Quantitative EEG Trends Surrounding Cardiopulmonary Arrests in Children: Insights for Prevention and Prognosis

Addison Schwamb^{a,*,†}, Carley Gilman^{b,*}, Rebekah Landre^c, Zoe Krug^a, Talie Fulton^d, Stuart Tomko^d, ShiNung Ching^a, Réjean M. Guerriero^d

April 18, 2024

Abstract

Objective: In this study, we investigate the ways in which brain electrophysiology responds to sudden cardiopulmonary arrest. We also investigate differences in brain dynamic response which correspond to mortality, as well as potential age differences between infants and adolescents who experience cardiopulmonary arrests.

Methods: We utilize multitaper spectral analysis to qualitatively analyze changes in the frequency structure of EEG signals. We also quantify changes in the alpha delta ratio and spectral edge frequency prior to and during cardiopulmonary arrest.

Results: We identify a narrowband frequency structure characterized by a strong 2Hz rhythm. This structure localizes temporally to the arrest event, and its strength reflects differences in arrest mortality. We also note that the alpha-delta ratio (ADR) decreases prior to arrest, and the spectral edge frequency increases during arrest.

Conclusions: Changes in frequency structure of electrophysiological activity reflect changes in physiology present during cardiopulmonary arrest and correspond in strength. The strength of the narrowband structure we observed corresponds to mortality in our cohort, indicating its potential usefulness as a prognostic aid.

Significance: These results contribute insight into the ways in which the brain reacts to and recovers from cardiopulmonary arrest, enabling clinicians to identify patients requiring more aggressive care.

Highlights:

- We identified a narrowband structure localizing to time of arrest and corresponding to outcome using EEG spectral analysis.
- Alpha delta ratios decreased prior to arrest, while spectral edge frequencies increased during arrest.
- EEG monitoring can provide valuable prognostic information prior to, during, and in the wake of cardiopulmonary arrest.

Keywords— quantitative EEG, brain dynamics, pediatric neurology, cardiopulmonary arrest, spectral analysis

1 Introduction

Cardiopulmonary arrest is an extreme physiological event which can lead to devastating neurologic injury and death. In survivors of arrest events, many will later die of complications secondary to hypoxic-ischemic brain injury (HIBI)

^{*}These authors contributed equally.

^aDepartment of Electrical & Systems Engineering, Washington University in St. Louis, 1 Brookings Dr., Saint Louis, MO 63130, USA. Z.K.: krug@wustl.edu, S.C.: shinung@wustl.edu

^bDivision of Neurology, Children's Hospital of Philadelphia, 3401 Civic Center Blvd. Philadelphia, PA 19104, USA. gilmanc@chop.edu

^cPediatric Neurology, St. Louis Children's Hospital, 1 Children's Pl., Saint Louis, MO 63110, USA. rebekah.landre@bjc.org

^dDepartment of Neurology, Washington University School of Medicine, 660 S. Euclid Ave., Saint Louis, MO 63110, USA. T.F.: e.fulton@wustl.edu, S.T.: s.tomko@wustl.edu, R.G.: r.guerriero@wustl.edu

[†]Corresponding author: a.l.schwamb@wustl.edu

(Nolan et al, 2021; Sekhon et al, 2017; Sandroni et al, 2022). Thus, cardiac arrest has a significant impact on brain physiology and function. However, the matter of how brain electrophysiology responds to and recovers from cardiopulmonary arrest is less well-studied. It stands to reason that acute effects on cerebral oxygenation would impact neural firing. Characterization of the neurophysiological response to hemodynamic changes and metabolic stress of cardiopulmonary arrest could help us understand neurologic recovery after these events. Additionally, given the high morbidity and mortality associated with arrest events, there is a call for further monitoring modalities, particularly in hospitalized patients receiving intensive care, to help identify patients at high risk for decompensation and facilitate possible interventions before neurologic harm is done (Pollack et al, 2018).

Despite this potential for arrest prevention and prognosis, previous research into human brain electrophysiology during cardiac arrest have been limited due to the challenge of identifying subjects who have experienced an arrest event while undergoing continuous electroencephalogram (CEEG) monitoring (Roberti et al, 2023). Currently, CEEG is utilized primarily for the detection of non-convulsive seizures in particularly vulnerable populations, such as post-cardiac arrest. In the pediatric intensive care unit, there has been increasing utilization of CEEG monitoring over time in other high-risk populations due to the improved sensitivity for seizure detection and survival outcomes reported with continuous monitoring (Ney et al, 2013; Abend et al, 2013). As such, there is more neurophysiologic data being gathered in patients that ultimately experience arrests while on CEEG.

Many previous works analyzing CEEG in these patients focus on time domain analyses, identifying patterns such as voltage suppression, burst suppression, and rhythmic and periodic patterns associated with poorer outcomes (Sadaka et al, 2015; Søholm et al, 2014; Benghanem et al, 2022; Sandroni et al, 2020; Monteiro et al, 2016; Reagan et al, 2018). While these analyses can be informative, it is often difficult to investigate the brain's more complex oscillatory dynamics through time domain analysis alone (Babadi and Brown, 2014).

