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Clinical paper

Integrating rSO_2 and EEG monitoring in cardiopulmonary resuscitation: A novel methodology

Samantha Shellen[a,*], *Sam Parnia*[a,b], *Elise L. Huppert*[a], *Anelly M. Gonzales*[a], *Kenna Pollard*[a]

Abstract

Despite improvements in cardiopulmonary resuscitation (CPR), survival and neurologic recovery after cardiac arrest remain poor due to ischemia and subsequent reperfusion injury. As the likelihood of survival and favorable neurologic outcome decreases with increasing severity of ischemia during CPR, developing methods to measure the magnitude of ischemia during resuscitation is critical for improving overall outcomes. Cerebral oximetry, which measures regional cerebral oxygen saturation (rSO_2) by near-infrared spectroscopy, has emerged as a potentially beneficial marker of cerebral ischemia during CPR. In numerous preclinical and clinical studies, higher rSO_2 during CPR has been associated with improved cardiac arrest survival and neurologic outcome. There is also emerging evidence that this can be integrated with electroencephalogram (EEG) monitoring to provide a bimodal system of brain monitoring during CPR. In this method's review, we discuss the feasibility, application, and implications of this integrated monitoring approach, highlighting its significance for improving clinical outcomes in cardiac arrest management and guiding future research directions.

Keywords: Cardiopulmonary resuscitation, Cardiac arrest, Electroencephalography, Hypoxic ischemic brain injury, Cerebral oximetry

Introduction and background information

Despite significant medical advancements over the last six decades, there has been little improvement in cardiac arrest (CA) survival.[1] In the inaugural multicenter analysis of adult in-hospital cardiac (IHCA) arrest published in 1953, the overall mortality rate stood at 72%.[2] In contrast, a 2006 US study involving 36,902 adults revealed a mortality rate of 82%.[3] Similarly, a contemporary UK study encompassing 24,132 IHCA reported an overall mortality rate of 71%.[4] Furthermore, the mortality rate in 2021 among 45,815 IHCA remained at 81%.[5] Among survivors, long-term neurological impairments are frequently observed. As a result, only 3–7% of CA patients survive and regain their pre-arrest functional status.[1,6,7]

Adverse survival and neurological outcomes result from a two-step process known as ischemia/reperfusion injury. The ischemic phase, initiated by the loss of heartbeat, induces a no-/low-flow state.[6,8–10] Upon return of spontaneous circulation (ROSC), the reintroduction of oxygen contributes to reperfusion injury and inflammation, compounded by vasoconstriction in the immediate post-resuscitation period. This leads to significant reduction in cerebral blood flow (CBF), causing further ischemia.[8] As the severity of the secondary injury process is proportional to the magnitude of the

Abbreviations: ACLS, Advanced Cardiovascular Life Support, AHA, American Heart Association, BSA, Burst Suppression & Attenuation, CA, Cardiac Arrest, CBF, Cerebral Blood Flow, CPC, Cerebral Performance Category, CPR, Cardiopulmonary Resuscitation, ECMO, Extracorporeal Membrane Oxygenation, E-CPR, Extracorporeal Membrane Oxygenation Assisted Cardiopulmonary Resuscitation, EEG, Electroencephalogram, ETCO2, End-Tidal Carbon Dioxide, HIPAA, Health Insurance Portability and Accountability Act, IHCA, In-Hospital Cardiac Arrest, IRB, Institutional Review Board, LPD, Lateralized Periodic Discharges, LAR, Legally Authorized Representative, NIRS, Near-Infrared Spectroscopy, OHCA, Out-of-Hospital Cardiac Arrest, ROSC, Return of Spontaneous Circulation, rSO2, Regional Cerebral Oxygen Saturation, RDA, Rhythmic Delta Activity, V/Q, Ventilation/Perfusion

* Corresponding author at: Critical Care & Resuscitation Research Associate, Division of Pulmonary, Critical Care and Sleep Medicine, 462 1st Ave, Suite CD 636, New York, NY 10016, USA.

E-mail address: samantha.shellen@nyulangone.org (S. Shellen).

