Neurological Monitoring for Congenital Heart Surgery

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The incidence of neurological complications after pediatric cardiac surgery ranges from 2% to 25%. The causes are multifactorial and include preoperative brain malformations, perioperative hypoxemia and low cardiac output states, sequelae of cardiopulmonary bypass, and deep hypothermic circulatory arrest. Neurological monitoring devices are readily available and the anesthesiologist can now monitor the brain during pediatric cardiac surgery. In this review we discuss near-infrared cerebral oximetry, transcranial Doppler ultrasound, and electroencephalographic monitors for use during congenital heart surgery. After review of the basic principles of each monitoring modality, we discuss their uses during pediatric heart surgery. We present evidence that multimodal neurological monitoring in conjunction with a treatment algorithm may improve neurological outcome for patients undergoing congenital heart surgery and present one such algorithm.

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The reported incidence of neurological complications after heart surgery in children ranges from 2% to 25% (1–4). A retrospective report of 706 children undergoing heart surgery found that 2.3% had acute neurological complications (3). In contrast to adults undergoing heart surgery with cardiopulmonary bypass (CPB), who develop postoperative neurological sequelae that are largely embolic in nature, the etiology of neurological dysfunction in children is multifactorial (5–8). Techniques such as deep hypothermic circulatory arrest (DHCA) and low-flow bypass, which have allowed successful correction of complex cardiac defects in neonates and infants, may themselves contribute to neurological damage in this vulnerable population (9,10). Furthermore, the details of the conduct of CPB contribute to potential brain injury after CPB (7). Such details include arterial blood gas (ABG) management: α-stat (not correcting ABG for temperature) versus pH stat (correcting ABG for temperature), hematocrit on bypass, and the rate and extent of cooling and rewarming.

When assessing neurological outcome in children after open-heart surgery, clinicians and investigators often assume that these children are neurologically normal before surgery. However, central nervous system (CNS) malformations are more frequent in patients with congenital heart disease, specifically those with hypoplastic left heart syndrome (HLHS), where brain dysgenesis may approach 30% (6,11). In addition, children with chromosomal defects, particularly those with microdeletions of chromosome 22, have a more frequent incidence of CNS abnormalities, as do neonates with coarctation of aorta (12,13). Hence, these developmental brain disturbances contribute to the incidence of brain injury in the perioperative setting.

Although vital organs are routinely monitored during congenital heart surgery with CPB, the brain is not typically monitored. Any strategy for prevention or rescue from adverse neurological events during CPB must start with the routine use of neurological monitoring systems that allow easy, reliable, and reproducible detection of these events. Despite the availability of several modalities of monitoring for almost 20 years, in our opinion neurological monitoring during CPB remains in its infancy. In this article, we review the currently available modalities for neurological monitoring during congenital heart surgery in children and present preliminary evidence that such monitoring improves neurological outcome in this high-risk population.

Electroencephalographic Monitors

The electroencephalogram (EEG) during cardiac surgery in infants with CPB has been well characterized

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(14). The standard EEG using between 2–16 channels has been used in congenital heart surgery (4). The major disadvantage of using scalp EEG is the requirement for a dedicated technician to place the electrodes and interpret the EEG, which is neither practical nor cost-effective in busy congenital heart surgery centers. The EEG provides a rough guide to anesthetic depth and can be used to determine electrocerebral silence before using DHCA (15). The EEG is affected by several factors, including anesthetics, temperature, and CPB. Impracticalities of the use of an intraoperative EEG include electrical signal interference, complexity of placement and difficulty in interpretation. Newer devices using processed EEG technology are more user-friendly.

The Bispectral Index (BIS) monitor (Aspect Medical Systems, Newton, MA) is one device approved by the United States Food and Drug Administration (FDA) currently used to assess the depth of anesthesia. BIS sensor electrodes are applied to the forehead and temple, producing a frontal-temporal montage that connects to a processing unit. The device is easy to use; electrode placement is not difficult, and the monitor requires no calibration or warm up time. Via a proprietary algorithm of Aspect Corporation based on the normal adult EEG, BIS uses Fourier transformation and bispectral analysis of a one-channel processed EEG pattern to compute a single number, the BIS (16). This index ranges from 0 (isoelectric EEG) to 100 (awake) with mean awake values in the 90–100 range in adults, infants, and children (17). The real-time unprocessed EEG wave form of the BIS can be used to recognize EEG burst suppression or electrical silence, which could be useful in alerting the anesthesiologist of the need to continue cooling before the initiation of DHCA. Even this use has limitations; rarely, for example, an isoelectric EEG in the newborn infant may not correlate with a lack of all cortical activity (18). The BIS is subject to motion artifact, electromyographic activity, and radiofrequency interference from electrical equipment in the operating room. BIS values are anesthetic-specific; for example, the BIS value in children at 1 MAC halothane is 56, versus 36 for 1 MAC isoflurane, although at awakening the values are identical (19).

During CPB, hemodilution and temperature changes alter pharmacokinetics and pharmacodynamics of opioid anesthetics, which can lead to awareness under anesthesia (20). The overall incidence of awareness in adults undergoing cardiac surgery varies from 1.1% (21) to 23%, which is more than that reported for general surgical procedures (22,23). Although there are no documented reports of awareness under anesthesia in children undergoing heart surgery, BIS or other EEG monitoring is potentially useful to detect a level of anesthetic depth associated with awareness. In a cohort of children undergoing open-heart surgery with an anesthetic tailored for "fast-tracking," BIS increased during rewarming, a period considered at risk for awareness under anesthesia (24). However, in this study, and in a similar study in infants <1 year of age, BIS did not correlate with stress hormone levels, a surrogate for light levels of anesthesia, nor with plasma fentanyl levels (25). Additional studies are needed to determine the utility of the BIS monitor in infants and children undergoing CPB with or without DHCA.

