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# Hemispheric Cerebral Oximetry Monitoring During Pediatric Seizure Activity in a Pediatric Emergency Department

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**Background:** Sustained neuronal activity during seizures causes cellular perturbations, alterations in cerebral physiology, and potentially neurological injury, a neurological emergency. With variable clinical manifestations of seizures, frequent failure of seizure recognition by providers in pediatric and developmentally challenged patients can increase seizure complications. Neuroresuscitation should include rapid cerebral physiology assessment for increased seizure recognition and optimal neurological outcomes. In neurological emergencies, cerebral oximetry has demonstrated its utility in altered cerebral physiology and a standard combat neurological assessment tool. During adult seizures, cerebral oximetry (regional cerebral oxygen saturation [ $r_cSO_2$ ]) has been shown as a useful neurological assessment tool, but research is lacking in pediatric emergency department (PED) seizure patients.

**Objective:** The aim of this study was to identify trends in  $r_cSO_2$  readings for patients presenting to the PED with seizure activity and in the post-seizure state in order to evaluate usefulness of  $r_cSO_2$  as a neurological assessment tool in pediatric seizure patients.

**Methods:** This was a PED observational case series comparing hemispheric  $r_cSO_2$  readings in first-time clinically evident generalized and focal seizure patients to first-time postseizure patients with no PED seizures.

**Results:** Generalized or focal seizure ( $n = 185$ ) hemispheric  $r_cSO_2$  revealed significant differences compared with nonseizure and controls'  $r_cSO_2$  readings ( $n = 115$ ) ( $P < 0.0001$ ). Generalized and focal seizure  $r_cSO_2$ 's were either less than 60% or greater than 80% compared with nonseizure  $r_cSO_2$  ( $P < 0.0001$ ). Ipsilateral focal seizure  $r_cSO_2$  correlated to seizure side ( $P < 0.0001$ ) and was less than the contralateral  $r_cSO_2$  ( $P < 0.0001$ ), with

interhemispheric  $r_cSO_2$  discordance greater than 16 ( $P < 0.0001$ ). Seizure to pre-seizure  $r_cSO_2$  discordance was as follows: generalized 15.2, focal: left 19.8, right 20.3 ( $P < 0.0001$ ).

**Conclusions:** Hemispheric during-seizure  $r_cSO_2$  readings significantly correlated with generalized and focal seizures and reflected altered cerebral physiology. Ipsilateral focal seizure  $r_cSO_2$  readings correlated to the focal side with wide interhemispheric  $r_cSO_2$  discordance. All postseizure  $r_cSO_2$  readings returned to pre-seizure readings, showing altered cerebral physiology resolution. Overall, in generalized or focal seizure,  $r_cSO_2$  readings were less than 60% or greater than 80%, and in focal seizure, interhemispheric  $r_cSO_2$  discordance was greater than 10. During seizures, hemispheric  $r_cSO_2$  readings demonstrated its potential pediatric seizure utility. Utilizing  $r_cSO_2$  readings related to seizure activity could expedite pediatric and developmentally challenged patients' seizure recognition, cerebral assessment, and interventions especially in pharmacoresistant seizures.

**Key Words:** cerebral physiology, focal seizure, generalized seizure, hemispheric cerebral oximetry,  $r_cSO_2$  (regional cerebral oxygen saturation), neuroresuscitation, seizure, seizure activity

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## WHAT IS ALREADY KNOWN ON THIS SUBJECT

Pediatric seizure is common in the pediatric emergency department (PED) and clinically presents in multiple forms. Sustained neuronal activity causes cellular perturbations and alterations in cerebral physiology, potentially causing neurological injury. In limited adult and pediatric cerebral oximetry seizure studies, change in multichannel regional cerebral oxygen saturation ( $r_cSO_2$ ) reading correlated with seizure activity in non-ED settings.

## WHAT THIS STUDY ADDS

This study showed significantly decreased or increased hemispheric  $r_cSO_2$  readings compared with pre-seizure and postseizure events during generalized and focal seizure. During seizure activity, there was an alteration in cerebral hemispheric cerebral tissue oxygenation and physiology. Also in the postseizure period, these altered hemispheric during-seizure  $r_cSO_2$  readings return to pre-seizure readings. In focal seizure patients, the ipsilateral  $r_cSO_2$  readings correlated to the hemispheric focal seizure side and were significantly different from the contralateral  $r_cSO_2$  readings.