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ischemic phase, one method that may help improve survival and neurological outcomes is a monitoring system to detect the depth of ischemia.[1,6,8–10] This would enable clinicians to implement real-time changes to reduce the degree of ischemia during CA, and consequently mitigate injury during the ischemia/reperfusion injury processes.

The current American Heart Association (AHA) guidelines recommend end-tidal carbon dioxide ($ETCO_2$) to monitor cardiopulmonary resuscitation (CPR) quality.[11] $ETCO_2$ tracks changes in pulmonary blood flow and cardiac output during CPR.[12] While $ETCO_2$ correlates with chest compression depth and is associated with ROSC, it does not provide information about the depth of ischemia.[13] Therefore, measuring oxygen delivery and uptake could be a more meaningful marker of resuscitation quality. Additional limitations are that $ETCO_2$ cannot be readily used in non-intubated patients and the measurements can be impacted by the use of epinephrine and sodium bicarbonate. Changes in ventilation in combination with underlying pulmonary disorders can also cause ventilation/perfusion (V/Q) mismatch.[14–18]

Traditionally, electroencephalogram (EEG) monitoring has been used in clinical settings to detect the depth of cerebral ischemia.[19] Studies have shown that as CBF drops below 25–35 ml/100 g/min, there is suppression of higher frequency brain waves (for example, beta and alpha waves).[20] Subsequently, slower activity (theta, delta) emerges, eventually progressing to full suppression. However, traditional EEG cannot be used during CPR with significant motion artifact, and these systems are time-consuming to setup. Even if traditional EEG could be used, bedside physicians managing CA would not be able to readily interpret changes in EEG.

Within this context, there has been great interest in cerebral oximetry using near-infrared spectroscopy (NIRS). Cerebral oximetry reflects the balance of oxygen delivery and uptake, influenced primarily by hemoglobin concentration, arterial oxygen saturation, and cardiac output.[21] While physiological conditions maintain constant oxygen transport through compensatory mechanisms, CA overwhelms these mechanisms, causing a notable increase in oxygen extraction and a subsequent drop in cerebral oxygen saturation. Emerging data supports the use of cerebral oximetry during CPR. Multiple *meta*-analyses show a positive association between mean regional cerebral oxygen saturation (rSO_2) and subsequent ROSC. A 2022 review of 13 studies involving 678 CA patients, comprising 300 IHCA and 378 out-of-hospital cardiac arrest (OHCA) cases, revealed that patients who achieved ROSC had higher initial and mean rSO_2 levels during CPR than those without ROSC.[22] In a study of 2,436 CA cases, ROSC was rare (2.7%) when mean rSO_2 was below 30%.[23] Moreover, patients who were discharged and achieved favorable neurological outcomes exhibited higher combined initial and mean rSO_2 values than their counterparts (SMD = 1.63; 95% CI = 1.34 to 1.92; and SMD = 2.12; 95% CI = 1.14 to 3.10).

In a 2014 study, Ito et al. investigated the association between rSO_2 levels in 672 OHCA patients upon hospital arrival and their neurological outcomes 90 days after arrest.[28] The study found that the patients who exhibited positive neurological outcomes (cerebral performance category (CPC) 1 and 2) three months post-arrest had higher rSO_2 levels upon arrival at the hospital compared patients with poorer neurological outcomes (55.6 ± 20.8% vs. 19.7 ± 11.0% , $p < 0.001$). A study of 183 IHCA also found higher mean rSO_2 was associated with the 62 patient who achieved ROSC versus 121 with no ROSC (51.8% ± 11.2% vs 40.9% ± 12.3%, $p < 0.001$). In addition, there was a statistical significance in mean rSO_2 values in those that survived and achieved CPC 1–2 at discharge ($n = 13$) versus CPC 3–5 ($n = 170$) (56.1% ± 10.0% vs 43.8% ± 12.8%, $p < 0.001$).[24]