Other previous works use the bispectral index (BIS) as an indicator of outcome in cardiac arrest (Feng et al, 2016; Chawla et al, 2009; Goodman et al, 2009; Stammet et al, 2009). The BIS is a scalar value ranging from 0-100, an aggregate metric which includes measures of the power spectrum, burst suppression ratio, and phase coupling in the EEG (Bruhn et al, 2000). The BIS has been observed to decrease during cardiac arrest and indicate patient prognosis (Feng et al, 2016; Chawla et al, 2009; Goodman et al, 2009; Stammet et al, 2009). However, while changes in the BIS may indeed be manifest, they do not provide specific information on dynamical changes in brain activity associated, e.g., with specific oscillations or rhythmic structure. Frequency domain analyses including power spectrograms, can provide a more holistic insight into the oscillatory dynamics which occur prior to, during, and after a cardiopulmonary arrest, and have proved useful in neurocritical care (Babadi and Brown, 2014; Claassen et al, 2013).

In this paper, we apply both time and frequency domain analyses to EEG recordings from 16 patients who experienced cardiac arrest while undergoing CEEG monitoring. We identify and characterize the alpha-delta ratio, a narrowband frequency structure, and a change in spectral edge frequency in the data which is temporally localized to the time of arrest to investigate how these changes relate to patient outcomes as well as potential opportunities for intervention to avoid clinical decompensation.

2 Methods

2.1 Patient Population

We retrospectively examined a cohort of 17 patients at St. Louis Children's Hospital who experienced a cardiac arrest event while undergoing EEG monitoring. We excluded one patient who was in status epilepticus at time of arrest, providing a confound to the EEG data, resulting in a final cohort size of 16. The patients ranged in age from 38 week post-menstrual age to 16 years old, though 9 were under one year old and the rest were 7 years old or older. Patient demographics are given in Table 1. 58.8% (n = 10) survived their arrest. Each patient had a minimum of one hour of EEG data surrounding the arrest event. Further clinical information is included in Table 2. This study was approved by the Institutional Review Board (IRB) at Washington University in St. Louis.

	Infant Group (n=9)	Child Group (n=7)
Male, N (%)	5 (55)	3 (43)
Ethnicity		
White	7 (78)	4(57)
Black	1 (11)	3(43)
Asian	1 (11)	0
Age at time of arrest, median (IQR)	3 months (3.5)	13 years (5)
Type of arrest, N (%)		
Ventricular Fibrillation	1 (11)	2(28)
Bradycardiac	3(33)	2(28)
Hypotensive	2(22)	2(28)
Other	3(33)	1 (15)
Resuscitation duration (minutes), median (IQR)	3(9)	9 (15)
Arrest survival, N (%)	7 (78)	3 (34)

Table 1: Patient Demographics

Patient	Age at time of arrest	Ethnicity	Hispanic?	Reason for hospitalization	Cause of decompensation	Resuscitation time (m)	Arrest survival
1	15 years	Black or African American	No	Sickle Cell Crisis	Acute diffuse lung injury secondary to multiorgan failure	20	No
2	11 years	White	Yes	Diabetic ketoacidosis	Ventricular fibrillation secondary to hypokalemia	6	Yes
က	$\begin{array}{c} 1 \text{ month} \\ (38 \text{ weeks} \\ \text{PMA}) \end{array}$	White	No	Bronchiolitis	Hypoxemia secondary to respiratory mucus plug	11	Yes
4	16 years	White	No	Neuromuscular crisis	Hypotension	6	$N_{\rm o}$
7	7 years	White	No	Inflammatory bowel disease	Disseminated into intravascular coagulation leading to bradycardia	4	No
∞	13 years	Black or African American	No	Status epilepticus	Bradycardia during intracranial shunt sampling	∞	Yes
6	1 month	White	No	Alveolar capillary dysplasia	Bradycardia during ECMO transition	2	No
10	16 years	Black or African American	No	Congenital heart disease complicated by coronary artery thrombosis	Ventricular fibrillation during induction of anesthesia	19	$_{ m O}$
11	4 months	Asian	$N_{\rm o}$	Pulmonary hypertension	Hypoxemia due to poor ECMO circulation	က	Yes
12	13 years	White	No	Sepsis	Hypotension	2	Yes
13	2 months	White	No	New onset epilepsy	Bradycardia after secretion suctioning	င	Yes
14	6 months (4 months PMA)	White	No	Congenital heart disease with pulmonary hypertension	Pulmonary hypertension	18	m No
15	2 weeks (38 weeks PMA)	Black or African American	No	Viral meningoencephalitis complicated by myocarditis	Hypotension	4	Yes
16	3 months	White	No	Congenital heart disease and respiratory distress	Ventricular fibrillation during ECMO cannulation	11	Yes
17	6 months	White	No	Bronchiolitis	Hypotension due to hemorrhage	2	Yes
18	5 months	White	$N_{\rm O}$	Multiple intracranial abnormalities complicated by apneic events	Apnea during blood draw	П	Yes
DMA -	noct monetrn	- nost-monstrus age ECMO	- Oxfraggarous	more a mombre no oxizone tion			

PMA = post-menstrual age, ECMO = extracorporeal membrane oxygenation

Table 2: Patient clinical information

To examine the interactions between brain activity and other key variables, we split the patient cohort in two ways. We split the cohort based on age into a group of infants under one year old, and a group of children and adolescents 7 years old and older, in order to investigate a possible age difference. We also separately split the cohort into surviving and nonsurviving patients, in order to investigate any indications of outcome in the brain's electrophysiology.