## INTRODUCTION

Pediatric seizures presenting to the pediatric emergency department (PED) or emergency department (ED) can be generalized (which can be easily identifiable), focal, convulsive, or non-convulsive, or status epilepticus.<sup>1–4</sup> Subtle clinical or nonconvulsive seizure activity can be unrecognized by emergency medical services (EMS) and ED providers, given the lack of overt clinical signs and symptoms. Seizures can cause neuronal compromise and altered cerebral physiology, be pharmacoresistant, and cause

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neurological complications, a neurological emergency.<sup>1–8</sup> Seizure manifestations are variable, and failure to recognize and treat prolongs the seizure activity, thus increasing the neurological complications.<sup>3–8</sup> These “hard to clinically recognize” seizures can be exacerbated in the neonate, nonverbal pediatric patients and especially nonverbal/developmentally challenged patients.

A false seizure assumption is that the brain's physiology is not altered if there is global glucose and oxygen normalcy.<sup>6–12</sup> Persistent cerebral physiology abnormalities can continue during the seizure and can be undetected by current ED monitoring systems.<sup>2–12</sup> Neuroresuscitation should strive to quickly assess for altered cerebral physiology coupled with immediate therapeutic response assessment.<sup>2–12</sup> These objectives are paramount to neuronal preservation and improved neurological outcomes.<sup>3–14</sup> With a rapid objective cerebral physiology assessment tool's correlation with the patient's corresponding clinical neurological activity, this seizure misperceptions could be significantly decreased and augment the provider's critical thinking and decision making, which ED or EMS monitoring systems currently lack.<sup>7–15</sup>

During seizures, especially those with underlying neuronal mitochondria dysfunction, an increase in neuronal metabolism occurs causing regional oxygen and glucose depletion, resulting in regional tissue hypoxia and altered cerebral physiology.<sup>2–9,16–22</sup> Cerebral oximetry ( $r_cSO_2$ ) detects and reflects regional dynamic cerebral physiologic changes (tissue perfusion, oxygenation metabolism, and oxygen extraction).<sup>12–15,23–25</sup> Normal pediatric hemispheric (left and right)  $r_cSO_2$  is 60% to 80%. A low  $r_cSO_2$  reading less than 60% or a high  $r_cSO_2$  reading greater than 80% or an interhemispheric discordance  $r_cSO_2$  reading greater than 10 represents abnormal hemispheric cerebral physiology and pathology and an increased hypoxic brain injury risk.<sup>12–15,23–26</sup> In pediatric and adult neurological emergencies, cerebral oximetry has been validated for identifying altered hemispheric cerebral physiology and changes, neurological insults, and cerebral pathology detection.<sup>12–15,23–26</sup> Adult cerebral oximetry seizure studies suggest that cerebral  $r_cSO_2$  differences exist between generalized seizure and nonseizure  $r_cSO_2$  readings but have never been investigated in pediatric patients.<sup>15,16,23–27</sup>

**TABLE 1A.** Study and Control Patients' Inclusion and Exclusion Criteria

Study subject inclusion criteria (stepwise selection process)

1. PED patients: First-time clinically evident generalized or focal seizure activity: upon presentation to PED, EMS seizure activity (seizure and postseizure) with subsequent clinically evident seizures in the PED
2. Postseizure patients: patients in a postseizure state presenting by EMS or triage or during PED stay and had another clinically evident seizure while in the PED
3. Must have continuous hemispheric (left and right)  $r_cSO_2$  readings without lapsed data during their PED stay
4. Must have documented seizure activity times in patient's PED EMR as recorded by PED bedside nursing staff during PED stay
5. No PED intubation (before cerebral oximetry monitoring or during monitoring)

Study subject exclusion criteria (in stepwise selection process)

