

# Cerebral Near-Infrared Spectroscopy Use in Neonates: Current Perspectives

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**Abstract:** Conventional clinical practice in the neonatal intensive care unit (NICU) often fails to actively monitor the brain, relying on reactive strategies and imprecise risk indicators. The introduction of Near-Infrared Spectroscopy (NIRS) enhances current approaches to brain monitoring, offering non-invasive, real-time, continuous, and tissue-specific measures of oxygen saturation. NIRS leverages the physics of light to provide a comprehensive evaluation of oxygen delivery and consumption. This review covers the principles of NIRS, normative values for cerebral oximetry, and its applications in various clinical scenarios. Current clinical applications of NIRS span diverse areas, including intraventricular hemorrhage, white matter injury, anemia, congenital heart disease, and hypoxic-ischemic encephalopathy (HIE). NIRS demonstrates its potential in predicting and preventing adverse outcomes, particularly in optimizing cerebral oxygenation during cardiac surgery and guiding respiratory support in neonates. Key highlights of this review include the role of NIRS for the detection of cerebral hypoxia, even when other monitors do not show signs of clinical deterioration, a discussion of new methods for quantifying cerebral autoregulation and the connection to brain injury, and the potential utility NIRS monitoring offers for critically ill infants, such as those with congenital heart disease. The comprehensive insights provided by NIRS, if translated effectively into clinical practice, have the potential to improve the care and outcomes of neonates in the NICU.

**Keywords:** NIRS, neonatal, brain injury, intraventricular hemorrhage, white matter injury, hypoxic ischemic encephalopathy, seizures, congenital heart disease

## Introduction

Avoidance of brain injury and prediction of neurodevelopmental outcomes remain some of the highest priorities for parents and providers of infants admitted to the neonatal ICU (NICU). Infants are susceptible to distinct forms of brain injury; this includes intraventricular hemorrhage (IVH),<sup>1</sup> cerebellar hemorrhage (CH), and white matter injury<sup>2</sup> for preterm infants and hypoxic ischemic injury in term infants who experienced perinatal ischemic events. However, despite the importance placed on these outcomes, in standard clinical practice, the brain often goes unmonitored during the NICU stay, with the notable exception of EEG monitoring when seizures are suspected.

Typical clinical practice involves screening for injury that has already occurred in populations of at-risk infants, judged primarily on fixed and imprecise risk indicators (eg, gestational age, sepsis) with little personalization. While head ultrasound screening is practically universal in preterm infants, it provides little information beyond gross anatomic injury.<sup>3-5</sup> Term equivalent head imaging has been well described in the literature but is limited by poor positive predictive value.<sup>3,6-8</sup> MR imaging in HIE is less controversial, and although systems for scoring injury have gradually demonstrated improved predictive performance, the simultaneous increase in complexity of interpretation has meant limited translation to daily clinical practice.<sup>9-11</sup> Most importantly, imaging (regardless of modality) is a *reactive* strategy, employed after injury has already occurred when there is little chance to prevent or mitigate adverse impact.

Near-infrared spectroscopy (NIRS) monitors provide non-invasive, real-time, continuous, tissue-specific measures of oxygen saturation. Unlike pulse oximetry (SpO<sub>2</sub>), these devices measure oxygen saturation in all vascular compartments (arterial, venous, capillary) which provides an advantageous evaluation of oxygen delivery and consumption. While NIRS has been available for nearly two decades, interest and utilization for the NICU population have only begun to increase recently.

The work of many clinical studies and several large, randomized trials provide greater information about how best to use the information provided by the monitor in a *proactive* rather than *reactive* strategy.

For this review, neonatal NIRS literature from the last 20 years was reviewed with a special focus on clinical trials, reference studies, and large observational studies with brain injury as the primary outcome. This review summarizes the underlying physics principles of the NIRS monitor, examines the types and meaning of data which can be obtained from these devices, examines the role of NIRS in many important areas of NICU clinical care, and summarizes the results of recent large, randomized trials.