2.2 Electrophysiological signal processing and analyses

We first preprocessed the EEG data by applying a standard bipolar montage LB-18.1 (Acharya et al, 2016), subtracting the mean, and dividing by the mean absolute deviation. We then computed a multi-taper spectrogram (Babadi and Brown, 2014) of each channel, and clipped all spectrograms to times ranging from 40 minutes prior to arrest to 40 minutes after arrest, where arrest is defined as time of CPR. In some patients, recordings were not present for this entire 80-minute window. In these cases, we zero-padded the spectrograms and timeseries in order to provide recordings of a uniform length with arrests centered at 0.

To evaluate the central tendency of spectral activity across the brain in a patient, we calculated the spectrogram for each channel and took the median across channels for each time-frequency point. This is similar to the mean spectrogram of a given patient, but using the median rather than the mean makes it more robust to outlying signals such as motion artifact. The median spectrogram for eight of our 16 patients is shown in Fig. 1. We then took the median spectrogram across all patients and channels, in order to examine the spectral structures common across all patients. Time points which consist entirely of padding zeros do not figure in the median calculation. This cross-patient median spectrogram is shown in Fig. 2.

In addition to using the spectrogram as a tool of analysis, we also used the 90% spectral edge frequency (Szeto, 1990) (SEF90) as a low-dimensional quantification of spectral changes. The SEF90 is the frequency below which 90% of the power in the spectrogram resides. The SEF90 can account for changes in the band-specific power structure, and can provide a low-dimensional proxy for spectral changes observed by eye. Figs. 1 and 2 overlay the SEF90 on top of the spectrogram itself in order to show the edge changes alongside the full spectral changes.

To analyze the temporal changes in brain electrophysiology as the body enters cardiac arrest, we take the SEF90 for each patient and channel, and categorize them as pre-arrest, peri-arrest, and post-arrest. We define pre-arrest time points as 40 minutes prior to arrest time to 2 minutes prior to arrest time, peri-arrest as 2 minutes prior to arrest time to 12 minutes post arrest time, and post-arrest as 12 minutes post arrest time to 40 minutes post arrest. After making these divisions, we then compare the distributions of the SEF90 in each category, and can test for significant differences using two-sample t-tests.

3 Results

3.1 Alpha Delta Ratio Decreases Prior to Arrest

The alpha delta ratio (ADR) decreases, indicating a higher proportion of delta range frequencies (0.5-2Hz) two minutes prior to arrest in both infants and children. The ADR decreases from baseline (calculated at 20 minutes prior to arrest) by 27% in the infant group and by 63% in the child group.

3.2 Narrowband Structure Localizes to Time of Arrest

As shown in Fig. 1, each arrest is individualized. Nevertheless there are some common structures which appear in multiple spectrograms in Fig. 1, as well as the median spectrogram in Fig. 2. Most noticeably, there is narrowband activity in the delta and theta frequency ranges with a strong 2Hz rhythm which emerges around the time of arrest in many of the patients (e.g., Patients 1, 2, 3, 7, 12, and 14 in Fig. 1) and in the median spectrogram across patients (Fig. 2). This narrowband structure is characterized by a transition in the power spectrogram from typical diffuse activity to a highly rhythmic structure, characterized by a 2Hz oscillation and harmonics occurring at multiples of 2Hz. These harmonics steadily decrease in power as they reach into the low theta frequency range. These higher harmonics appear to be patient-specific: in the median across all patients, they are not present, but the 2Hz oscillation is still observable (Fig. 2). Since this oscillation is occurring during CPR, there is a possible confound due to motion artifact from chest compressions. We believe this is not the case, and provide a fuller discussion below 4.2.

3.3 Cardiac Arrest is Associated with Increase in Spectral Edge Frequency

In addition to this narrowband activity, we observed a loss of power in the lower delta frequency range (0.5 - 1.5Hz) during arrest. This is reflected in a rise in the spectral edge frequency, since power is less concentrated at these

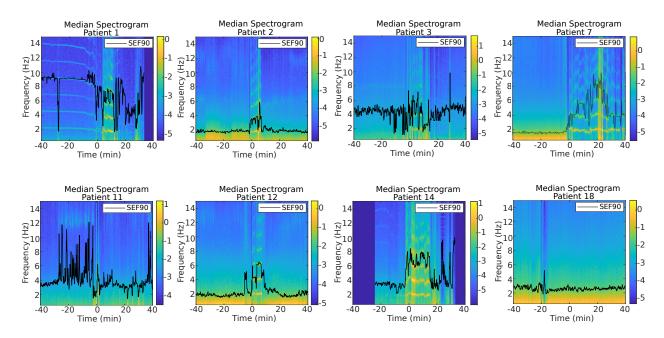


Figure 1: Cardiopulmonary arrest is evident in frequency-domain EEG analysis. Median spectrogram and 90% spectral edge frequency (SEF90) for eight of the sixteen cardiac arrest patient. Recordings are zero-padded (solid dark blue) when the recording does not cover the entire 80-minute window surrounding the arrest. Each arrest occurs at t=0 min.

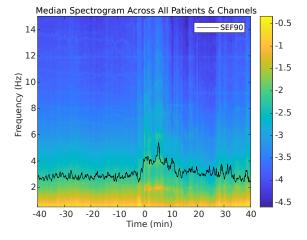


Figure 2: Narrowband frequency structure is observed in the cross-patient median. Median spectrogram and SEF90, calculated across all patients and channels. Arrest occurs at t=0.

