1. Citerio, G., Oddo, M., & Taccone, F. S. Recommendations for the use of multimodal monitoring in the neurointensive care unit. Current Opinion in Critical Care 2015; 21: 113–9
2. Makarenko S, Griesdale DE, Gooderham P, Sekhon MS. Multimodal neuromonitoring for traumatic brain injury: A shift towards individualized therapy. J Clin Neurosci 2016; 26: 8-13
3. Le Roux, P., Menon, D. K., Citerio et al. The International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: A List of Recommendations and Additional Conclusions: A Statement for Healthcare Professionals From the Neurocritical Care Society and the European Society of Intensive Care Medicine. Neurocritical Care 2014; 21: 282-96
4. Teasdale G, Maas A, Lecky F, et al. The Glasgow Coma Scale at 40 years: standing the test of time. Lancet Neurol 2014; 13: 844-54
5. Kirkman MA, Smith M. Intracranial pressure monitoring, cerebral perfusion pressure estimation, and ICP/CPP-guided therapy: a standard of care or optional extra after brain injury? Br J Anaesth. 2014; 112: 35-46
6. Kirkman, M. A. Brain Oxygenation Monitoring. Anesthesiology Clinics 2016; 34: 537–56

7. Nangunoori R, Maloney-Wilensky E, Stiefel M, et al. Brain tissue oxygen-based therapy and outcome after severe traumatic brain injury: a systematic literature review. Neurocrit Care 2012; 17: 131-8
8. Ghosh A, Elwell C, Smith M. Review article: cerebral near-infrared spectroscopy in adults: a work in progress. Anesth Analg 2012; 115: 1373-83
9. Bouzat P, Oddo M, Payen JF. Transcranial Doppler after traumatic brain injury: is there a role? Curr Opin Crit Care 2014; 20: 153-60
10. Hutchinson PJ, Jalloh I, Helmy A, et al. Consensus statement from the 2014 International Microdialysis Forum. Intensive Care Med 2015; 41: 1517-28

Figure 1

Management protocol for brain tissue oxygen-guided therapy after acute brain injury

CPP, cerebral perfusion pressure; EEG, electroencephalography; FiO_2, fractional inspired oxygen; ICP, intracranial pressure; $PtiO_2$, brain tissue pO_2.

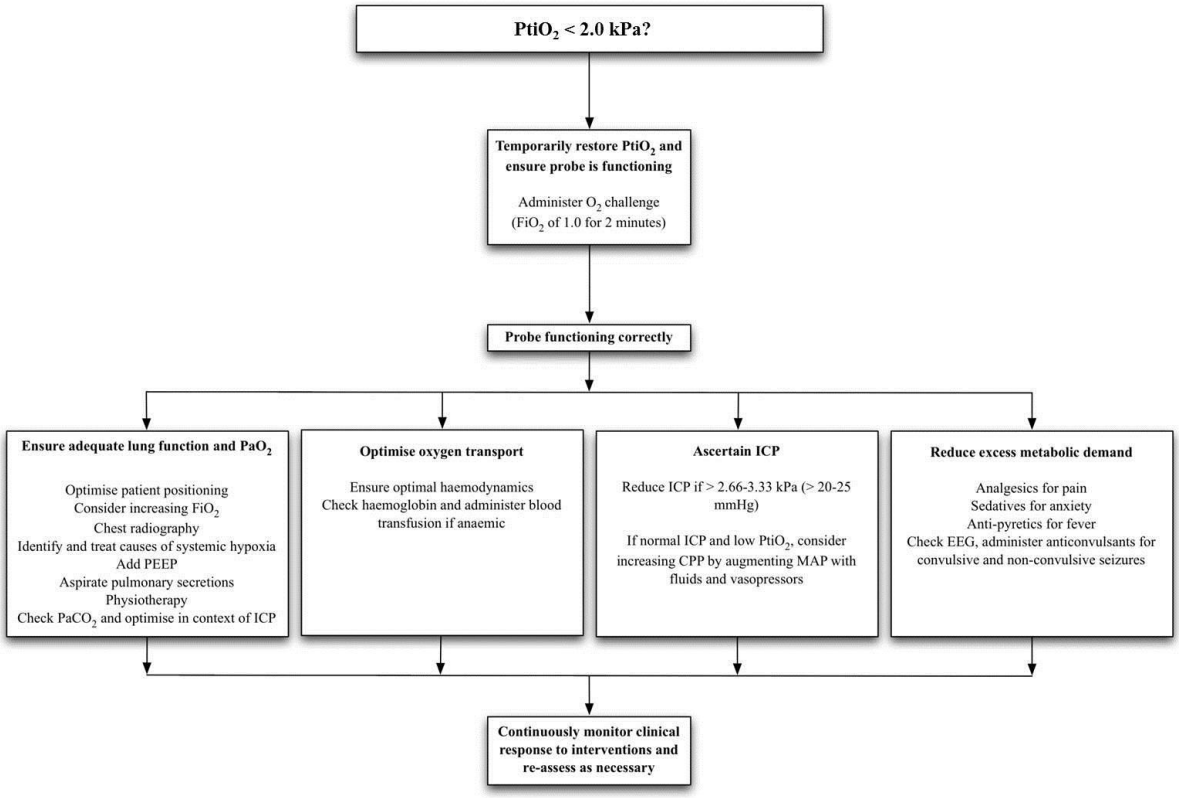

Figure 2

Multimodality signature of transient intracranial hypertension

Note that the increase in ICP and reduction in CPP is accompanied by a reduction in $PbtO_2$ brain extracellular fluid glucose and increases in lactate. Brain oxygen and metabolism recover as ICP and CPP return to baseline.