1. Lapse or lack of corresponding left and right  $r_cSO_2$  every 5-s readings during patient's PED stay
2. Positive history of neurological disorder (hydrocephalus, cerebrospinal fluid shunts, brain tumor newly diagnosis or resected, and central nervous system malformation, cerebral vascular abnormalities)
3. Head computed tomography scan positive for cerebral pathology if done
4. Positive prior history of prematurity of less than 36 wk, neonatal intensive care unit stay, neonatal intubation, trauma especially head trauma, child abuse, concussion, traumatic brain injury, congenital heart disease, immunocompromised, chronic lung disease, acute or prior history of bacterial or aseptic meningitis, and abnormal genetic or inborn error of metabolism
5. History of ingestion induced seizure activity, hypoglycemia-induced seizure activity
6. History of drowning present or in the past history
7. History of hypoxia-induced seizure activity
8. History of post-cardiopulmonary resuscitation
9. History of syncope-associated seizure activity

Control subject inclusion criteria

1. Documented pre-PED seizure activity in EMS run sheet or by parents and no clinically evident seizure activity upon PED arrival or during the PED stay
2. Must have continuous hemispheric (left and right)  $r_cSO_2$  readings without lapsed data during PED stay  $r_cSO_2$
3. Must have had a normal computed tomography scan of the head if done
4. No PED intubation (before cerebral oximetry monitoring or during monitoring)

Control subject exclusion criteria

Positive history of

1. Lapse or lack of corresponding left and right  $r_cSO_2$  every 5-s readings during patient's PED stay
2. Documented PED seizure times in patient's PED EMR as recorded by PED bedside nursing staff during PED stay
3. History of prior seizures, seizure disorder, febrile seizure, pseudoseizure, or viral meningitis/encephalitis
4. Cerebrovascular accident history, hydrocephalus or cerebrospinal fluid shunts, new brain tumors or previously diagnosed, cerebral vascular anomalies
5. Prematurity at <36 wk, neonatal intensive care unit stay, neonatal intubation, trauma especially head trauma, child abuse, concussion, traumatic brain injury, congenital heart disease, immunocompromised, chronic lung disease, acute or prior history of bacterial or aseptic meningitis, and genetic abnormalities or inborn error of metabolism

Study patients' inclusion and exclusion criteria: PED, EMR, and PED Cerebral Oximetry REDCap (Research Electronic Capture Database).<sup>11</sup>

This preliminary hemispheric cerebral r<sub>c</sub>SO<sub>2</sub> study's primary aim was to investigate the relationship of hemispheric cerebral r<sub>c</sub>SO<sub>2</sub> readings to clinically evident generalized and/or focal seizure activity in PED seizure patients with no prior seizure history. These seizure r<sub>c</sub>SO<sub>2</sub> readings were also compared with readings of PED postseizure patients with clinically evident seizures prior to PED arrival and no seizures during their PED stay.<sup>4-12</sup> The secondary aim was to investigate generalized and focal seizures' hemispheric r<sub>c</sub>SO<sub>2</sub> reading time pattern behavior. We hypothesized that there would be significantly different hemispheric r<sub>c</sub>SO<sub>2</sub> readings during these clinically evident seizure events compared with the nonseizure events. Analysis for cerebral oximetry age matching, sensitivity, specificity, and positive and negative predictive values for seizures was not the scope of this preliminary study.

**METHODS**

This is an observational retrospective case series from 2009 to 2016 in 2 academic PEDs (Arkansas Children's Hospital and Monroe Carrol Vanderbilt Children's Hospital) (annual census: 56,000 and 55,000 patient visits) examining hemispheric r<sub>c</sub>SO<sub>2</sub>

readings in 2 PED clinically evident seizure groups: focal and generalized patients and nonseizure PED patients. The seizure groups were (1) PED patients presenting with seizure activity and (2) PED patients who developed clinically evident seizure activity during their PED stay with continuous hemispheric r<sub>c</sub>SO<sub>2</sub> readings. The control patients had clinically evident seizure activity prior to their PED arrival and no subsequent seizure activity during their PED stay and had continuous hemispheric r<sub>c</sub>SO<sub>2</sub> readings.<sup>12,14</sup> To avoid potential underlying abnormal cerebral physiology causing underlying cerebral oximetry sampling bias, the seizure and control patients' inclusion and exclusion criteria were selected with the objective of underlying normalcy of the patients' nervous system (vascular and architecture) and cerebral physiology. More detailed study and control patient inclusion and exclusion criteria are presented in Table 1A.<sup>10</sup> The study and control patients were selected by one of the primary investigators from the PED (Arkansas Children's Hospital and Monroe Carrol Vanderbilt Children's Hospital) Cerebral Oximetry REDCap (Research Electronic Data Capture) database and screened with the inclusion and exclusion criteria of neurological normalcy, seizure activity, and continuous hemispheric r<sub>c</sub>SO<sub>2</sub> readings (Table 1A).<sup>10</sup>