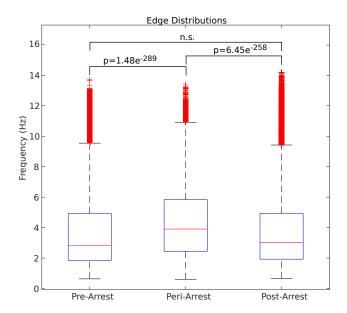


Figure 3: Spectral edge frequency is significantly elevated during arrest. Distribution of spectral edge frequencies at pre-arrest time points, peri-arrest time points, and post-arrest time points. Significance calculated using two-sample t-test in MATLAB.

low frequencies. The comparison of the SEF90 prior to, during, and after arrest is shown in Fig. 3. We observed a significant change in the edge distributions between the pre-arrest and peri-arrest periods, and between the peri-arrest and post-arrest periods.

3.4 Intensity of Observed Spectral Effects Reflects Differences in Outcome and Age

When we split the cohort by outcome and calculated the median spectrogram for each group (Fig. 4), we noticed that both the observed narrowband activity and the rise in SEF90 were stronger and more persistent in the patients who did not survive than in the patients who did. To a lesser extent, this same difference in narrowband activity is seen between the children and infant populations (Fig. 5).

Our observations about the strength of the effects of arrest is also reflected in the changes in spectral edge frequency. We observed that the change in median SEF90 from pre-arrest timepoints to peri-arrest timepoints is 160% larger in nonsurviving patients than in the whole cohort, and 95.5% larger in children (Fig. 6). Additionally, the SEF90 returns to levels close to the original levels in surviving patients, but remains high in nonsurviving patients, indicating that it is capturing a level of pathology.

4 Discussion

4.1 Changes in Alpha Delta Ratio Herald Clinical Decompensation

The ADR in both infants and children decreases from baseline in the minutes prior to cardiopulmonary arrest. This change reflects a relative increase in delta-range frequencies which are seen with neurologic dysfunction. Thus, these results suggest that there are CEEG markers of physiologic changes prior to the need for resuscitation. As the ADR is a computed value that can be accessible at the bedside by non-neurologists, our results suggest that tracking the ADR could provide additional neurologic monitoring for critically ill patients.

4.2 Observed EEG Spectral Patterns are Independent of CPR

Since the observed 2Hz narrowband structure is a strong effect occurring at the same time as CPR was being performed on the patients, we wondered if perhaps it was just artifact caused by the CPR. To investigate this, we compared the time domain EEG signals from each channel with their respective spectrograms, to see if artifact from CPR could account for this structure. While we did observe CPR artifact as described by time domain studies

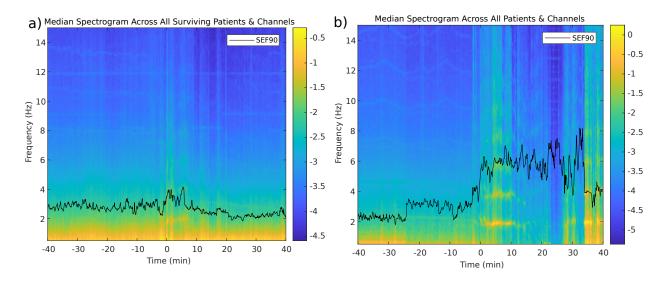


Figure 4: Narrowband structure is stronger and more persistent in nonsurviving patients. Median spectrogram and SEF90, calculated across all channels in a) surviving patients, b) nonsurviving patients.

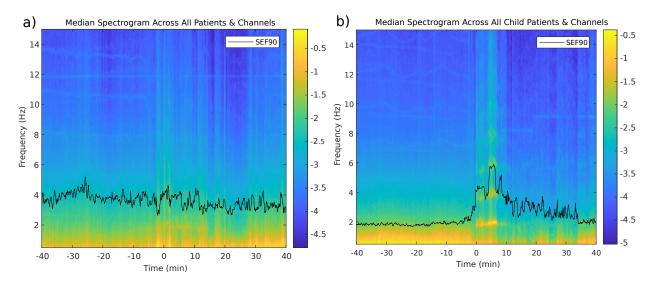


Figure 5: Narrowband structure is stronger in older patients. Median spectrogram and SEF90, calculated across all channels in a) infant patients under 2 years old, b) child & adolescent patients 7 years old and older.

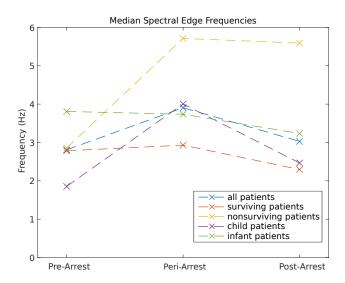


Figure 6: Median change in SEF90 reflects qualitative changes in spectrograms. Median spectral edge frequencies at pre-arrest, peri-arrest, & post-arrest time points for each cohort.

(Schäuble et al, 2002; Sethi et al, 2008) in the patients, the CPR interventions overall did not correspond well with the narrowband activity we observed. In some patients (e.g., Fig. 7a), the CPR lasts longer than the narrowband activity. In other channels, the reverse is true (e.g., Fig. 7b). Some patients who did not receive CPR compressions did exhibit the narrowband activity (Fig. 7c), and some patients who received CPR compressions did not exhibit this activity (Fig. 7d). As a result, we can conclude that this narrowband activity spectral pattern is likely a true physiological effect proximal to the time of arrest and not merely a result of CPR.

