Quantitative Electroencephalogram Patterns During Neonatal Antegrade Cerebral Perfusion and Deep Hypothermic Circulatory Arrest that Suggest Neurologic Injury

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Take-home points

- What is already known:
  - Antegrade cerebral perfusion (ACP) and deep hypothermic circulatory arrest (DHCA) are associated with postoperative neurologic injury following neonatal cardiac surgery.
  - Cerebral ischemia has been associated with characteristic quantitative EEG (qEEG) changes including decreases in Alpha:Delta Ratio (ADR) and increased asymmetry percentage.
  - Interhemispheric ADR differences have been associated with neurologic injury in neonates undergoing arch reconstruction.

- What this study adds:
  - ADR remains stable during ACP but decreases within minutes of the onset DHCA and becomes significantly different from neonates undergoing ACP after 15 minutes at a nadir temperature of 20°C.
  - There are significant differences in absolute posterior and hemispheric asymmetry percentages during ACP, but no significant differences in the duration of a left versus right ADR difference > 25% or incidence of an asymmetry percentage > 50% between groups.
  - DHCA, longer CPB time, and total duration of anterior left v right ADR difference > 25% are associated with postoperative neurologic injury in multivariate analysis.

Introduction

Over the past several decades, patients born with congenital heart disease (CHD) have seen greatly improved survival and are now largely expected to live to adulthood. Neurodevelopmental outcomes, however, have seen only modest improvement over the same period despite an increasing understanding of factors that increase neurodevelopmental risk. Known perioperative risk factors include significant brain injury on imaging, postoperative seizures, cardiac resuscitation, mechanical support, prolonged hospitalization during infancy, and heart transplantation. (Sood, 2024) Although the degree of impact and interaction with one another remain largely unknown, some of these risk factors continue to be quite common. Pre-operative brain injuries have been demonstrated by brain magnetic resonance imaging (MRI) in nearly 25% of neonates with CHD, with almost 70% of patients showing new or worsening injuries in the first two weeks after neonatal cardiac surgery. (Mahle, 2008) Postoperative seizures occur in 6% and 18% of neonates with biventricular and single ventricle physiology, respectively. (Hsia, 2023)

Anesthesiologists are uniquely positioned to control modifiable risk factors during the intraoperative period, but outcomes improvement can only occur if they know what risk factors to focus on and what interventions are beneficial. Efforts to minimize the deleterious effects of cardiopulmonary bypass (CPB) and optimize end-organ oxygen delivery have focused on surgical timing; temperature, hematocrit, and acid-base management; and CPB duration and technique (i.e. deep hypothermic circulatory arrest (DHCA) and/or antegrade cerebral perfusion (ACP)). (Sood, 2024). Multiple neuromonitoring modalities, including electroencephalogram (EEG), transcranial doppler, near infrared spectroscopy (NIRS), and jugular venous oximetry, have been utilized in the quest to detect and prevent neurologic injury. Each modality has its pros and cons, especially in smaller patients and during non-standard cardiopulmonary bypass (CPB) strategies such as antegrade cerebral perfusion (ACP) and deep hypothermic circulatory arrest (DHCA).

The use of traditional EEG during neonatal cardiac surgery has been limited by signal suppression (and eventual loss) during deep hypothermia and circulatory arrest. (Reilly, 1974) Newer, quantitative methods of EEG analysis may offer a solution. Measurements of the Alpha:Delta ratio (ADR), comparing faster alpha and slower delta frequencies, and the asymmetry percentage on asymmetry spectrogram, may provide useful metrics for assessing ischemia in real time. It has been previously demonstrated that right v. left hemispheric differences in regional and hemispheric ADR > 25% were associated with neurologic injury in neonates undergoing arch reconstruction. (Lansinger, 2025) In the recently published "Quantitative Electroencephalogram Patterns During Neonatal Antegrade Cerebral Perfusion and Deep Hypothermic Circulatory Arrest that Suggest Neurologic Injury," Orie *at al* sought to build upon this finding and characterize the quantitative EEG (qEEG) patterns seen in neonates undergoing arch reconstruction with ACP and/or DHCA in order to understand what patterns are associated with a diagnosis of neurologic injury in the post-operative period (Orie, 2026).