## NIRS Principles

NIRS leverages the physics of light to measure tissue oxygen saturation. Each monitor consists of a display unit with one or more data channels, each attached to a patient sensor. Sensors contain an emitter, which produces multiple wave lengths of light in the red and near-infrared frequency bands, and two receivers which are located at different distances from the emitter.<sup>12–14</sup>

While hemoglobin light absorption is a foundational element of both NIRS and pulse oximetry, there are key differences in how the devices are implemented, resulting in significant clinical ramifications. As light is transmitted through tissue, it is scattered, reflected, and absorbed.<sup>15</sup> Hemoglobin is a chromophore, meaning that it is a compound which absorbs light in a predictable fashion. Importantly for both NIRS and pulse oximetry, different oxidative states of hemoglobin (ie, oxy- and de-oxyhemoglobin) have distinctive absorption patterns.<sup>16</sup> Oxyhemoglobin absorbs more infrared light and less red light, when compared to deoxyhemoglobin. Thus, if a known quantity of specific wavelengths of light pass through a tissue, the ratio of absorption at each wavelength can be used to calculate oxygen saturation in the tissue under the sensor.<sup>17–19</sup> Although typically between 700 and 800 nm, the number of discrete wavelengths of light utilized by devices varies by manufacturer (INVOS 730, 810nm; ForeSight 690, 780, 805, 850 nm; EQUANOX 730, 760, 810, 880nm; NIRO 735, 810, 850 nm; OxyPrem 760, 805, 870 nm).<sup>20,21</sup>

Pulse oximetry evaluates absorption as light is linearly transmitted through a tissue, passing from one side to the other. With each cardiac cycle, the volume of arterial blood rapidly increases then decreases, generating a cyclical change in oxyhemoglobin absorption set against an unchanging absorption background of venous blood, skin, muscle, and bone.<sup>22</sup> In contrast, the NIRS sensor lies flat on the surface of the skin and two or more receivers detect changes in absorption as photons return back to the sensor following a curved path.<sup>23</sup> It is not pulse synchronized and thus measures oxygenation in arterial, venous, and capillary beds simultaneously. Given that only 30% of blood is intra-arterial at any given time, the measured values represent a 30% to 70% arterial to venous-weighted estimate and approximate a mixed-venous saturation (SvO<sub>2</sub>).<sup>24</sup> NIRS has been extensively validated against other measurements of cerebral blood flow including transcranial Doppler ultrasound,<sup>25</sup> xenon-enhanced CT,<sup>26</sup> and MRI.<sup>27</sup>

NIRS monitoring necessarily involves the use of a sensor applied directly to the skin. As with any medical device, safety is an important priority. Fortunately, the prevailing experience is that these devices can be safely used even in smallest of infants. In the SafeBoosC-II trial, 16/166 (14%) infants experienced temporary red marks at the site of the sensor, with no further adverse events reported.<sup>28</sup> In the much larger SafeBoosC-III trial, 7/772 (1%) infants experienced sensor-related skin issues.<sup>29</sup> All other reported adverse events were common complications of prematurity and were not different between the intervention and control groups. To avoid skin-related sensor issues, some recommend frequent (every 12–24 hours) replacement of the sensor and the use of underlying clear barrier dressings.<sup>14</sup>

## Normative or Reference Values for Cerebral Oximetry

Clinical accessibility and application of NIRS requires information about the expected range of values experienced by neonates. As NIRS is a mixed-venous measure, values from pulse oximetry cannot be used and new normative values must be separately established including tissue-specific patterns (eg, cerebral vs renal).

### Preterm Infants

The largest reference dataset in neonates was published in 2015 by Alderliesten et al<sup>30</sup> and is based on cerebral NIRS values obtained in the first 72 hours after birth in 999 very low birth weight (VLBW) infants. In this cross-sectional sample, the median cerebral saturation was 65% with the 95% confidence interval spanning 55–85%. This range has been

widely adopted in clinical practice and formed the basis for at least two clinical trials. A similar reference dataset of cerebral NIRS values in the delivery room was published in 2013 by Pichler et al.<sup>31</sup> Similar to the pulse oximetry curves developed for targeted oxygen saturation management during resuscitation,<sup>32</sup> cerebral saturations rise rapidly over the first minutes of life and stabilize by approximately 10 minutes.