4.3 Age Difference in Observed EEG Activity Confounded By Survival Rate

We notes differences in the spectrogram patterns and SEF90 in children compared to infants, as well as surviving patients compared to nonsurviving patients. These results indicate that there could be an age difference and an outcome difference, but they are confounded by the survival rates of the two age cohorts. Four of the seven children in the cohort did not survive their arrest, but only two of the nine infants in the cohort did not survive their arrest. Since the effect is strongest between the surviving and nonsurviving populations, it seems more likely that this is an effect related to outcome rather than related to age.

4.4 Observed EEG Activity Corresponds to Negative Outcomes

The changes that we see in the spectrogram at time of arrest clearly indicate that the brain electrophysiology is changing in response to a dramatic change in hemodynamics caused by the arrest. This is consistent with previous work which has noted changes in electrophysiology in the time domain. Reagan et al noted several patterns which occur during cardiac arrest, including delta background activity and rhythmic delta activity (Reagan et al, 2018). In this study, the authors used NIRS to provide a measurement of regional cerebral oxygen saturation (rSO₂), and were able to relate the observed electrophysiology to level of rSO₂. They noted that delta background activity was only present at rSO₂ levels higher than 40%, which corresponded to a more positive overall outcome. Our observations in the spectral domain support this - we observed a decrease in the background delta activity seen in the minutes prior to arrest, which was more pronounced in nonsurviving patients (Fig. 4). This loss of low frequency power is reflected in the sharp increase in SEF90 between pre-arrest timepoints and peri-arrest timepoints (Fig. 3). This loss of low-delta power follows a decrease in the ADR, which indicates a loss of alpha power relative to delta power during the arrest.

In addition to a loss of low-delta power, we also see a broadband loss of power during and after arrest, especially at timepoints 20-35 minutes after time of arrest in the nonsurviving patients (Fig. 4b). A broadband loss of power such as this is an indication of an attenuation in EEG amplitude, known as suppression. In general, suppression is associated with poor outcomes post cardiac arrest (Sadaka et al, 2015; Søholm et al, 2014). This can indicate a general lack of cortical activity (Benghanem et al, 2022; Sandroni et al, 2020; Monteiro et al, 2016), and potentially a lack of rSO₂ (Reagan et al, 2018).

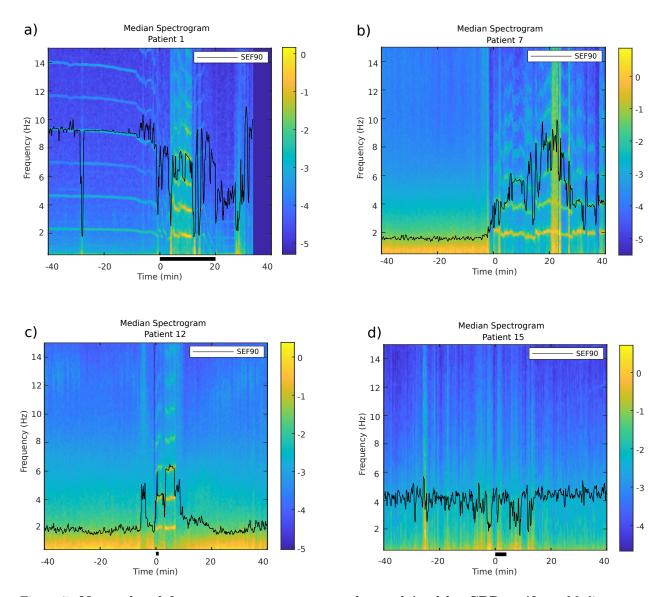


Figure 7: Narrowband frequency structure cannot be explained by CPR artifact. Median spectrogram plots with CPR times indicated by the thick black line for 4 patients. a) Patient 1, who received 20 minutes of CPR. b) Patient 7, who did not receive CPR compressions due to being in ECMO cannulation surgery at time of arrest. c) Patient 12, who received 1 minute of CPR. d) Patient 15, who received 4 minutes of CPR.

In addition to the broadband and low-delta losses of power, the main activity we observed is highly synchronous, characterized by a narrowband activity with a strong 2Hz rhythm. Often, rhythmic or periodic patterns such as this are an indication of pathology. They can be an indication of epileptic activity (Maciel and Hirsch, 2018), and have been specifically noted to correlate to negative outcomes post cardiac arrest (Benghanem et al, 2022; Sandroni et al, 2023; Rossetti et al, 2016). The rhythmic structures we observed during arrest are stronger in the nonsurviving group than the surviving group, whose spectral activity was more diffuse throughout the arrest. This indicates that the spectral pattern could be an indicator of worse outcomes, or of a more severe effect of the arrest on brain physiology, and further confirms that these rhythmic patterns can be a useful indication of outcome for cardiac arrest patients.

In particular, Reagan et al noted rhythmic delta activity in their patients (Reagan et al, 2018), which is characterized by a strong rhythm in the delta range. This could be similar to the narrowband activity we observed, with its 2Hz rhythm firmly in the delta frequency band. However, they only observed it in 12.5% (n=2/16) of their patients, whereas we observed the 2Hz narrowband activity in 62.5% (n=10/16) of our patients. This discrepancy could be due to the differences in observing frequency activity in the time domain (as in (Reagan et al, 2018)), and in the frequency domain as we have. The rhythmic delta activity observed by Reagan et al did not correspond significantly to rSO₂ as delta background activity did. By identifying this narrowband activity characterized by a strong 2Hz rhythm associated with poorer outcomes, we set the stage for asking more specific questions about how highly synchronized delta activity relates to outcome in cardiac arrest patients.