CPP, cerebral perfusion pressure; ICP, intracranial pressure; MD, cerebral microdialysis; $PbtO_2$, brain tissue PO_2

(Reproduced with permission from Elsevier – Lazardis and Robertson, Neurosurg Clin N Am 2016; 27: 509-17)

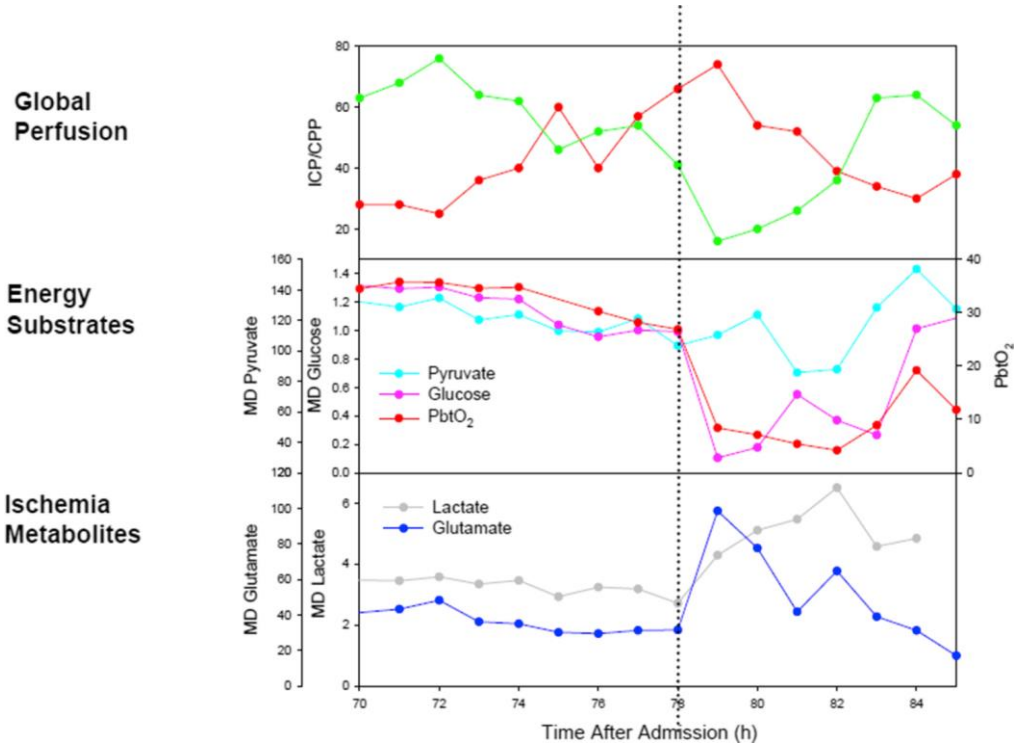

Table 1

Advantages and disadvantages of bedside neuromonitoring techniques

Technique	Advantages	Disadvantages
Intracranial pressure		
Ventricular catheter	• Gold standard • Measures global pressure • Therapeutic drainage of CSF • *In-vivo* calibration	• Placement technically difficult • Risk of haemorrhage • Risk of infection
Microsensor	• Intraparenchymal/subdural placement • Easy to place with low procedural complication rate • Low infection risk	• *In-vivo* calibration not possible • Measures localized pressure
Transcranial Doppler	• Non-invasive • Real time with good temporal resolution	• Measures relative rather than absolute cerebral blood flow • Operator dependent • Failure rate of 5-10% (absent acoustic window)
Jugular venous oximetry	• Assesses balance between oxygen delivery (blood flow) and demand (metabolism) • Easy to perform	• Global and insensitive to regional changes • Risk of vein thrombosis, haematoma, carotid puncture
Brain tissue pO_2	• Bedside gold standard for brain oxygenation monitoring • Assesses balance between oxygen delivery (CBF) and demand (metabolism) • Continuous	• Invasive • Measures regional oxygen tension so utility dependent on probe location

Near infrared spectroscopy	• Non-invasive • Real time • Assessment of regional cerebral oxygenation over multiple regions of interest	• Dependent on manufacturers algorithms • Signals affected by extracerebral tissue
Microdialysis	• Measurement of local brain tissue biochemistry • Early detection of hypoxic/ischaemic injury • Monitor of cellular bioenergetic distress	• Focal measure • Thresholds for abnormality uncertain
Electroencephalography	• Non-invasive • Real time • Correlates with ischaemic and metabolic changes • Assessment of non-convulsive seizures/status epilepticus	• Skilled interpretation required • Affected by anaesthetic/sedative agents

Table 2

The Glasgow coma score

Eye opening (E)

1 None
2 To pressure
3 To speech
4 Spontaneous

Verbal response (V)

1 None
2 Sounds
3 Words
4 Confused
5 Orientated

Best motor response (M)

1 None
2 Extension
3 Abnormal flexion
4 Normal flexion (withdrawal)
5 Localising
6 Obeying commands

Note: *Each component of the GCS is assessed in turn using standardised physical and verbal stimuli. The score for each component, rather than only the sum score, should be reported. In intubated patients or those with a tracheostomy verbal response should be recorded as* V_T*, and not assigned a score of 1.*