The impact of other clinical factors becomes apparent when looking at longitudinal cerebral oxygenation extending further into the NICU stay. Several studies<sup>33,34</sup> have demonstrated a steady decline in cerebral regional oxygen saturation (rSO<sub>2</sub>) over the first 6–8 weeks following birth, which closely parallels anemia of prematurity over the same period. Injury also has an impact, with persistently lower cerebral saturations following intraventricular hemorrhage, an effect lasting for at least two months.<sup>34</sup>

## Term Infants

Fewer studies have examined similar longitudinal trends in term neonates. In contrast to preterm infants, cerebral saturations for term infants are higher, likely reflective of a lower metabolic demand in a more developed brain. In one report of 26 normal newborns, mean cerebral rSO<sub>2</sub> was approximately 80% soon after birth, falling slightly over the first few days.<sup>35</sup> Infants with perinatal asphyxia seem to exhibit the opposite pattern, with lower initial cerebral rSO<sub>2</sub> then rising over the first few days.<sup>36</sup>

## Cerebral Autoregulation

The concept of cerebral autoregulation was first described by Claassen in 1961, who conceived of the idea that the cerebral vasculature maintains homeostasis of cerebral blood flow, despite fluctuations in cardiac output.<sup>37</sup> This has been summarized in the now classic sigmoidal “autoregulatory curve” where constant cerebral blood flow is maintained across a wide range of blood pressures, with rapid changes at the limits of autoregulation. The cerebral NIRS signal is an indirect measure of cerebral blood flow and thus can be used as a proxy for more invasive measures of cerebral blood when investigating cerebral autoregulatory function in neonates.

## Time Domain Methods

Several different strategies have been employed to quantify autoregulation. The most straightforward approach evaluates correlation between the mean arterial blood pressure and the cerebral rSO<sub>2</sub>. When autoregulation is intact, the correlation between these two measures should be either zero or negative. In the method pioneered at University College London,<sup>38</sup> the correlations between cerebral NIRS and mean arterial blood pressure are analyzed in serial 10-minute windows and assigned to “bins” corresponding to the mean blood pressure during the window. After analysis is complete, the mean correlation value for each of the blood pressure “bin” is calculated. Intact autoregulation would demonstrate zero or negative correlations across the middle range of blood pressures, with increasing or even positive values at the extremes.<sup>39–41</sup> This method can also be used to identify the “optimal” blood pressure, defined as the mean arterial blood pressure at which the most negative correlation is found.<sup>42</sup> Increased time spent with blood pressure outside the optimal range has been associated with an increased burden of brain injury in neonates.<sup>43,44</sup>

## Coherence Methods

Coherence is a mathematical technique for assessing correlation in the frequency domain, essentially the degree to which low-frequency oscillations in blood pressure are dampened before transmission to the brain. Intact and functioning autoregulation should reshape blood supply to match the metabolic demands of the brain, thus little or no coherence should be seen.<sup>45</sup> Several groups<sup>46,47</sup> have applied this method to neonates, using similar 10-min windows to calculate the value of coherence with a range between 0 (no correlation) and 1 (complete correlation). Autoregulatory function is then assessed by evaluating the time spent with coherence above a pre-defined threshold, described as a “pressure passive” state by Soul et al.<sup>46</sup> Although there is some disagreement about the selection of the threshold,<sup>39,45,48</sup> multiple studies have demonstrated that increased pressure passivity (increase time spent above coherence threshold) is associated with smaller, sicker preterm infants<sup>46</sup> and with adverse outcomes in infants suffering from HIE.<sup>47</sup>

## Transfer Function Methods

One additional method that has been used to quantify autoregulation builds on the concepts of coherence and frequency domain analysis. There are well-described low-frequency oscillations in cardiovascular signals, most notably at 0.1 Hz (once every ten seconds) often called the Mayer wave frequency.<sup>49</sup> The oscillations at 0.1 Hz (and other frequencies) are thought to be the manifestation of intrinsic and extrinsic vascular autoregulation, influenced by the autonomic nervous system and local metabolic demands, amongst others.<sup>50–52</sup> Autoregulatory mechanisms should dampen these oscillations as they pass from the central circulation into the cerebral circulation. A method called transfer function analysis<sup>53,54</sup> can quantify this dampening curve across the frequency spectrum. This method has been used to study autoregulation in neonates, finding both a developmental effect, with increased dampening capacity as gestational age increases and a loss of dampening in the setting of IVH.<sup>55,56</sup>

Although this technology is far from utilization in clinical practice, an improved ability to quantify autoregulation will help to better explain mechanisms of brain injury and could eventually be employed at the bedside. Real-time measures of autoregulation could guide hemodynamic management or periods where handling should be avoided (eg, pressure passive periods).