Brief Summary of Study

The study by Orie *et al* is a retrospective study of prospectively collected EEG and post-operative clinical data. It included 86 neonates who underwent intraoperative EEG monitoring during aortic arch reconstruction using ACP (n = 72; enrolled between 2015 and 2021 as part of current ACP standard of care) or DHCA +/- ACP (n = 14; enrolled between 2006 and 2009 as part of an earlier study on the incidence of seizures during CPB). A standard international 10-20 system of EEG electrodes (with the exception of 2 frontal electrodes, FP1 and FP2) was applied; baseline, intraoperative, and postoperative recordings (48 hours) were recorded. The EEG was reviewed by an attending neurologist and quantitative analysis was performed retrospectively using Persyst software (Persyst Development Corporation, Solana Beach, CA, USA) per the manufacturer's specifications. Intraoperative EEG data was quantified every 5 minutes throughout CPB, starting at cannulation, with the initiation of ACP or DHCA considered as time zero.

Between groups, there were no differences in demographics or non-DHCA perfusion times except for the incidence of chromosomal and genetic syndromes, attributed to the differences in genetic testing practices between study epochs. ADR remained stable during ACP but decreased within minutes of the onset DHCA. ADR signal dropouts only occurred during DHCA. The regional and hemispheric differences in ADR between ACP and DHCA groups became significant at 15 minutes with the greatest difference observed between the right and left anterior ADRs at 15min. The asymmetry percentage, on the other hand, increased during ACP and remained similar during DHCA. Although there were significant differences in absolute posterior and hemispheric asymmetry percentages during ACP, there were no significant differences in the duration of a left v right ADR difference > 25% or incidence of an asymmetry percentage > 50% between groups. The authors attributed asymmetry changes to differences in hemispheric perfusion, autoregulatory reserve, and/or metabolic suppression during cooling and either ACP or DHCA.

Known seizure or stroke occurred in 12.8% of patients (9.7% ACP v 28.6% DHCA; p = 0.07) and was not significantly different between groups. DHCA (OR 21.487, 95% CI 2.180,211.828; p = 0.009), longer CPB time (OR 1.1017, 95% CI 1.004, 1.030; p = 0.009) and total duration of anterior left v right ADR difference > 25% (OR 1.044, 95% CI 1.010, 1.080; p = 0.012) were associated with postoperative neurologic injury in multivariate analysis.

Opinion

The study by Orie *et al* describes normative qEEG patterns (baseline through 48 hours post-op) in neonates undergoing ACP or DHCA and begins to establish injury thresholds. It builds upon previous work done at the authors' center which examined changes in qEEG measurements during the cooling and rewarming phases of CPB for neonatal arch reconstruction and demonstrated that 1) ADR directly correlated with cerebral oximetry and 2) neurologic injury was more often preceded by an interhemispheric ADR difference > 0.1. (Lansinger, 2025) Both studies are important, albeit early, steps towards developing qEEG into an intraoperative neuromonitoring modality capable of detecting periods of cerebral vulnerability that could potentially be intervened upon to mitigate injury and improve neurodevelopmental outcomes.

In the current study, the authors hypothesized that 1) ADR would decrease during DHCA, 2) the asymmetry percentage would increase during ACP, and 3) interhemispheric differences in ADR would precede neurologic injury, defined as seizure or stroke. qEEG abnormalities concerning for ischemia were found in both study groups. ADR was found to decrease during DHCA in this study; however, a significant decrease was not immediate as was the case in previous studies of patients undergoing carotid endarterectomy. As the authors point out, this is likely due to the protective effect of hypothermia and corroborates prior studies that demonstrate a lower incidence of postoperative neurologic injury with DHCA duration of less than 20 minutes. Although the asymmetry percentage did increase during ACP, this finding was not consistent across all regions and time points. The rates of neurologic injury diagnosed postoperatively (12.8%) were consistent with previous studies with the total duration of anterior left v right ADR difference > 25% determined to be one of several risk factors for postoperative neurologic injury.