4.5 Practicality of EEG as a Prognostic Tool

CEEG captures information relating to the clinical status of the brain, and, therefore, can provide important information related to survival of cardiopulmonary arrest and subsequent brain injury. Most researchers agree that using EEG as a prognostic tool in cases of cardiac arrest is feasible (Roberti et al, 2023; Feng et al, 2016; Reagan et al, 2018; Benghanem et al, 2022), though there are still challenges to be addressed.

Artifact is a significant barrier to the interpretation of CEEG given the amount of interference from both patient care and other machines used in the ICU (Chollet-Xémard et al, 2009; Dumans-Nizard et al, 2010; Nitzschke and Schmidt, 2012), particularly in the time domain. As we addressed in section 4.2, however, the artifact from CPR did not interfere significantly with the large scale frequency features we observed. Even in the time domain, researchers have found that CPR artifact is often limited to a few channels and has a stereotyped form (Schäuble et al, 2002; Sethi et al, 2008). When CPR artifact can be identified, it can be ignored or removed for the prognostic analysis of the data.

Another challenge in using EEG as a prognostic tool is the difficulty of connecting EEG leads while the patient is undergoing CPR, particularly in out of hospital cardiac arrests. This is an ongoing challenge, though Reagan et al conducted promising work using a 4-lead EEG system which was applied to the patients' foreheads at time of CPR. To test the potential for using a smaller montage, we calculated the median spectrogram and SEF90 for the surviving and nonsurviving patients using only the 4 frontal and anterior temporal leads, montaged to the first 3 channels of the standard transverse bipolar montage TB-18.1 (Acharya et al, 2016). As shown in Fig. 8, the structures we observed with the full montage data are also present in the frontal lead only data, indicating that these results are robust to a reduction to frontal leads only. In hospital cardiac arrests may also benefit from this simplified EEG system as a useful tool for prognosis in cardiac arrest cases.

Studies have found that vital sign changes trended over time can signal an impending in-hospital cardiopulmonary arrest even 20 minutes prior to clinical decompensation (Kennedy et al, 2015). Cerebral near-infrared spectroscopy (NIRS) has become a standard monitoring modality in the PICU to allow for neurologic monitoring in critically ill children. NIRS measures regional oxyhemoglobin saturation which has been correlated with SVC oxygenation (Loomba et al, 2022), increased lactate levels (Chakravarti et al, 2009) and, therefore, global tissue perfusion. However, population limitations have been noted with this modality, particularly children with congenital heart disease and profound cyanosis (Finucane et al, 2020). This poses a significant limitation in utility as these population represent an important part of infants and children in the ICU. Given the variable sensitivity and the specificity of NIRS as well as the complexity of neurologic response to critical illness, successful neurologic monitoring in the ICU likely lies within a robust multimodality monitoring system (Finucane et al, 2020; Massey et al, 2024). We believe that the prognostic information given by EEG monitoring prior to, during, and in the wake of cardiopulmonary arrest demonstrates the value of including CEEG in such a multimodal monitoring system.

4.6 Limitations

This was a retrospective analysis of children who experienced cardiopulmonary arrest while undergoing EEG monitoring, and thus is limited in several aspects. First, this is a low-n study and should be extended to analysis in a larger population. Second, due to the low number of patients, there is a confound present in the age difference analysis since many of the older children did not survive their arrests, and many of the infants did. Finally, all the

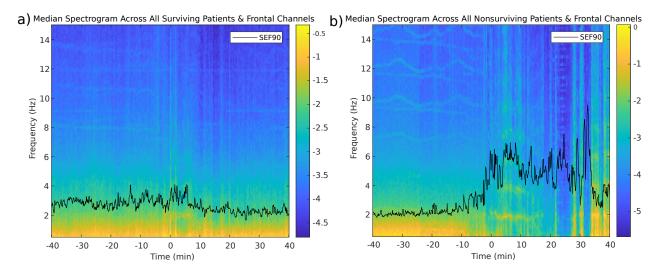


Figure 8: Results remain consistent when limited to frontal leads only. Median spectrogram and SEF90, calculated across the four frontal channels in a) surviving patients, b) nonsurviving patients.

patients had existing medical conditions prior to arrest indicating a need for EEG monitoring. Given the limited size and heterogeneous nature of the current cohort, further studies are needed for replication and generalizability of these findings.

4.7 Future Directions

This work can be extended in a few different ways. Larger studies with more subjects should examine the frequency-domain characteristics of EEG prior to and during cardiopulmonary arrest in order to understand the utility of CEEG in neurologic monitoring of patients at risk for cardiopulmonary decompensations, to understand the significance of rhythmic patterns in patients who experience an arrest event, and to investigate a potential age difference without the confound of survival rate. Additionally, this work sets the stage for more general questions about the brain's relationship to hemodynamics. Understanding how patterns in electrophysiology during cardiac arrest relate to patterns in electrophysiology during less extreme events can help us gain a better understanding of the relationship between the heart and brain more generally.

4.8 Conclusion

In conclusion, we have characterized frequency structures observed surrounding cardiopulmonary arrest in infants and children. By noting these changes in electrophysiology, we can conclude that brain activity is indeed linked to hemodynamics, and is significantly disrupted in cases of extreme reduction in cerebral blood flow. Further investigation of these responses, in both cardiac arrest and less severe clinical decompensations, can lead to greater understanding of how the brain responds to systemic changes. Additionally, we associated the strength of certain frequency structures with worse outcomes post-arrest. Understanding the prognostic significance of these trends can be useful in understanding the ways in which the brain recovers from hemodynamic instability, subsequent neurologic injury, and in identifying patients who require more aggressive care than others.