In an ideal setting, the concurrent use of rSO_2 and EEG in CPR would offer complementary brain oxygen and brain function monitoring capabilities, respectively. While traditional EEG is not feasible, there is growing evidence that portable EEG devices may be practically employed in critical care settings. Our group has pioneered the use of rSO_2 and portable EEG during CPR, first through a feasibility study among 16 subjects and, more recently, in a study of 85 IHCA.[29,30] This study found that while rSO_2 levels below ~15–20% were only associated with no measurable EEG activity, higher frequency alpha activity was only identified when rSO_2 levels exceeded 35–40%. Furthermore, we found that near-normal EEG activity can emerge up to 35–60 min into CPR, including delta, theta, alpha, and beta rhythms. This suggest there may be specific rSO_2 thresholds that correspond with the restoration of electrocortical activity, and highlights the potential of combining rSO_2 and EEG as prognostic indicators and real-time markers for assessing brain perfusion during CPR. This paper aims to describe the methods underlying the use of rSO_2 and EEG monitoring in CA.

Patient identification

Eligible patients are typically identified using the hospital's paging system. At our institution, following a CA alert, a research team member is dispatched to the location of the CA and brings the portable EEG and cerebral oximeter for immediate use.

Consenting

Given the unpredictable nature of CA events, obtaining informed consent from the unconscious patient is not feasible in real-time. As cerebral oximetry and portable EEG monitoring are noninvasive procedures that do not interfere with clinical care, a waiver of consent for minimal-risk research authorized by the Institutional Review Board (IRB) is applied. Informed consent is sought from survivors who have regained decisional capacity. If the patient cannot provide informed consent, the study team attempts to contact the legally authorized representative (LAR). If the patient or LAR declines to consent, any previously collected data is discarded.

Devices

Portable EEG and rSO_2 devices are crucial for the success of this research. While there are various models of these devices on the market, we have experience in utilizing the SedLine Brain Function Monitor (Masimo, Irvine, CA) and the SenSmart Model X-100 M (Nonin, Plymouth, MN) for EEG and rSO_2 monitoring, respectively. The SedLine monitor has two temporal, two frontal, and two grounding electrodes integrated into an adhesive strip for convenient application across the patient's forehead. The SenSmart X-100 M employs an adhesive rSO_2 sensor applied to the patient's lateral forehead.

Equipment setup and application

In our experience, with training, the use of portable EEG and rSO_2 monitoring during CA does not impede the CPR process and takes approximately 5 min in total arrival and set-up time.[30] The preparation and setup of these devices are critical steps that ensure the equipment's readiness for immediate use during CA. Both the portable EEG and rSO_2 devices are routinely charged and tested on control subjects. The two devices undergo a regular maintenance to ensure the two clocks are synchronized. Another method to avoid this is to use newer generation devices that have combined EEG and rSO_2 capabilities, such as the SedLine Root Monitor with O3 Regional Oximetry (Masimo, Irvine, CA). The date of its last calibration and functional status is documented in a log for each device. Each pair of EEG and rSO_2 devices is allocated to a secure bag with supplies such as processing cables and compatible sensors. Upon arrival at the CA, the research staff tests the devices and ensures the patient's forehead is dry before carefully applying the adhesive strip of electrodes. Simultaneously, the rSO_2 sensor is placed on the lateral side of the forehead (Fig. 1). The total time to place the EEG and rSO_2 sensors is roughly 30 s. The researcher ensures that the sensors are correctly transmitting data to the monitoring devices.

Data collection

We collect EEG data only during standard Advanced Cardiovascular Life Support (ACLS)-mandated 3–5 s pauses in chest compressions, as these intervals present minimal motion interference.[31,32] These pauses allow medical staff to check for the return of a heartbeat and to analyze cardiac rhythms for potential defibrillation. In these moments, a researcher records data by capturing a screenshot of the EEG image (using SedLine, this is carried out by swiping across the EEG device screen from right to left with four fingers (Fig. 2)). Adaptations in data collection may be required based on the EEG device used. After CPR has ended, EEG data is extracted via USB, deidentified, and stored in the patient's file corresponding to a study identification number for analysis, focusing on raw EEG activity during CPR pauses to identify brain function indicators such as alpha, beta, delta, and theta waves, as well as to detect patterns like a 'flatlined' state, burst suppression, or seizure activity.