The Patient State Index (PSI) (Physiometrix, Inc, N. Billerica, MA) is a FDA-approved 4-channel processed EEG monitor also based on the adult EEG, which may have less dependence on the anesthetic used than the BIS (26). Comparison of the BIS and PSI in adults revealed a wide variation in individual values associated with loss of consciousness during induction of anesthesia, and there was a significant incidence of erroneous classification of the patient being unconscious when they could follow commands (27). The BIS and PSI demonstrated only about 70% accuracy in predicting loss or return of consciousness. Other drawbacks of the PSI include the larger area necessary for sensor placement on the front of the forehead compared with the BIS, which competes with other neurological monitors, such as near-infrared cerebral oximeter.

It is difficult to recommend EEG monitoring for routine use in infants and children undergoing pediatric CPB at this time. Reasons include the paucity of pediatric studies, particularly with the PSI, and the finding that EEG changes were responsible for only 5% of abnormal neurological monitor findings in a large pediatric study (4), and that these abnormal readings on the EEG did not appear to correlate with adverse postoperative outcomes.

Monitors of Cerebral Oxygenation

Near-Infrared Spectroscopy

Near-infrared spectroscopy (NIRS) is a noninvasive optical technique used to monitor brain tissue oxygenation. Most devices use 2–4 wavelengths of near-infrared light at 700–1000 nm, where the iron-porphyrin complexes of oxygenated and deoxygenated hemoglobin have distinct absorption spectra (28–30). Commercially available devices measure the concentrations of oxyhemoglobin and de-oxyhemoglobin and determine cerebral oxygen saturation. The cerebral oximeter probe is placed on the forehead below the hairline. A light emitting diode emits near-infrared light, which passes through a banana-shaped tissue volume of approximately 10 mL in the frontal cerebral cortex to 2 or 3 detectors placed 3–5 cm from the emitter. The terminology used to describe cerebral oxygen saturation as measured by NIRS varies, depending on the method and device used (2 versus 4

wavelengths, spatially resolved versus frequency domain spectroscopy). These terms include ScO_2 for cerebral cortical oxygen saturation, TOI for tissue oxygenation index, HbO_2 for oxygenated hemoglobin signal, and rSO_2i for regional cerebral saturation index. In this review, rSO_2i will be used to designate cerebral oxygen saturation for clarity and also because it is the designation used for the only FDA-approved device. Anatomical models predict that 75% of the cerebral blood volume in the light path is venous and 25% is arterial. Watzman et al. (31) attempted to verify this index in children with congenital heart disease by measuring jugular venous bulb and arterial saturations and comparing them with cerebral saturation measured with frequency-domain NIRS. The actual ratio in patients varied widely but averaged 85:15 venous:arterial blood ratio.

The proximal detector in the Somanetics INVOS system (Somanetics, Inc. Troy, MI) detects light absorbed by extracranial tissues and is subtracted from the total signal (detected by the distal electrode), leaving only the intracranial contribution. The pediatric model (INVOS 5100) is designed for patients weighing 4–40 kg and uses a different algorithm that takes into account the thinner skull and extracranial tissues of infants and children (32). This device is FDA-approved for use in children, is compact, simple to use, and requires no warm up. It uses two near-infrared wavelengths: 730 and 810 nm. The INVOS processor displays a numerical value; the rSO_2i, which is the ratio of oxyhemoglobin to total hemoglobin in the light path. The rSO_2i is reported as a percentage on a scale from 15% to 95%. A cerebral blood volume index, representing the total hemoglobin in the light path, can also be calculated. This measurement may be used as an estimate of cerebral blood volume, although currently it can be used for research purposes only because it is not FDA approved owing to insufficient data correlating it with other measurements of cerebral blood volume.

The NIRO 300 (Hamamatsu Photonics, Hamamatsu, Japan) uses spatially resolved spectrophotometry to calculate absolute concentrations of oxygenated hemoglobin and total hemoglobin rather than hemoglobin saturations. Theoretically, this could lead to improved accuracy; however, this device is not FDA approved. Prototype cerebral oximeters using frequency-domain technology are under development and have the potential to measure absolute rather than calculated rSO_2i (28).

Direct comparison of the INVOS 4100 and NIRO 300 in healthy anesthetized adults during normocapnia, hypocapnia, and hypercapnia revealed a positive correlation for data points in both absolute values, and change from baseline values ($r = 0.58$ and 0.85, respectively) (25). Bland-Altman comparison of the 2 devices demonstrated that although the correlation was good when all 60 values were combined, there may be large differences by individual comparison (33). The INVOS 5100 pediatric sensor tends to read significantly higher (by 14% ± 8%) than the NIRO 300 4 cm interoptode sensor (pediatric equivalent) (31). Regardless of the device used, it is important to note that all devices measure combined arterial and venous blood oxygen saturation and the values obtained will therefore not be identical to measured jugular venous bulb oxygen saturation ($SjvO_2$). Therefore, maneuvers that increase arterial oxygen saturation, e.g., increasing FIO_2, will increase cerebral oxygenation as measured by these devices, but may not change the $SjvO_2$. These devices are best used as trend monitors, with each patient serving as his or her own control, and a 20% relative decrease from baseline may be a clinically important change in the Somanetics system (4). Newer software versions continuously calculate and display the relative change from baseline and allow labeling of significant events, such as the start of CPB or DHCA.