Author Contributions

A.S. contributed to study design, EEG analysis, and manuscript preparation. C.G. contributed to study design, data collection, clinical data analysis, and manuscript preparation. R.L., T.F., and S.T. contributed to data collection and clinical data analysis. Z.K. contributed to EEG analysis. S.C. and R.G. contributed to study design and guidance. All authors have approved the final article.

Conflict of Interest Statement

None of the authors have potential conflicts of interest to be disclosed.

Acknowledgements

The authors would like to thank Samuel Brunwasser for his helpful comments during the preparation of this manuscript. This research was funded in part by the US National Institutes of Health [grant numbers R01NS130693, T32NS126157].

References

- Abend, NS, Chapman, KE, Gallentine, WB, Goldstein, J, Hyslop, AE, Loddenkemper, T, et al. Electroencephalographic monitoring in the pediatric intensive care unit. Curr neurol neurosci rep, 2013;13:1–10. https://doi.org/10.1007/s11910-012-0330-3.
- Acharya, JN, Hani, AJ, Thirumala, PD, Tsuchida, TN. American clinical neurophysiology society guideline 3: A proposal for standard montages to be used in clinical eeg. J Clin Neurophysiol, 2016;33:312–16. https://doi.org/10.1097/WNP.0000000000000317.
- Babadi, B, Brown, EN. A review of multitaper spectral analysis. IEEE Transactions on Biomedical Engineering, 2014;61:1555–64. https://doi.org/10.1109/TBME.2014.2311996.
- Benghanem, S, Pruvost-Robieux, E, Bouchereau, E, Gavaret, M, Cariou, A. Prognostication after cardiac arrest: how eeg and evoked potentials may improve the challenge. Ann Intensive Care, 2022;12:111. https://doi.org/10.1186/s13613-022-01083-9.
- Bruhn, J, Bouillon, TW, Shafer, SL. Bispectral index (bis) and burst suppression: revealing a part of the bis algorithm. J Clin Monit Comput, 2000;16:593–6. https://doi.org/10.1023/A:1012216600170.
- Chakravarti, SB, Mittnacht, AJ, Katz, JC, Nguyen, K, Joashi, U, Srivastava, S. Multisite near-infrared spectroscopy predicts elevated blood lactate level in children after cardiac surgery. J Cardiothorac Vasc Anesth, 2009;23:663–7. https://doi.org/10.1053/j.jvca.2009.03.014.
- Chawla, LS, Akst, S, Junker, C, Jacobs, B, Seneff, MG. Surges of electroencephalogram activity at the time of death: a case series. J Palliat Med, 2009;12:1095–100. https://doi.org/10.1089/jpm.2009.0159.
- Chollet-Xémard, C, Combes, X, Soupizet, F, Jabre, P, Penet, C, Bertrand, C, et al. Bispectral index monitoring is useless during cardiac arrest patients' resuscitation. Resuscitation, 2009;80:213–6. https://doi.org/10.1016/j.resuscitation.2008.10.011.
- Claassen, J, Taccone, FS, Horn, P, Holtkamp, M, Stocchetti, N, Oddo, M. Recommendations on the use of eeg monitoring in critically ill patients: Consensus statement from the neurointensive care section of the esicm. Intensive Care Med, 2013;39:1337–51. https://doi.org/10.1007/s00134-013-2938-4.
- Dumans-Nizard, V, Hamada, S, Fischler, M. Bispectral index during cardiopulmonary resuscitation: A poor indicator of recovery. two very different cases. Anaesthesia, 2010;65:196–8. https://doi.org/10.1111/j.1365-2044.2009.06163.x.
- Feng, G, Jiang, G, Li, Z, Wang, X. Prognostic value of electroencephalography (eeg) for brain injury after cardiopulmonary resuscitation. Neurol Sci, 2016;37:843–9. https://doi.org/10.1007/s10072-016-2475-3.
- Finucane, E, Jooste, E, Machovec, KA. Neuromonitoring modalities in pediatric cardiac anesthesia: a review of the literature. J Cardiothorac Vasc Anesth, 2020;34:3420–8. https://doi.org/10.1053/j.jvca.2020.02.054.
- Goodman, PG, Mehta, AR, Castresana, MR. Predicting ischemic brain injury after intraoperative cardiac arrest during cardiac surgery using the bis monitor. J Clinical Anesth, 2009;21:609–12. https://doi.org/10.1016/j.jclinane.2009.01.014.
- Kennedy, CE, Aoki, N, Mariscalco, M, Turley, JP. Using time series analysis to predict cardiac arrest in a picu. Pediatr Crit Care Med, 2015;16:e332–9. https://doi.org/10.1097/PCC.000000000000560.
- Loomba, RS, Rausa, J, Sheikholeslami, D, Dyson, AE, Farias, JS, Villarreal, EG, et al. Correlation of near-infrared spectroscopy oximetry and corresponding venous oxygen saturations in children with congenital heart disease. Pediatr cardiol, 2022;43:197–206. https://doi.org/10.1007/s00246-021-02718-7.
- Maciel, CB, Hirsch, LJ. Definition and classification of periodic and rhythmic patterns. J Clin Neurophysiol, 2018;35:179–88. https://doi.org/10.1097/WNP.0000000000000462.