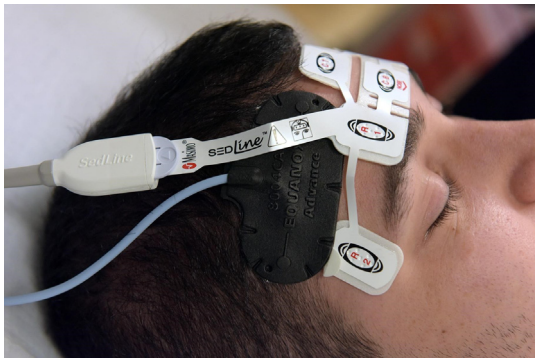

Fig. 1 – The integration of sensors for cerebral oximetry and electroencephalography (EEG) positioned on the forehead.

For rSO_2 monitoring, the device employs NIRS through a detector measuring hemoglobin saturation approximately 3 cm into the frontal lobe (Fig. 3). The device calculates % rSO_2 using the unique absorption spectra of oxy- and deoxyhemoglobin (detection range 0–100%).[33] The collection of cerebral oximetry data is continuous throughout the CA event until cardiac function is restored or CPR is halted. The data is later transferred to a study computer equipped with software provided by the oximeter manufacturer that converts the data into an Excel file associated with the patient's study identification number. Subsequently, the data is uploaded to the Health Insurance Portability and Accountability Act (HIPAA)-compliant platform for integration into the study's database.

It should be noted that during CPR, both rSO_2 and portable EEG possess dedicated functions for specific event marking, which allow for meaningful data analysis after the event.

Data analysis

EEG data interpretation involves collaboration between a trained study team member and a board-certified neurophysiologist. EEG rhythms are categorized into three types: "near-normal" (encompassing alpha, beta, theta, delta waves), "pathologic" (including Rhythmic Delta Activity (RDA), lateralized periodic discharges (LPD), burst suppression & attenuation (BSA), epileptiform patterns), and "diffuse suppression" (indicating total suppression/unmeasurable activity). The term "near-normal" is chosen, despite some rhythms potentially being physiological (such as frontal beta waves or theta/delta waves during sleep), to reflect the limited scope of the 4-lead frontotemporal EEG monitoring. Any rSO_2 readings indicative of sensor malfunctions are excluded from analysis in addition to artifact values. These are typically determined by comparing any values that are $\geq$3 SD away from the mean. We analyze rSO_2 in this manner by examining the mean rSO_2 values every five seconds. Specific CPR-related events such as ROSC or administration of epinephrine are evaluated by examining EEG and rSO_2 values based on the precise timestamps using event marking functions.

Applications in clinical practice

As previously discussed, rSO_2 is strongly predictive of ROSC and there is emerging data that it is also predictive of survival and favorable neurological outcomes.[22–28] However, the question remains, can interventions be augmented to ameliorate rSO_2.

Studies have indicated that continuous rSO_2 monitoring effectively captures real-time fluctuations in resuscitation efforts and cerebral oxygen delivery. For instance, a study involving 34 IHCA cases revealed that automated CPR resulted in a more than 20% increase in rSO_2 compared to manual CPR (53.1% ± 23.4% vs 24% ± 25%, p = 0.002) (Fig. 4). Additionally, there was a significant difference in mean rSO_2 values between patients with ROSC (n = 15) and those without ROSC (n = 19) (47.4% ± 21.4% vs 23% ± 18.42%, $p < 0.001$).[25] In a separate investigation of 36 IHCA, the effects of epinephrine on rSO_2 were examined. Cerebral oxygenation values were measured during a five-minute period preceding epinephrine injection, followed by a five-minute interval after a 1 mg epinephrine injection. The rSO_2 values showed an average increase of 1.40% in the 5 min following epinephrine administration compared to the preceding 5 min ($p < 0.05$).[34] Furthermore, in an analysis of extracorpo-