In an attempt to validate the noninvasive measurement of rSO_2i in children with congenital heart disease $SjvO_2$ and rSO_2i have been compared. In one study of 40 infants and children undergoing congenital heart surgery or cardiac catheterization, the correlation for paired measurements was poor except for infants less than 1 year of age (34). In another study of 30 infants and children undergoing cardiac catheterization, an excellent correlation ($r = 0.93$) was found (35). Greeley et al. (36) derived cerebral metabolic rate for oxygen consumption ($CMRO_2$) from cerebral blood flow measurements calculated using ^{133}Xe washout technology and jugular venous and arterial oxygen saturation measurements in infants and children undergoing congenital heart surgery. They compared $CMRO_2$ to changes in oxygenated hemoglobin (HbO_2) signal measured by NIRS and demonstrated important parallels. After DHCA, cerebral blood flow and $CMRO_2$ were depressed, whereas HbO_2 was increased when compared with patients undergoing continuous bypass without DHCA. Recovery from DHCA produced low $CMRO_2$ and a limited ability to use oxygen, resulting in an increased HbO_2 signal.

Near-infrared light is also absorbed by Cu^{++} atoms of cytochrome a,a_3, making NIRS a potentially useful monitor of cerebral intraneuronal oxygen delivery by assessing the redox state of cytochrome molecules in the electron chain of the mitochondria. The Hamamatsu NIRO 300 can measure cytochrome redox state. However, the light absorption by hemoglobin is an order of magnitude greater than that of cytochrome a,a_3, and the cytochrome a,a_3 absorption signal is highly dependent on hematocrit, bringing into question the validity of these readings (37).

Animal Models with Relevance to Pediatric Cardiac Surgery

Animal models have well known limitations; however, important data have been generated using such

models that support the use of NIRS as a monitor that measures meaningful changes in brain oxygenation that reflect disturbances in neuronal functioning. Low rSO_2i can lead to cell dysfunction, cell death, and by extension, poor neurological outcome in these models. These studies cannot be done in humans for obvious reasons. In a model of graded cerebral hypoxemia at normothermia in neonatal piglets with a baseline rSO_2i of 68%, Kurth et al. (38) determined that the threshold for half of the animals to experience an increased cerebral lactate concentration was a rSO_2i of 44%. Minor EEG changes occurred in half of the animals at an rSO_2i of 42%, major EEG change at an rSO_2i of 37%, and decreased brain adenosine triphosphate in half of the animals at an rSO_2i of 33%. rSO_2i also strongly correlated with sagittal sinus oxygen saturation, cerebral blood flow measured by laser Doppler flowmetry, and Pao_2.

In piglet models of DHCA, Sakamoto et al. (39,40) used NIRS under varying conditions: differing hematocrits (20% versus 30%) and temperatures (15°C versus 25°C), pH-stat versus α-stat blood gas management, and varying lengths of DHCA (60–100 minutes). They determined that the nadir of rSO_2i occurred sooner at higher temperatures, lower hematocrits, and with α-stat blood gas management. The time spent at the nadir of rSO_2i correlated with neurological outcome determined both behaviorally and on neuropathologic examination: all animals with rSO_2i nadir time <25 minutes were free of any evidence of neurological injury.

In another piglet model, NIRS detected cerebral desaturation when the superior vena cava (SVC) was partially or totally occluded during CPB. No other measurements were affected by this maneuver: arterial blood pressure, heart rate, SVC pressure measurements in the case of partial occlusion, or mixed venous oxygen saturation measured in the bypass circuit. Cerebral desaturation may develop in infants if they have SVC obstruction during SVC cannulation for bypass or in patients undergoing cavopulmonary anastomosis, where the SVC is often partially occluded (41).

Clinical Data in Pediatric Cardiac Surgery

Baseline preoperative rSO_2i as measured by a frequency-domain oximeter varies with different cardiac lesions (29). The baseline rSO_2i breathing room air is approximately 70% in acyanotic patients without large left to right intracardiac shunts; rSO_2i for cyanotic patients is usually 40%–60%. Ramamoorthy et al. (42) exposed neonates with unrepaired HLHS to two different inspired gas mixtures to control pulmonary overcirculation. Those treated with 17% inspired oxygen had rSO_2i averaging 53%, and those who received 21% oxygen and 3% inspired CO_2 had rSO_2i averaging 68%; however, there were no significant differences in the arterial saturation between groups. Significant decreases in rSO_2i occur during periods of hemodynamic instability or arterial desaturation (43). Increases in rSO_2i occur during cooling and vary with the rate of temperature change. Improvements in cardiac output and oxygen delivery result in an increase in rSO_2i. Characteristic changes in cerebral oxygenation occur during CPB in children with or without DHCA (Fig. 1) (43).