## Clinical Applications of NIRS

### IVH

Intraventricular hemorrhage is perhaps the most studied outcome in neonatal NIRS literature, and these investigations have revealed new insights into the genesis and longitudinal course of injury. First, cerebral NIRS monitoring has provided evidence of a biphasic pattern of injury, with early hyperperfusion and later tissue hypoxia. In at least two reports,<sup>57,58</sup> infants later diagnosed with IVH were found to have markedly elevated cerebral saturations during the period where the bleeding was presumed to occur, likely the effect of a stunned brain with reduced oxygen extraction and hyperemia from impaired cerebral autoregulation. However, after that acute period, infants with IVH have profoundly lower cerebral saturation, an effect which worsens with increasing grade and lasts for weeks to months in duration.<sup>34,59</sup>

In addition to acute changes in cerebral saturation during catastrophic hemorrhage, the NIRS monitor can detect the longitudinal burden of cerebral hypoxia experienced during the cardiorespiratory instability common in the first week of life for VLBW infants. Multiple reports<sup>60–62</sup> have shown a strong relationship between an increasing burden of cerebral hypoxia and increasing risk of IVH. More recently, advanced machine learning techniques have been applied<sup>63</sup> to the cerebral NIRS signal, quantifying the impact of prolonged periodic desaturations in a powerful prediction model for subsequent IVH. These results underscore the value of cerebral NIRS monitoring to identify and avoid acute and chronic changes in cerebral saturation, which may not be detectable with other monitoring devices.

### White Matter Injury

Intraventricular hemorrhage is an acute form of brain injury resulting from disruption in cerebral blood supply and/or autoregulation. In contrast, white matter injury is an indolent disease which takes weeks to become radiographically apparent and is strongly linked to chronic hypoxia and inflammation,<sup>64,65</sup> the course of which was succinctly described by Volpe in the “encephalopathy of prematurity” framework.<sup>66,67</sup> The cumulative impact of intermittent and partial prolonged hypoxia, particularly in the periventricular white matter where the short penetrating arteries provide insufficient blood supply,<sup>68</sup> creates an environmental milieu primed for injury. Although the exact threshold of the critical fractional tissue oxygen extraction (FTOE), beyond which metabolism switches from aerobic to anaerobic, is not precisely known, studies of adults suggest that it is approximately 0.60.<sup>69</sup> Many studies of preterm infants have identified a significantly elevated FTOE late in the NICU course for preterm infants, as high as 0.40–0.50.<sup>34,70,71</sup> When baseline extraction operates near to this limit, it is not surprising that common systemic desaturation events associated with apnea of prematurity or the stress of concurrent illness (such as necrotizing enterocolitis or sepsis) would exceed that threshold and expose the brain to ischemia, initiating, and/or perpetuating the cascade of preoligodendrocyte injury and loss that characterizes white matter injury.

## Anemia

Neonates admitted to the NICU have more than one potential mechanism of anemia—anemia of prematurity, physiologic anemia, and phlebotomy loss. In each case, it leads to the common result of lost oxygen carrying capacity. A strong correlation between anemia and cerebral desaturation or increased cerebral oxygen extraction has been described in multiple observational studies.<sup>71–74</sup> There is evidence that lower cerebral saturations are associated with worse anemia and transfusion restores cerebral oxygenation.<sup>75–78</sup> However, potentially unwarranted transfusions are associated with an increased risk of ROP.<sup>79</sup> It is important to note that pulse oximetry is of limited value in the setting of anemia, with essentially no differences between low and high hemoglobin groups.<sup>80,81</sup> This stands in contrast to the utility of cerebral NIRS which can detect both severity of anemia<sup>71,75,80,81</sup> and may provide more information about ROP risk.<sup>82</sup> Although additional study is needed, NIRS holds significant promise as a tool in transfusion decision-making.

## Congenital Heart Disease

Near-infrared spectroscopy also plays a role in the monitoring of infants with congenital heart disease (CHD), providing beneficial data during the peri-operative period to preempt acute decompensation, guide interventions, and predict neurodevelopmental outcomes.