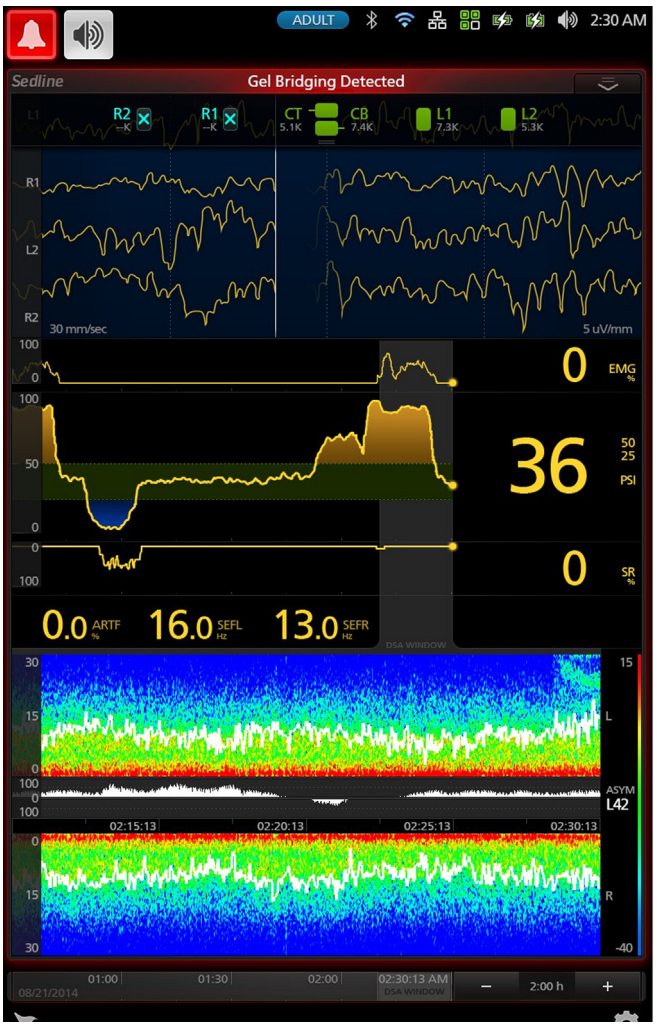

Fig. 2 – A screenshot of SedLine Root Patient Monitoring and Connectivity Platform displaying parameters and measurements as numeric values and graphical representations of the information acquired.

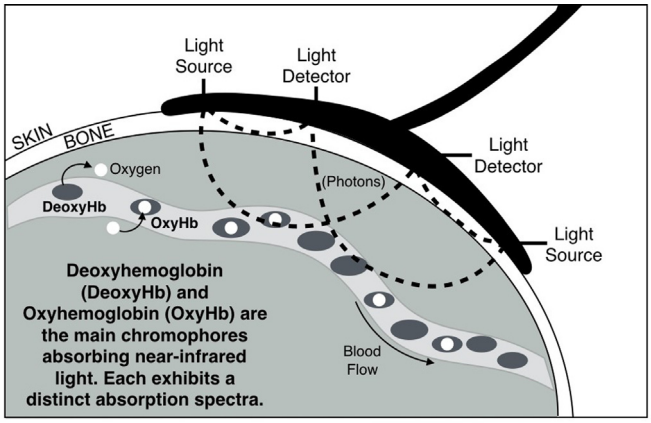

Fig. 3 – The use of NIRS to determine cerebral regional cerebral oxygen (rSO_2) saturation. Using algorithms, the cerebral oximeter subtracts oxygenation in bone, skin and dura (dark dashed curved line) and determines balance between cerebral oxy/deoxyhemoglobin.

real membrane oxygenation (ECMO) assisted CPR (E-CPR) involving 6 IHCA patients, rSO_2 values increased by an average of 20.8% in the 2.5 min after ECMO initiation ($p < 0.05$)[35] (Fig. 5).

These results have led our team at New York University to put forward a system of physiologically targeted resuscitation based on rSO_2 values. Recognizing that higher rSO_2 levels are associated with

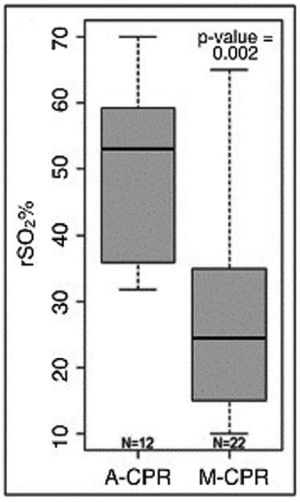

Fig. 4 – Impact of automated CPR and manual CPR on cerebral oxygen during CPR.