**TABLE 1B.** Study and Control Patients' Clinical Evident Seizure Duration (in Minutes) and Comparison Between the Study and Control Groups (*P*) Duration of Seizure Prior to PED Arrival, by Age, Generalized Seizures, Focal Seizures, and Frequency of Seizure Events: Generalized, Left Focal, and Right Focal

Seizure Patients	n	Median, min	<i>P</i>
1. Patients arriving in active seizure (EMS or private care), their seizure duration prior to PED arrival (EMS or private care)	141	23 (15.5, 44.7)	
2. All PED generalized seizure events	267	15.3 (15.5, 44.7)	
3. All PED focal seizure events	123	13.2 (15.5, 44.7)	
Comparison: all PED generalized to focal seizure events			0.13
4. Control patients: seizure duration before PED arrival	n		
Seizure duration prior to PED arrival (EMS or private care)	115	24 (17, 31)	
0-1 y	16	19.5 (16, 30.5)	
1-2 y	16	17.0 (13, 23)	
2-5 y	24	20.5 (14.5, 29)	
>5 y	60	29 (20, 32.5)	
All	115	24 (17, 31)	
5. Control patients: hemispheric r <sub>c</sub> SO <sub>2</sub> monitoring duration	n		
0-1 y	42	83.8 (73.8, 88)	
1-2 y	24	98.2 (62.8, 101)	
2-5 y	45	90.5 (75, 112)	
>5 y	74	80.3 (62.9, 141.4)	
All	115	87.6 (71, 105.3)	
6. Left focal seizure event	78	19.2 (16.3, 49.2)	
7. Right focal seizure event	45	16.7 (15.5, 44.7)	
Comparison left to right seizure event			0.23
8. For 1 seizure event: generalized seizure event	51	16.8 (15.5, 44.7)	
Focal seizure event	8	22.3 (15.5, 44.7)	
Comparison generalized to focal seizure events			0.7
9. For 2 seizure events: generalized seizure event	44	19.2 (15.5, 44.7)	
Focal	15	24.3 (15.5, 44.7)	
Comparison generalized to focal seizure event			0.42
10. 5 min before to seizure event: time (min) it took before the first 15% relative change in hemispheric r <sub>c</sub> SO <sub>2</sub> occurred before seizure			
Generalized seizures	267	1.33 (0.96, 1.83)	
Left focal seizure	45	1.75 (1.3, 2.4)	
Right focal seizure	78	1.98 (1.35, 2.92)	

The time (in minutes) it took for the first 15% change in the hemispheric r<sub>c</sub>SO<sub>2</sub> to occurred before the start of the seizure.

**TABLE 1C.** Comparison Analysis of All Left and Right Seizure's r<sub>c</sub>SO<sub>2</sub> Readings (as Independent Events) in All Generalized and Focal Seizure Patient Events

	10 to 0 min Before Start of Seizure Event		During Entire Seizure Event		0–10 min After Seizure Event Ends		P During, Before, and After Seizure Event
	n	Median	n	Median	n	Median	
Left r <sub>c</sub> SO <sub>2</sub>	352	66.0 (59.0, 72.7)	548	48.8 (42.2, 70.5)	496	66.4 (60.0, 71.9)	<0.0001
Right r <sub>c</sub> SO <sub>2</sub>	352	62.3 (52.6, 71.4)	548	41.2 (35.8, 70.9)	496	63.0 (55.5, 70.5)	<0.0001
Patients With Multiple Seizure	First Seizure's First 10-min r <sub>c</sub> SO <sub>2</sub>		Last Seizure's 10-min r <sub>c</sub> SO <sub>2</sub>				P
Left (n = 132)	47.2 (43.7, 76.9)		52.8 (43.9, 78.6)				0.37
Right (n = 132)	44.5 (36.3, 70.1)		45.3 (37.5, 81.4)				0.18

In patients with multiple seizure, compared their first 10 minutes of their first seizure's r<sub>c</sub>SO<sub>2</sub> readings with their first 10 minutes of their last seizure r<sub>c</sub>SO<sub>2</sub> readings.