Predictably, rSO_2i decreases during DHCA to a nadir approximately 60%–70% (relative change) less than baseline values obtained prebypass and the nadir is reached at 20–40 minutes, after which there is no further decrease (44). At this point it appears that there is no additional oxygen uptake by the brain. Interestingly, this time period correlates with clinical and experimental studies suggesting that 45 minutes is the safe duration for circulatory arrest (7). Reperfusion results in an increase in rSO_2i to levels seen at full bypass flow before DHCA. Andropoulos et al. (45) used bilateral NIRS to assess changes in rSO_2i during regional low-flow cerebral perfusion (RLFP) in neonatal patients undergoing aortic arch reconstruction. RLFP is a technique in which the brain is perfused via the right innominate artery, providing unilateral cerebral perfusion. During periods of perfusion via both carotid arteries (i.e., before and after RLFP, whether on or off bypass), bilateral rSO_2i values agreed closely, whereas during RLFP the mean rSO_2i was 6.3% lower on the left side, and about half of the patients experienced an absolute difference of more than 10% in rSO_2i values during RLFP, suggesting bilateral monitoring is useful during unilateral perfusion techniques, but not necessary when both carotid arteries are perfused under normal circumstances.

Recent studies using α-stat blood gas management for simpler surgeries (i.e., ventricular septal defect or tetralogy of Fallot repair) and mild or moderate hypothermia of 25°C–35°C have demonstrated a lower rSO_2i in the patients undergoing bypass with colder temperatures (25°C–28°C) versus warmer bypass at 32°C–35°C (46,47). This suggests that the cerebral vasoconstriction from decreased $Paco_2$ at the lower temperature decreases oxygen delivery more than the effect of cooling to decrease $CMRO_2$, resulting in lower rSO_2i. These studies demonstrate that NIRS may play a role in more moderate hypothermia because approximately 30% of patients in these studies experienced significant cerebral oxygen desaturation (absolute rSO_2i $<50\%$, or more than 20% relative decrease from baseline). Finally, in a study of cyanotic patients with aortopulmonary collaterals undergoing hypothermic CPB and randomized to α-stat versus pH stat blood gas management, rSO_2i was significantly lower in the α-stat group (48).