For infants with hypoplastic left heart syndrome (HLHS), standard monitoring plus NIRS have been linked to reduced pre-surgical mechanical ventilation requirements and improved evaluation of surgical timing.<sup>83,84</sup> Furthermore, lower preoperative cerebral rSO<sub>2</sub> values are associated with poorer outcomes after cardiac surgery and can predict need for extracorporeal membrane oxygenation.<sup>85,86</sup> NIRS monitoring has also proven beneficial in infants with aortic coarctation and transposition of the great arteries (TGA) to guide necessity and timing of interventions.<sup>87</sup> Specifically in infants with TGA, cerebral NIRS values improve after successful balloon atrial septostomy, providing insight on the response to intervention and underscoring the value of NIRS monitoring in perioperative planning and anticipation of long-term outcomes.<sup>88</sup>

The use of intra-operative NIRS monitoring may also lead to decreased post-operative neurologic sequelae and decreased length of stay by providing additional information to optimize cerebral oxygenation during cardiopulmonary bypass.<sup>89</sup> The validity of intra-operative NIRS monitoring was confirmed by its strong correlation with direct mixed venous blood sampling during cardiac surgery.<sup>90</sup>

Throughout the peri-operative period, NIRS monitoring offers prognostic insights into long-term neurodevelopmental outcome, with consistent patterns of low cerebral rSO<sub>2</sub> values or with minimal variability for patients with adverse neurodevelopmental indices.<sup>91–94</sup> Although the exact pathophysiology which links low cerebral saturation and adverse neurodevelopmental outcome is unclear, at least two mechanisms may provide explanation: low cerebral saturations may reflect ischemia and neuronal loss or alternatively, chronic insufficient delivery of oxygen to meet metabolic needs may interfere with the expected trajectory of brain development and growth without causing direct injury. For example, in infants with HLHS, prolonged rSO<sub>2</sub> values <45% were associated with new or worsening ischemic injury on post-operative MRI, and minimum intra-operative rSO<sub>2</sub> values were positively correlated with minimum measures of total intracranial volume, total brain volume, and white matter.<sup>95,96</sup>

## Hypoxic Ischemic Encephalopathy (HIE)

The capability of cerebral oxygen monitoring to provide information about both oxygen utilization and the cerebral autoregulation makes it potentially of great clinical and research value in the setting of HIE. Perinatal ischemia has wide-ranging deleterious effects on the brain. Beyond direct neuronal damage from the initial ischemic insult, this injury fundamentally alters cerebral metabolism. Cerebral NIRS provides a measure of oxygen delivery and consumption, where both low and high values of cerebral saturations are meaningful; exceptionally high values are predictive of severe injury<sup>97–99</sup> while low values may indicate cardiovascular insufficiency or seizures.<sup>100,101</sup> As with preterm infants, FTOE can provide valuable insights into adequate oxygen delivery to the brain in the setting of HIE, potentially indicating the need for inotropic support, blood transfusion, or increased respiratory support. To date, only one study has examined how NIRS monitoring might improve HIE outcomes, finding that the maintenance of blood pressure within NIRS-derived optimal values is associated with fewer MRI markers of brain injury.<sup>44</sup>



There has been significant study of the prognostic capabilities of NIRS for HIE infants. While there are many different technologies that provide prognostic value in the setting of HIE, the immediacy and ease of access to NIRS distinguishes it from aEEG/EEG, where predictive power is reached at 48 hours,<sup>102</sup> and MRI which is not typically performed until 3–4 days after birth. In a number of published studies, NIRS measures alone were predictive of brain injury and/or adverse outcomes.<sup>43,98,103–105</sup> The predictive ability of NIRS increased when used in combination with other monitoring technologies.<sup>106–109</sup>

## Silent Hypoxia and Respiratory Management

Pulse oximetry remains the mainstay of systemic saturation monitoring in neonates and plays a significant role in the approach to respiratory support, including the provision of supplemental oxygen. Numerous studies have sought to identify target oxygen saturation ranges which maximize survival while minimizing the risk of developing ROP with great success. However, pulse oximetry has significant limitations including a lack of end-organ specificity and limited insight into the consumption of oxygen, resulting in the potential for delivery-consumption mismatch. Silent or occult hypoxia may occur at the tissue level (ie, the brain) even during periods of normal systemic oxygenation on pulse oximetry. NIRS has the capacity to overcome these limitations, identifying tissue-level hypoxia far earlier than pulse oximetry.<sup>110,111</sup> Pulse oximetry is also a lagging indicator of response to intervention.<sup>112</sup>

Recently, this phenomenon in neonates has been studied in detail, demonstrating that silent cerebral hypoxia is common in neonates and paradoxically increases at lower levels of respiratory support.<sup>113</sup> These findings raise significant questions about the optimal management of less acutely ill infants later in the NICU course with regard to level of respiratory support, transfusion thresholds, and other interventions which might influence oxygen carrying capacity.

