The Role of Multimodal Invasive Monitoring in Acute Traumatic Brain Injury

Christos Lazaridis, MD[a,*], Claudia S. Robertson, MD[b]

KEYWORDS

• Intracranial pressure • Cerebral perfusion pressure • Brain tissue oxygen • Lactate/pyruvate ratio • Pressure reactivity index • Neuromonitoring

KEY POINTS

- Secondary injury is characterized by a cascade of biochemical, cellular, and molecular events, often compounded by the effects of systemic insults, such as hypotension and hypoxemia.
- ICP, CPP, PRx, CBF, $PbtO_2$, LPR, and electrophysiologic data are parts of an integrated, patient-specific approach.
- Incorporation of patient demographics, brain imaging, and multimodality data can lead to the creation of individualized patient trajectories and physiologic latent states.

INTRODUCTION

This article reviews the role of modalities that directly monitor the brain parenchyma in patients with severe traumatic brain injury (TBI). The physiology monitored involves compartmental and perfusion pressures, tissue oxygenation and metabolism, quantitative blood flow, pressure autoregulation, and electrophysiology. There are several proposed roles for this multimodality monitoring (MMM):

- Track, prevent, and treat the cascade of secondary brain injury (SBI), known to occur after primary TBI at the tissue and cell level.
- Monitor the neurologically injured, often heavily sedated, patient who may have no informative clinical examination. This takes into account the idea that irreversible brain injury may have occurred by the time clinical examination changes are noted at the bedside.
- Integrate clinical examination, neuroimaging, and MMM data into a composite, patient-specific and dynamic picture. Based on this, aim toward targeted management that optimally balances the timing and the benefit/risk ratio of medical-surgical interventions.
- Apply protocolized, pathophysiology-driven intensive care.
- Use as a prognostic marker.
- Understand the pathophysiologic mechanisms involved in SBI to develop preventive and abortive therapies, and to inform future clinical trials.

PATHOPHYSIOLOGIC RATIONALE

Secondary injury is characterized by a cascade of biochemical, cellular, and molecular events, including the endogenous evolution of cerebral damage and the effects of systemic insults, such as hypotension and hypoxemia.[1,2] Based on

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[a] Division of Neurocritical Care, Department of Neurology, Baylor College of Medicine Medical Center, Baylor College of Medicine, McNair Campus, 7200 Cambridge Street, 9th Floor, MS: NB302, Houston, TX 77030, USA;
[b] Department of Neurosurgery, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA
* Corresponding author.
E-mail address: lazaridi@bcm.edu

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experimental TBI models the mechanisms producing SBI can be grouped as (1) those associated with ischemia, excitotoxicity, energy failure, and resultant cell death cascades; (2) secondary cerebral swelling; (3) axonal injury; and (4) inflammation and regeneration.[1] At the core of these mechanisms a resultant tissue hypoxia and/or dysoxia is believed to underlie a state of cellular energy failure.

Oxidative metabolism is based on convective oxygen transport from ambient air to blood capillaries, with hemoglobin and erythrocytes as vehicles; oxygen diffusion from erythrocytes in the capillaries to mitochondria in the cells; and oxygen reduction in the mitochondria via the electron transport chain.[3] Failure in any of these three steps could result in similar clinical manifestations; nevertheless, targeted and differentiated management requires distinguishing the actual mechanisms involved. The main types, causes, and neuromonitoring profiles of tissue hypoxia are summarized in **Table 1**. In clinical practice, it is difficult to determine the exact nature of tissue hypoxia without integration of data from MMM and neuroimaging.[4]

Among the different types of hypoxia, ischemia has long been regarded as the central cause of SBI. Studies in the 1970s demonstrated low cerebral blood flow (CBF) in the first few hours after injury, and postmortem examination of patients with fatal head injuries provided evidence of ischemic necrosis.[5,6] These findings led to management strategies directed at augmenting cerebral perfusion, blood flow, and oxygen delivery. These strategies, however, have not reliably proven to positively impact clinical outcomes, although they are known to potentially carry significant morbidity. The finding of a high rate of acute respiratory distress syndrome in patients treated with hemodynamic augmentation as an antiischemia regimen is a prime example.[7,8]

There are further mechanistic objections to the current model of ischemic hypoxia as the predominant mechanism.[9] It seems that except for cases of extremely low cerebral perfusion pressure (CPP) the presence of ischemia, using a variety of techniques, has remained elusive.[5] Recent observations have highlighted alternative mechanisms: dysperfusion hypoxia as a result of increased mean diffusion length from erythrocytes to mitochondria caused by intracellular or interstitial edema,[10] uncoupling hypoxia caused by intrinsic mitochondrial dysfunction,[11] and shunt hypoxia in the forms of capillary transit time heterogeneity and thoroughfare channel shunt flow.[12,13] Increases in capillary transit time heterogeneity were shown to reduce the maximum achievable oxygen extraction fraction (OEF) for a given CBF and tissue oxygen tension. This overview provides the context for the discussion that follows on the different components of MMM.

Table 1
Types of brain hypoxia in TBI

Type	Pathophysiology	Neuromonitoring Profile
Ischemic	Inadequate CBF	↓CBF, ↓$PbtO_2$, ↑LPR (high lactate/low pyruvate), ↑OEF
Low extraction	Low arterial Po_2 (hypoxemic hypoxia) Low hemoglobin concentration (anemic hypoxia) Low half-saturation tension P50 (high-affinity hypoxia)	≅CBF, ↓$PbtO_2$, ↑LPR (high lactate/low pyruvate), ≅OEF
Shunt	Arteriovenous shunting (microvascular shunt)	↑CBF, ≅$PbtO_2$, ↑LPR (high lactate/low pyruvate), ↓OEF
Dysperfusion	Diffusion barrier (intracellular or interstitial edema)	≅CBF, ≅$PbtO_2$, ↑LPR (high lactate/low pyruvate), ↓OEF
Uncoupling	Mitochondrial dysfunction	≅CBF, ≅$PbtO_2$, ↑LPR (high lactate/normal pyruvate), ↓OEF
Hypermetabolic	Increased demand	↑CBF, ↓$PbtO_2$, ↑LPR (high lactate/low pyruvate), ↑OEF

Abbreviations: ≅, no change or in either direction; CBF, cerebral blood flow; LPR, lactate/pyruvate ratio; OEF, oxygen extraction fraction; P50, oxygen half-saturation of hemoglobin; $PbtO_2$, partial brain tissue oxygen tension; Po_2, arterial oxygen tension.