Although this study's identification of qEEG patterns during neonatal arch surgery using ACP or DHCA is novel, it has several limitations including its single-center retrospective design, small study size (especially the DHCA group), and lack of long-term neurodevelopmental follow-up. Another notable limitation is the temporal separation of the study groups, with the ACP cohort enrolled from 2015 – 2021 the DHCA cohort enrolled from 2006 – 2009. Analysis may therefore be confounded by changes in monitoring, surgical technique, and/or monitoring strategies that occurred between these two time periods. Larger, multicenter prospective studies will be needed to confirm the authors' findings and to determine whether real-time ADR-guided interventions in perioperative care lead to improved neurologic outcomes.

What do we as anesthesiologists do with these findings? The results add evidence that qEEG abnormalities concerning for ischemia are present during both ACP and DHCA but were not limited to these time periods in patients who go on to develop neurologic injury. Although this study suggests that DHCA places the neonates at a higher risk of brain injury compared to ACP alone, the difference in neurologic injury was not found to be significant, which is consistent with the current evidence showing equivocal outcomes between techniques. (Sood, 2024) This is likely because many other factors beyond perfusion technique contribute to neurologic injury such as patient-specific preoperative factors, perioperative hemodynamic instability, and postoperative complications. Although anesthesiologists are unable to effect interventions during DHCA, advocating for hypothermia and limiting DHCA time are supported by this study and others. (Orie, 2026; Alkhatip, 2021) With regards to ACP, because the qEEG analysis was conducted retrospectively and interventions were not studied, it is not known if changes to flow or cooling strategy during ACP could lead to reduced asymmetry during the cooling and re-warming portions of ACP. Although the results of this study align with what we would expect electroencephalographically during ACP and DHCA, the author's description of the ADR changes that occurred outside of the ACP and DHCA are limited. These EEG changes would be easier targets for real-time ADR-guided intervention aimed at optimizing perfusion and oxygen delivery. Overall, there is little guidance to guide anesthesiologists to make practice changes at this time and the association between qEEG metrics and cerebral injury is weak.

The authors conclude that this manuscript (and others) provide early support for the use of qEEG monitoring during neonatal aortic arch surgery and postulate that incorporating practical real-time EEG metrics into standardized protocols with established thresholds and evidence-based neuroprotective strategies would improve neurologic outcomes in vulnerable, high-risk populations. Unfortunately, we believe that there is not enough data or guidance for most centers to jump to incorporating qEEG monitoring based on this study alone. In combination with this study, the authors' previous work demonstrating a strong correlation between ADR and cerebral oximetry could be seen as supporting the use of the less resource-intensive cerebral oximetry as a surrogate measure until such time as there is better data to support when and how to intervene on real-time qEEG metrics.

Conclusion

Characteristic qEEG patterns concerning for cerebral ischemia are present in neonates undergoing arch reconstruction with ACP and/or DHCA with longer anterior right versus left ADR difference found to have a weak, positive association with neurologic injury diagnosed in the immediate postoperative period. Incorporating the use of real-time qEEG monitoring during high-risk neonatal cardiac surgery has the potential to help guide intraoperative interventions in order to optimize perfusion and end-organ oxygen delivery and/or to identify patients most in need of enhanced postoperative screening or tailored neuroprotective care. Further prospective studies will be needed to develop evidence-based management strategies built around qEEG metrics in order for qEEG use to become routine. The search for an intraoperative neuromonitoring modality that allows for individualized neuroprotective perfusion strategies is ongoing.

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