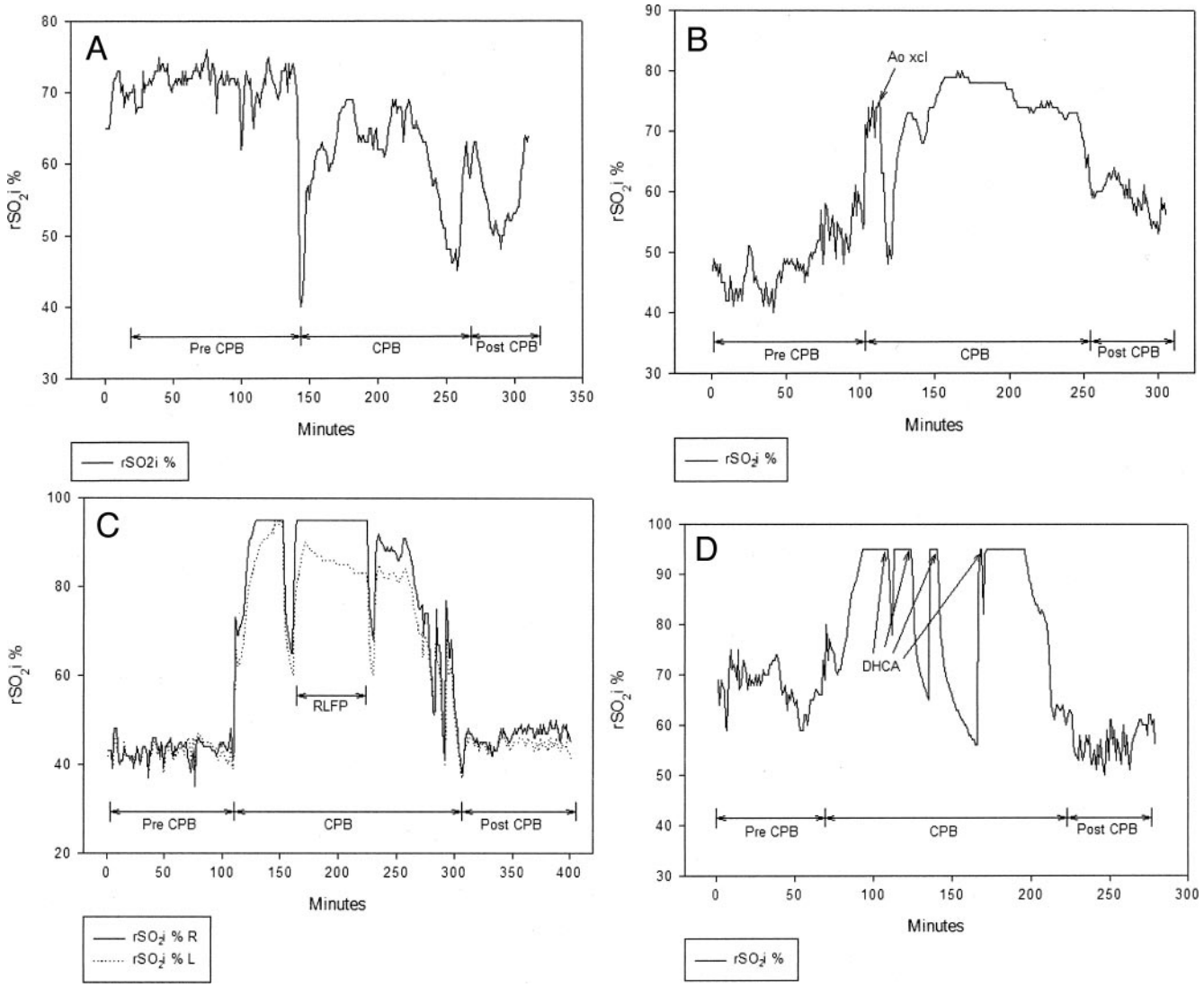

Figure 1. Typical changes in regional cerebral oxygen saturation index (rSO_2i) in congenital heart surgery with cardiopulmonary bypass (CPB) with a) mild hypothermia, b) moderate hypothermia, c) deep hypothermia with regional low-flow cerebral perfusion (RLFP), and d) deep hypothermic circulatory arrest (DHCA). pH stat blood gas management was used in all cases. Cases b–d had slow cooling over 20–30 min, and hematocrit 25%–30% when the lowest temperature was reached. Hemofiltration and transfusion were used to achieve hematocrit 40%–45% before separation from bypass for cases b–d. Figure 1a: rSO_2i in a 13-yr-old undergoing right ventricle to pulmonary artery conduit replacement at 32°C with hematocrit 22% on bypass. With the onset of bypass, acute hemodilution from hematocrit of 35% to 22% resulted in a decrease in rSO_2i from 74% to 45%. Cooling to 32°C increased rSO_2i to >60%. b, rSO_2i in a 7-mo-old undergoing repair of complete atrioventricular canal with moderate hypothermic bypass to 28°C. A brief period (60 s) of circulatory arrest was used when the aortic cross-clamp (Ao xcl) was applied at 31°C, resulting in a decrease in rSO_2i from 75% to 48%. c, typical changes in right and left-sided rSO_2i during cardiac surgery with CPB, regional cerebral low flow perfusion, and DHCA at 18°C, in a neonate undergoing the Norwood Stage I palliation for hypoplastic left heart syndrome. There is a brief period of DHCA before and after the period of RLFP, and the left-sided rSO_2i is lower than the right during RLFP. d, rSO_2i in a neonate with unbalanced, left-ventricle dominant complete atrioventricular canal and infradiaphragmatic total anomalous pulmonary venous return. This patient underwent four periods of DHCA at 18°C of 3, 12, 26, and 1 min, for a total of 42 min.

Relationship Between Low rSO_2i and Adverse Neurological Outcome

Clinical evidence suggests a correlation between low rSO_2i and adverse neurological outcome. A study of 26 infants and children undergoing surgery with bypass and DHCA found that the 3 patients with low rSO_2i had acute postoperative neurological changes: seizures in 1 and prolonged coma in 2 (44). In these 3 patients the increase in rSO_2i was much less after the onset of CPB (average 3% relative increase versus 33% increase in patients without neurological deficit) and the duration of cooling before DHCA was shorter. Austin et al. (4) studied 250 pediatric patients undergoing cardiac surgery with bypass and found that 41% of patients experienced prolonged periods of relative cerebral oxygen desaturation, defined as more than 20% decrease

less than prebypass baseline. One-quarter of these patients with cerebral desaturation had postoperative adverse neurological events consisting of prolonged coma, seizures, or hemiparesis.

It would be intuitive to conclude that low rSO_2i as measured by NIRS leads to adverse neurological outcomes and therefore should be monitored and treated. The studies cited above support this notion. However, additional prospective outcome data in infants and children using this modality are necessary. An additional limitation of the NIRS monitor is that it measures rSO_2i in only a small tissue volume of the frontal cerebral cortex; other areas of the cortex and deeper structures in the brain are not assessed by this technique. It would be useful to attempt to correlate abnormal rSO_2i with the frequency of changes detected by magnetic resonance imaging after CPB in newborns, specifically periventricular leukomalacia (49).

Other Uses of NIRS

Other important areas of investigation include correlating the rSO_2i with mixed venous oxygen saturation (SvO_2) to assess whether it can be used as a noninvasive measure of SvO_2. Preliminary data suggest that measured SVC HbO_2 saturation correlates well in infants with congenital heart disease after cardiac surgery (50). Other potential uses of this technology include measuring HbO_2 saturation in subdiaprhagmatic viscera (e.g., kidney and intestines). There is evidence that these values decline significantly during aortic cross-clamping for coarctation repair (51) and are preserved during cerebral RLFP; this may have implications for end organ function (52,53).

Transcranial Doppler Ultrasound

Transcranial Doppler ultrasound (TCD) is a sensitive, real-time monitor of cerebral blood flow velocity (CBFV) and emboli during congenital heart surgery. Currently available instruments use pulsed-wave ultrasound at 2 MHz frequency that is range-gated, emits a power of 100 mW, and has a sample volume length of up to 15 mm. A display of the frequency spectrum of Doppler signals is easily interpreted, and peak systolic and mean flow velocities, in cm/s, are displayed, as well as a pulsatility index that is equal to the peak velocity minus the end-diastolic velocity, divided by the mean velocity. As with cardiac ultrasound, the advantage of pulsed-wave Doppler ultrasound is that a precise sample volume can be selected which insonates only the arteries of interest without contamination from other sources.

The most consistent and reproducible technique for clinical use in patients of all ages is to monitor the middle cerebral artery (MCA) through the temporal window, which can usually be found just above the zygoma and just anterior to the tragus of the ear (54). Several transducer probes are available, ranging from very small disk probes suitable for infants and children, to larger, heavier probes for adolescents and adults. The depth of the sample volume and angle of insonation is adjusted until the bifurcation of the MCA and the anterior cerebral artery (ACA) is detected. This is heralded by a maximal antegrade signal (positive deflection, toward the transducer) from the MCA, accompanied by a retrograde signal from the ACA (negative deflection, away from the transducer) of the same or very similar velocity and wave form as the MCA flow.