ROSC and survival,[22–28] we have proposed a stepwise algorithm focused on changes in chest compressions and the use of epinephrine, vasopressors, corticosteroids and ECMO to augment rSO_2 signals (Fig. 6). While the AHA recommends compressions of at least 100/min and a depth of 5 cm,[11] a study of 10,371 OHCA found that compression rates between 100–120 and depths ≥5.1–6 cm were associated with greatest survival to hospital discharge.[36] Thus, some patients may benefit from increased rate and depth of compressions (up to a rate of 120 and depth of 6 cm). Furthermore, a randomized controlled trial of ECMO vs standard ACLS in 30 OHCA concluded that survival to hospital discharge was higher with ECMO ($p < 0.0001$).[37] Another study of 100 IHCA showed the use of vasopressin, epinephrine and corticosteroid when compared to epinephrine correlated with ROSC ($p = 0.003$) and improved survival to hospital discharge ($p = 0.02$).[38] The most effective resuscitation strategy may vary depending on changing physiological conditions. Clinicians may alter their interventions in response to this, by increasing the rate or depth of the compressions, implementing

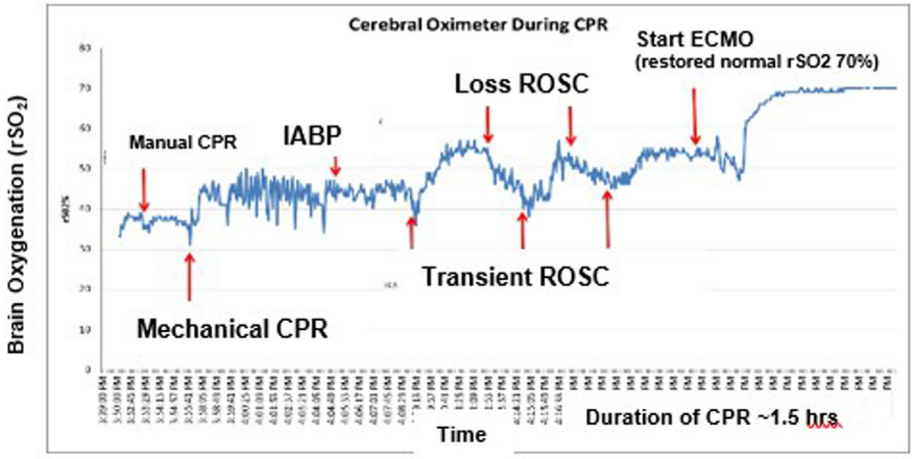

Fig. 5 – Impact of automated CPR and manual CPR on cerebral oxygen during CPR.

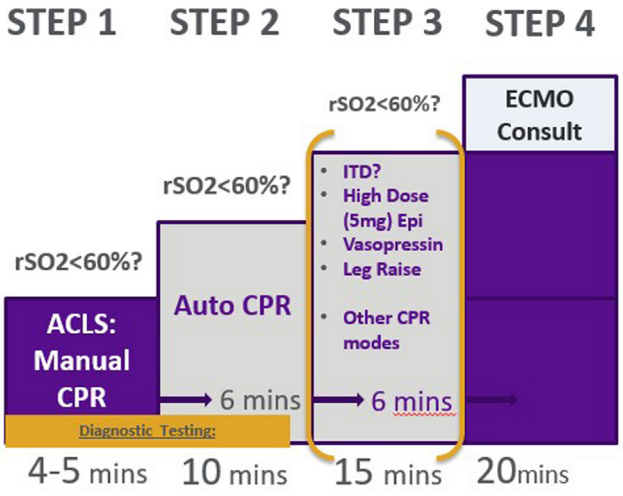

Fig. 6 – The NYU resuscitation algorithm, a step wise approach to brain targeted resuscitation.

mechanical CPR, and the combined use of epinephrine, vasopressins, and corticosteroids.