- Massey, SL, Weinerman, B, Naim, MY. Perioperative neuromonitoring in children with congenital heart disease. Neurocrit Care, 2024;40:116–29. https://doi.org/10.1007/s12028-023-01737-x.
- Monteiro, ML, Taccone, FS, Depondt, C, Lamanna, I, Gaspard, N, Ligot, N, et al. The prognostic value of 48-h continuous eeg during therapeutic hypothermia after cardiac arrest. Neurocrit Care, 2016;24:153–62. https://doi.org/10.1007/s12028-015-0215-9.
- Ney, JP, van der Goes, DN, Nuwer, MR, Nelson, L, Eccher, MA. Continuous and routine eeg in intensive care: utilization and outcomes, united states 2005–2009. Neurology, 2013;81:2002–8. https://doi.org/10.1212/01.wnl.0000436948.93399.2a.
- Nitzschke, R, Schmidt, GN. Electroencephalography during out-of-hospital cardiopulmonary resuscitation. J Emerg Med, 2012;43:659–62. https://doi.org/10.1016/j.jemermed.2010.05.098.
- Nolan, JP, Sandroni, C, Böttiger, BW, Cariou, A, Cronberg, T, Friberg, H, et al. European resuscitation council and european society of intensive care medicine guidelines 2021: Post-resuscitation care. Resuscitation, 2021;161:220– 69. https://doi.org/10.1016/j.resuscitation.2021.02.012.
- Pollack, MM, Holubkov, R, Berg, RA, Newth, CJ, Meert, KL, Harrison, RE, et al. Predicting cardiac arrests in pediatric intensive care units. Resuscitation, 2018;133:25–32. https://doi.org/10.1016/j.resuscitation.2018.09.019.
- Reagan, EM, Nguyen, RT, Ravishankar, ST, Chabra, V, Fuentes, B, Spiegel, R, et al. Monitoring the relationship between changes in cerebral oxygenation and electroencephalography patterns during cardiopulmonary resuscitation: A feasibility study. Crit Care Med, 2018;46:757–63. https://doi.org/10.1097/CCM.00000000000003014.
- Roberti, E, Chiarini, G, Latronico, N, Adami, EC, Plotti, C, Bonetta, E, et al. Electroencephalographic monitoring of brain activity during cardiac arrest: a narrative review. ICMx, 2023;11:4. https://doi.org/10.1186/s40635-022-00489-w.
- Rossetti, AO, Rabinstein, AA, Oddo, M. Neurological prognostication of outcome in patients in coma after cardiac arrest. Lancet Neurol, 2016;15:597–609. https://doi.org/10.1016/S1474-4422(16)00015-6.
- Sadaka, F, Doerr, D, Hindia, J, Lee, KP, Logan, W. Continuous electroencephalogram in comatose postcardiac arrest syndrome patients treated with therapeutic hypothermia: Outcome prediction study. Journal of Intensive Care Medicine, 2015;30:292–6. https://doi.org/10.1177/0885066613517214.
- Sandroni, C, Cronberg, T, Hofmeijer, J. Eeg monitoring after cardiac arrest. Intensive Care Med, 2022;48:1439–42. https://doi.org/10.1007/s00134-022-06697-y.
- Sandroni, C, D'Arrigo, S, Cacciola, S, Hoedemaekers, CW, Kamps, MJ, Oddo, M, et al. Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review. Intensive Care Med, 2020;46:1803–51. https://doi.org/10.1007/s00134-020-06198-w.
- Sandroni, C, Grippo, A, Westhall, E. The role of the electroencephalogram and evoked potentials after cardiac arrest. Curr Opin Crit Care, 2023;29:199–207. https://doi.org/10.1097/MCC.0000000000001031.
- Schäuble, B, Klass, DW, Westmoreland, BF. Resuscitation artifacts during electroencephalography. American Journal of Electroneurodiagnostic Technology, 2002;42:16–21. https://doi.org/10.1080/1086508X.2002.11079371.
- Sekhon, MS, Ainslie, PN, Griesdale, DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: A "two-hit" model. Crit Care, 2017;21:90. https://doi.org/10.1186/s13054-017-1670-9.
- Sethi, NK, Torgovnick, J, Sethi, PK, Arsura, E. Cardiopulmonary resuscitation artifact during electroencephalography. Clin EEG Neurosci, 2008;39:214–6. https://doi.org/10.1177/155005940803900413.
- Stammet, P, Werer, C, Mertens, L, Lorang, C, Hemmer, M. Bispectral index (bis) helps predicting bad neurological outcome in comatose survivors after cardiac arrest and induced therapeutic hypothermia. Resuscitation, 2009;80:437–42. https://doi.org/10.1016/j.resuscitation.2009.01.008.
- Szeto, HH. Spectral edge frequency as a simple quantitative measure of the maturation of electrocortical activity. Pediatr Res, 1990;27:289–92. https://doi.org/10.1203/00006450-199003000-00018.
- Søholm, H, Kjær, TW, Kjaergaard, J, Cronberg, T, Bro-Jeppesen, J, Lippert, FK, et al. Prognostic value of electroencephalography (eeg) after out-of-hospital cardiac arrest in successfully resuscitated patients used in daily clinical practice. Resuscitation, 2014;85:1580–5. https://doi.org/10.1016/j.resuscitation.2014.08.031.