In infants, an alternative site for monitoring is through the anterior fontanelle, using a hand-held pencil-type probe, placing the probe over the lateral edge of the fontanelle, and aiming caudally, at a greater depth than for the temporal window, at the internal carotid artery. The depth of measurement and normal flow velocities for the MCA through the temporal window are listed in Table 1 (55). These normal velocities were determined in awake children without cardiovascular disease, under perfect examination conditions. Lesions producing large diastolic runoff (e.g., large patent ductus arteriosus) will decrease diastolic blood flow to the brain. Hemodynamic instability, less than optimal probe positioning, and general anesthesia may reduce these velocities in clinical practice. Typically the clinician must accept a stable baseline for the individual patient and use it as the basis for comparison. Fixation of the probe in the optimal position is problematic. There are several commercial devices available for fixation in larger patients (Table 2), but in practice it is often simpler to affix a small disk Doppler probe with a clear adhesive dressing and clear tape over the temporal window of infants and children, assuring access and some mobility to the probe for the frequent adjustments that may be necessary. Currently available FDA approved TCD manufacturers are listed in Table 2.

TCD has been used extensively in pediatric cardiac surgical research to examine cerebral physiology in response to CPB, hypothermia, low-flow bypass, RLFP to the brain, and DHCA. Hillier et al. (56) used TCD to study cerebrovascular hemodynamics during hypothermic bypass with DHCA in 10 infants. CBFV did not return to baseline levels after DHCA. Calculated cerebral vascular resistance (mean arterial blood pressure − central venous pressure/CBFV) was increased immediately after DHCA and remained increased until the end of bypass. The observed decrease in CBFV during cooling was presumed to be attributable to decreased metabolic demand by the brain and thus less blood flow. In this study an α-stat blood gas

Table 1. Normal Transcranial Doppler Velocities for Infants and Children

Age	Depth (mm)	Mean velocity (cm/s)	Peak systolic velocity (cm/s)	End-diastolic velocity (cm/s)
0–3 mo	25	24–42 ± 10	46–75 ± 15	12–24 ± 8
3–12 mo	30	74 ± 14	114 ± 20	46 ± 9
1–3 yr	35–45	85 ± 10	124 ± 10	65 ± 11
3–6 yr	40–45	94 ± 10	147 ± 17	65 ± 9
6–10 yr	45–50	97 ± 9	143 ± 13	72 ± 9
10–18 yr	45–50	81 ± 11	129 ± 17	60 ± 8

Normal transcranial Doppler velocities in the middle cerebral artery obtained through the temporal window in awake children without cardiovascular disease, expressed as mean ± SD. From Reference 55.

Table 2. Transcranial Doppler Manufacturers

Manufacturer	Internet address	Small intraoperative 2 MHz monitoring probes available?	Probe fixation devices
Nicolet Vascular, Inc (Madison, WI)	www.nicoletvascular.com	Yes	Yes—elastic headband, adjustable halo device, or Velcro® device with plastic headpiece
DWL Systems, Inc., (Sterling, VA)	www.dwldoppler.com	Yes	Yes—elastic headband, or adjustable headframe; pediatric models available
Spencer Technologies, Inc. (Seattle, WA)	www.spencertechnologies.com	Yes	Yes—adjustable halo device
NewTech Industrial Corporation (Minneapolis, MN)	www.newtech-medical.com	Yes	No
Multigon Industries, Inc. (Yonkers, NY)	www.multigon.com	Yes	Yes—malleable adhesive probe fixation device
Rimed Ltd. (Los Gatos, CA)	www.rimed.com	Yes	No

strategy was used, which can produce relative cerebral vasoconstriction during cooling in smaller arterioles downstream to the MCA and ACA (57). TCD of the MCA through the temporal window was used to describe the cerebral pressure-flow velocity relationship during hypothermic bypass in 25 neonates and infants <9 months old. CBFV was examined over a wide range of cerebral perfusion pressure varying from 6 to 90 mm Hg at 3 temperatures: normothermia (36°C–37°C), moderate hypothermia (23°C–25°C), and profound hypothermia (14°C–20°C). Cerebral pressure flow autoregulation was preserved with normothermia, partially affected with moderate hypothermia, and totally lost with profound hypothermia; these results agree with previous research performed using xenon washout to quantitate cerebral blood flow (58).

TCD has also been used to determine the threshold of detectable cerebral perfusion during low-flow CPB. Zimmerman et al. (59) studied 28 neonates during bypass undergoing the arterial switch operation with α-stat blood gas management. At 14°C–15°C, bypass flow was sequentially reduced to 0 $mL \cdot kg^{-1} \cdot min^{-1}$. All patients had detectable CBFV more than 20 $mL \cdot kg^{-1} \cdot min^{-1}$, although one had no perfusion at 20 $mL \cdot kg^{-1} \cdot min^{-1}$ and 8 had none at 10 $mL \cdot kg^{-1} \cdot min^{-1}$, leading the authors to conclude that 30 $mL \cdot kg^{-1} \cdot min^{-1}$ was the minimum acceptable flow in this population. Andropoulos et al. (60) used TCD of the MCA to determine the level of bypass flow necessary during RLFP for neonatal aortic arch reconstruction. They studied 34 neonates and established a baseline mean CBFV under full flow bypass (150 $mL \cdot kg^{-1} \cdot min^{-1}$) using pH stat management at 17°C–22°C: a mean of 22 cm/s. These authors then used the TCD signal to determine the necessary bypass flow during RLFP, a mean of 63 $mL \cdot kg^{-1} \cdot min^{-1}$. Interestingly, this level of bypass flow did not correlate with mean arterial blood pressure in the radial artery or rSO_2i measured by NIRS. The necessary CPB flow as determined by TCD varied widely, leading the authors to conclude that TCD was a valuable monitor to ensure adequate but not excessive cerebral blood flow during this complicated perfusion technique. The TCD is a useful monitor to detect acute decreases in CBFV; this can allow for adjustment of bypass cannulae, which might avert a neurological disaster (61,62).