Discussion

This paper delineates a methodological framework developed in our laboratory for the integration of rSO_2 and EEG during CPR. The incorporation of this bimodal monitoring may contribute to a deeper understanding and enhancement of resuscitation strategies. Findings from our research indicate a possible role of cerebral oxygenation and brain activity in influencing CPR outcomes. The observed association between rSO_2 levels and EEG patterns during CA indicates that higher rSO_2 levels may correlate with certain EEG rhythms, suggesting improved brain perfusion and possibly more favorable outcomes.

Overall, higher rSO_2 is associated with ROSC.[22–27] Furthermore, data indicates that rSO_2 is a good measure of changes in resuscitation treatments such as epinephrine, automatic CPR, and ECMO.[25,34,35] This suggests that optimizing oxygen delivery and perfusion to the brain relies on the overall quality of circulation. However, larger studies are needed to investigate the effects of these interventions on rSO_2 levels, survival rates and neurological outcome.

While there is more evidence for the integration of cerebral oximetry in practice, there is also data emerging about the utility of combining this method with EEG.[29,30] Although brain oximetry provides data on the balance between oxygen delivery and uptake, it does not address how the brain responds to this stimulus. EEG is also a useful marker of metabolism, since the restoration of physiological EEG rhythms is indicative of metabolic activity. Thus, it can serve as an additional monitoring tool to reflect the brain's metabolic response to changes in CBF and oxygen delivery. The appearance of physiological EEG patterns during CPR may represent sufficient CBF and oxygen supply to meet the metabolic needs of the cerebral cortex. Additionally, the ability to generate physiological EEG activity would further indicate the preservation of viable cortical brain tissue, signifying it is not irreversibly damaged. While there is limited data on how EEG could inform resuscitation decisions, the absence of brain activity despite the highest level of treatment, ECMO, could be considered a potential indicator of poor recovery, while the emergence of physiological EEG activity may be associated with improved survival and neurological outcomes.

A notable challenge in the bimodal approach is the practical employment of EEG during CA. Motion artifacts inherent in CPR can substantially impact the quality of EEG data. Our approach, focusing on data capture during brief pauses in chest compressions, has demonstrated potential in mitigating this issue and capturing EEG data. The total time required for the arrival and setup of the two monitoring devices is approximately 5 min, however this will depend on staff training and may not be realistic for patients with shorter duration of compressions. It is worth noting that 3–5 min also serves as an approximate estimate for the arrival time of any CA team to the scene of the CA, contingent upon the location and size of the hospital. Furthermore, portable EEG, while advantageous for its suitability in emergent settings, offers less comprehensive data compared to traditional EEG. The limited lead system of the portable EEG restricts the breadth of cerebral activity that can be monitored, potentially affecting the depth of insights that can be derived from the data.

Based on the need to enhance treatments using physiological markers, such as cerebral oximetry, our group is pursuing additional studies, including a pilot randomized control trial that examines the effects of physiologically driven CPR compared to conventional CPR, where the physiological group receives augmented treatment in response to the need to reach a physiological target. Looking ahead, our laboratory is committed to further refining these monitoring techniques. Our objective is to extend our research to a more diverse and larger population to confirm and broaden the applicability of our findings. Larger studies are needed to investigate the role of integrated EEG and rSO_2 monitoring in guiding the optimization of CPR, which will be vital in the progress of this field.

Conclusion

The use of rSO_2 and EEG during CPR is practical and feasible and offers a novel approach to measuring ischemia and the quality of resuscitation, which may be complementary to $ETCO_2$ monitoring.

Consent/ethical approval

Not required for this review.

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CRediT authorship contribution statement

Samantha Shellen: Writing – review & editing, Writing – original draft, Project administration. **Sam Parnia:** Writing – review & editing, Visualization, Supervision, Methodology, Funding acquisition, Conceptualization. **Elise L. Huppert:** Writing – original draft. **Anelly M. Gonzales:** Project administration, Methodology. **Kenna Pollard:** Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: NYU Langone Health Department of Medicine.

Author details

[a]*Critical Care and Resuscitation Research Program, New York University Grossman School of Medicine, NYU Langone Health, New York, NY, USA* [b]*Division of Pulmonary, Critical Care & Sleep Medicine, New York University Grossman School of Medicine, NYU Langone Health, New York, NY, USA*

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