## Clinical Trials of NIRS in the NICU

Although most clinical NIRS research in neonates is observational, there have been two major clinical trials comparing standard of care monitoring to standard monitoring plus NIRS monitoring in the delivery room (COSGOD) and early NICU course (SafeBoosC) for VLBW infants. Both studies completed smaller phase-II pilot studies before subsequent large multicenter randomized trials and used similar endpoints of death or severe brain injury.

In the Cerebral regional tissue Oxygen Saturation to Guide Oxygen Delivery (COSGOD) Phase II trial, 60 premature infants were placed on a NIRS monitor immediately after birth. The display was blinded at random in half of the infants and their resuscitation proceeded using standard of care monitoring (targeted SpO<sub>2</sub>). For those infants where the NIRS display was randomized to be visible, PEEP and FiO<sub>2</sub> were manipulated following a standardized treatment algorithm. This strategy led to a relative reduction of cerebral hypoxia by 55% compared to SpO<sub>2</sub> alone.<sup>114</sup> A larger Phase III trial of 607 infants was conducted at 11 centers in Europe and Canada using a similar study design, although in this study, only infants randomized to the NIRS arm had sensors placed (ie, no blinded displays). Survival without brain injury was 4.3% greater in the NIRS arm of the study, however this failed to reach statistical significance.<sup>115</sup>

The SAFEGuarding the Brain Of Our Smallest Children (SafeBoosC) trials followed the same paradigm of the COSGOD trials; in the phase II SafeBoosC study, 166 infants were placed on cerebral NIRS monitors, half of which were blinded. For those where the monitor was visible, infants received one or more treatments according to a standardized treatment algorithm when cerebral saturations were persistently less than the defined threshold. The NIRS visible group had a threefold reduction in hypoxia burden (58 vs 16%), lower mortality (25 vs 14%), and less severe brain injury on ultrasound (23 vs 13%).<sup>28</sup> A phase III trial followed using the same study design and included 1601 infants from 70 centers in 17 countries. As with the COSGOD trial, only the standard of care plus NIRS monitoring group was placed on NIRS monitors in the phase III trial. The primary outcome of death or severe brain injury on ultrasound was not statistically different between the two groups (35.2 vs 34%,  $p = 0.64$ ).<sup>29</sup>

## Conclusion and the Future of NIRS in the NICU

NIRS has emerged as a beneficial non-invasive tool in the management of infants with a wide range of risk factors for brain injury and adverse neurodevelopmental outcome, including prematurity, HIE, and congenital heart disease. A considerable body of evidence supports NIRS as a monitoring tool to identify cerebral hypoxia not detected using other monitoring devices. NIRS also

provides a correlation between cerebral hypoxia and a range of brain injury, a mechanistic understanding of cerebral autoregulation in the normal and injured state, and a method to assess response to interventions. However, despite the strength of these data, they have not yet translated to clinical trials showing a definitive benefit in outcomes, which must be considered in the ethical context of adding monitoring to guide interventions in a vulnerable population. A limitation of this review is a general lack of NIRS clinical trials in the neonatal population; outside of SafeBoosC and COSGOD, there have been none. As the next generation of clinical trials is developed, it is important for the community of researchers to reach consensus on a target population and target intervention to enable strong multicenter trials with rapid potential for translation to clinical practice. We propose several strategies for further development of NIRS to improve the neurologic outcomes of neonates.

1. Future devices should incorporate multiple sources of data. This will allow real-time calculation of autoregulation in the clinical setting (as opposed to research calculations made after hospital discharge) and develop insights from multiple organ systems.
2. Clinical trials should be narrowly focused on infants at the highest risk for injury.
3. The relationship between cerebral hypoxia and brain injury requires further exploration. The definition of a simple threshold is likely insufficient—duration, frequency, timing, and degree of hypoxia may be more relevant and should be intentionally incorporated in study designs.
4. An international consensus guideline which defines a) which infants should be monitored, b) how long monitoring should last, and c) what goals should be accomplished (eg, avoid cerebral hypoxia) is urgently needed.

With continued investigations, further refinement of NIRS monitoring and intervention strategies will strengthen the benefit of its use in the clinical setting to optimize neonatal neurocritical care.

## Disclosure

Dr. Vesoulis has received compensation from Medtronic for consulting and educational services. Dr Valerie Chock reports grants from NICHD/NIH, grants from Research Institute at Nationwide Children's Hospital/Abbott, grants from Washington University in St. Louis, outside the submitted work. The authors report no other conflicts of interest in this work.

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