Isolated cerebral emboli are a frequent occurrence during open-heart surgery in children. Emboli are easily detected by TCD, although false positive artifacts from electrocautery and physical contact with the ultrasound transducer occur (63). True emboli have characteristic audio and visual signals and are designated as high intensity transient signals (HITS) that

can be counted by the TCD software. The HITS counter can be an accurate gauge of the number of emboli detected in the artery being monitored; however, it does not distinguish false positive artifacts, and if a large number of emboli are detected in a short period of time, the number counted is meaningless. In actual practice, the anesthesiologist can observe the monitor intermittently and decide whether the number of emboli detected is clinically significant and initiate treatment. Despite the potential utility of this monitor to detect emboli, one study found that the number of emboli detected in the carotid artery during pediatric congenital heart surgery does not appear to correlate with acute postoperative neurological deficits (63). Another limitation of emboli detection is that it only occurs after the fact; however, limitation of further emboli may be possible with this monitor.

One caveat when usng TCD clinically is that this device measures CBFV rather than blood flow. CBFV is dependent on the diameter of the blood vessel, whereas cerebral blood flow depends on cerebral vascular resistance, which changes in response to changes in CO_2, temperature, cerebral perfusion pressure, and bypass flow. Thus, changes in CBFV often correlate well with changes in cerebral blood flow in the individual patient, particularly at deep hypothermia when autoregulation is lost and the caliber of the blood vessels is unchanged. However, the clinician must always estimate the state of the patient's cerebral vascular resistance to translate TCD into meaningful information for clinical decision-making.

Multimodality Neurological Monitoring

Simultaneous neurological monitoring—NIRS, TCD, and processed EEG—may hold the greatest promise in detecting and correcting neurological abnormalities during congenital heart surgery, just as pulse oximetry combined with capnography is more effective at preventing morbidity from ventilation mishaps than either modality alone (64). With combined use of TCD to measure blood flow in the MCA/ACA and NIRS to measure rSO_2i of blood in the frontal lobe, it is possible to monitor up to 70% of the blood flow distribution to a cerebral hemisphere. A study by Austin et al. (4) showed that 70% (176 of 250) of pediatric patients experienced a significant change in one or more variables when multimodality neurological monitoring—NIRS, TCD, and four-channel qualitative EEG—was used during cardiac surgery. Abnormal neurological monitor values were not treated during the initial observational phase of this study, when multimodality monitoring was of unproven benefit and 26% of patients experienced adverse early neurological outcomes (seizures, prolonged coma, or hemiparesis). As experience was gained with multimodality monitoring and abnormal values appeared to correlate with adverse outcomes, a treatment algorithm was developed. The investigators in this study originally intended to randomize patients to treatment according to the algorithm or to receive standard care without monitoring. However, given the correlation of adverse outcomes with abnormal neurological monitor values, the investigators felt that it would be unethical to leave the obvious changes they observed untreated. They then began the next phase of the study, which treated patients according to the algorithm. When the abnormal monitoring values were treated, the incidence of adverse neurological outcomes decreased to 7%. This decreased incidence was very similar to that in the group that did not experience abnormal values on their neurological monitors (6%).

In this study EEG changes were responsible for only 5% of the monitoring abnormalities, with NIRS changes responsible for 58% and TCD 37%. The 26% incidence of acute neurological complications in the pretreatment phase of this study is more than most other reports of neurological outcomes after congenital heart surgery (3). Although this study was prospective, it was neither randomized nor controlled. However, it represents the best evidence that multimodality neurological monitoring, particularly NIRS and TCD, in conjunction with a treatment algorithm can reduce adverse neurological outcomes during congenital heart surgery. A modification of the treatment algorithm used in the Austin et al. study (4) is presented in Table 3. These modifications account for the anesthesiologist being the interpreter of the monitors (instead of a dedicated technician as used in the Austin et al. study) and the use of these monitors in the pre- and post-CPB periods. Eliminating the need for a separate technician obviates the problems of technician availability and third-party reimbursement for placement and interpretation of the neurological monitors. It should be noted that although low rSO_2i values have been correlated with acute gross neurological outcomes, there are no data correlating low rSO_2i with either more subtle neuropsychological dysfunction or long-term neurodevelopmental outcomes in congenital heart disease.

In patients younger than 2 years of age the BIS is not used not only because of space limitations on the forehead but also because of insufficient data confirming its utility in this age group. Anesthesiologists can learn to place and interpret these monitors and treat the patient according to the algorithm presented in this review or another algorithm. For the NIRS monitor, a relative decrease of rSO_2i of more than 20% from a stable baseline obtained preincision is the primary indication for treatment. Other critical values are an absolute value of rSO_2i $<30\%$ or an absolute value of 95% accompanied by a significant increase in CBFV. It should be noted that the recommendation to reperfuse the patient at a NIRS nadir of 30 minutes will not be possible in some cases; i.e., the Norwood Stage I palliation where the aorta is opened

Table 3. Neurological Monitoring Treatment Algorithm for Congenital Heart Surgery

Monitor	Change	Intervention pre/post bypass	Intervention on bypass	Intervention on DHCA
NIRS (rSO_2i%)	≥20% relative to preincision baseline	Cardiac output, hgb, FIO_2, $Paco_2$	Bypass flow, $Paco_2$, MAP, temp, hgb, √CBFV adjust cannulae	–
	DHCA: rSO_2i < 30%, or at nadir > 30%	–	–	Reperfuse if possible
	rSO_2i ≥ 95%	–	None, or √CBFV− bypass flow or $Paco_2$ if >25% above baseline	–
	rSO_2i <30%	Rapid institution bypass, aggressive measures to O_2 delivery	Aggressive treatment: bypass flow, $Paco_2$, MAP, temp, hgb, √CBFV-adjust cannulae	Reperfuse if possible
TCD (mean CBFV, cm/s)	≥25% from preincision baseline	√ transducer; √NIRS—if low, cardiac output, $Paco_2$, MAP	√ transducer; √NIRS—if low: bypass flow, $Paco_2$, MAP, adjust cannulae	–
	≥25% from preincision baseline	$Paco_2$, anesthetic depth MAP	$Paco_2$, anesthetic depth, MAP	–
	Emboli: more than isolated HITS	De-air all infusions, Trendelenberg, stop rapid fluid boluses, search for and treat air entrainment in surgical field, assess TEE for air, return to bypass for de-airing	De-airing maneuvers, Trendelenberg, assess TEE for air, slow wean from bypass	–
BIS	≥80	Anesthetic depth	Anesthetic depth	
	No isoelectric EEG prior to DHCA		Additional cooling time; lower temperature before DHCA	
	<30 during rewarming bypass		Reduce or discontinue volatile agent on bypass pump	

Modified from Reference 4.

DHCA = deep hypothermic circulatory arrest; NIRS = near-infrared spectroscopy; rSO_2i = regional cerebral oxygen saturation index; hgb = hemoglobin; MAP = mean arterial blood pressure; √ = assess variable and adjust as necessary; TCD = transcranial Doppler ultrasound; CBFV = cerebral blood flow velocity; HITS = high-intensity transient signals; TEE = transesophageal echocardiogram; EEG = electroencephalogram. Baseline rSO_2i and CBFV refer to preincision values during hemodynamically stable period with optimal blood gases. Frequent adjustments of TCD transducer position may be necessary to obtain the optimal signal before making interventions based on abnormally low values.

during reconstruction. In our institutions, low rSO_2i values are responsible for approximately 90% of the abnormal monitor values that result in treatment and frequently correlate with decreases in CBFV values. The TCD alone is responsible for approximately 10% of interventions, either as the result of cerebral emboli or significant increases in CBFV during deep hypothermia when the rSO_2i is at its maximum value of 95%, placing the patient at risk for overperfusion to the brain. The BIS values are rarely responsible for initiating treatment. BIS values of >80 are frequently observed during rewarming on CPB, but BIS is typically not altered by benzodiazepines and opioids administered into the bypass circuit. It is only after bypass when small-dose volatile anesthetic gases are administered that the BIS value declines, again emphasizing the dependence of the BIS values on anesthetic. We have not recognized a case of awareness under anesthesia during rewarming with BIS >80.

Adverse Effects of Neurological Monitoring

No adverse effects from intraoperative neurological monitoring have been reported. In clinical practice of up to 12 hours use, there may be minor skin irritation associated with the adhesives used for the NIRS and BIS monitors and fixation devices for the TCD, but these are self-limited. The TCD should be used at the lowest power (i.e., scale setting) possible and should not be directed near the orbit because of potential effects on the eye (65).

Conclusion

The anesthesiologist can now monitor the brain during congenital heart surgery with commonly available clinical monitors, potentially improving neurological outcome with appropriate treatment strategies. More careful outcome studies, assessing both acute and long-term neurodevelopmental changes, including the common neuropsychological dysfunction seen after bypass, are clearly needed. These outcome studies will be complicated by the frequent occurrence of congenital neurological abnormalities and by neurological events occurring in the perioperative period outside of the operating room. Other problems with outcome studies include the fact that gross early neurological insults are far less common in the modern era in experienced centers (3). This improvement in acute outcomes has occurred in the absence of the use of neurological monitoring in most centers. The study size necessary to prove a significant decrease from the current 1%–2% incidence of early adverse events will

be difficult to achieve. It may be that the greatest benefit will be in the subtler, long-term neurodevelopmental outcomes, which are difficult to quantify but of obvious importance to the patients' quality of life. Isolated case reports of the prevention of neurological disasters during CPB (66) or of changing the surgical approach (67) add to the evidence of the benefit of using neurological monitoring. All of this evidence taken together suggests that neurological monitoring should become routine during congenital heart surgery. If the anesthesiologist places the monitors and interprets the monitoring values, the cost savings in preventing a small number of neurological complications with routine monitoring will more than pay for the cost of the monitoring hardware and disposable sensors (4). The vulnerable immediate postoperative period in high-risk patients should also be studied. Because a high survival rate after complex heart disease in children is no longer in question, the goal should be to improve the quality of life of these children with complex heart disease through better detection of neurological events and their expeditious treatment.

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