Patients meeting inclusion criteria had their PED electronic medical record (EMR) abstracted by one of the primary investigators for demographic data, EMS seizure activity, seizure activity upon PED presentation, generalized or focal seizure, seizure frequency, and various other seizure parameters. Patients' EMRs were reviewed for the neurologist's final diagnosis and final hospital or PED discharge diagnosis. The acknowledgement of patients' clinically evident seizure activity (whether tonic clonic or fine motor seizure activity) was by the PED attending physician or pediatric emergency medicine fellow and documented as seizure activity only in the patient's PED nursing EMR. The patient's clinically evident seizure recorded times from the PED nursing EMR were matched to the patient's cerebral oximetry hemispheric r<sub>c</sub>SO<sub>2</sub> times by one of the one of the investigators. Correlating subclinical seizure activity to the patient's hemispheric cerebral oximetry readings was not a study objective. The patient's r<sub>c</sub>SO<sub>2</sub> readings were not blinded to the PED providers and often not recorded in the PED EMR. The 2 PEDs had identical seizure protocols: normalizing blood sugar, supplemental oxygen, and anticonvulsants, and protocols were driven by the patient's clinically evident seizure activity, not by r<sub>c</sub>SO<sub>2</sub> recording protocol.

Health Insurance Portability and Accountability Act compliance for all aspects of patient data was maintained. The institutional review board at each facility granted study approval including a waiver of informed consent, and this study was registered at ClinicalTrials.gov (NCT 02950181).

**Cerebral Oximetry Sampling**

At both facilities, hemispheric cerebral oximetry monitoring was standard during pediatric neurological emergencies 24 hours, 7 days a week. Patients had left and right forehead cerebral oximetry probes (INVOS 5100C Medtronic, Minneapolis, MN) with simultaneous r<sub>c</sub>SO<sub>2</sub> recordings at 5-second intervals during their PED stay and did not delay patient's resuscitation endeavors.

The patient's seizure times were recorded in the cerebral oximetry device as event marks.

**Statistical Analysis**

Single patient data consist of hemispheric r<sub>c</sub>SO<sub>2</sub> readings at 5-second intervals over the patient's PED stay. Patient groups were formed according to the median r<sub>c</sub>SO<sub>2</sub> in the first 5 minutes after PED arrival as less than 60%, between 60% and 80%, and greater than 80%, as adult cerebral oximetry seizure studies show an increase or decrease in regional cerebral blood flow (CBF) occurs just before and during a seizure.<sup>16–18,24–27</sup> Patient r<sub>c</sub>SO<sub>2</sub> data were split in periods around clinically evident seizure events as (1) 10 to 5 minutes before seizure start, (2) 5 to 0 minutes before seizure start, (3) during seizure, (4) 0 to 5 minutes after seizure ends, and (5) 0 to 10 minutes after seizure end. For each patient, 5-second r<sub>c</sub>SO<sub>2</sub> reading data for periods defined were collapsed as median r<sub>c</sub>SO<sub>2</sub>, yielding a single number per period per patient. Analyses of r<sub>c</sub>SO<sub>2</sub> behavior over periods defined around seizure events and corresponding comparisons of groups of interest (eg, control vs seizure, r<sub>c</sub>SO<sub>2</sub> levels upon arrival in PED <60%, 60%–80%, >80%) were carried out by a mixed model (nonparametric repeated measures) followed by Tukey procedure. P < 0.05 was considered statistically significant; corresponding confidence intervals are provided. Medians and first (Q1) and third (Q3) quartiles were obtained. Setup of analytical data sets and analyses were carried out in SAS 9.4 (SAS Institute Inc, Cary, NC).

**RESULTS**

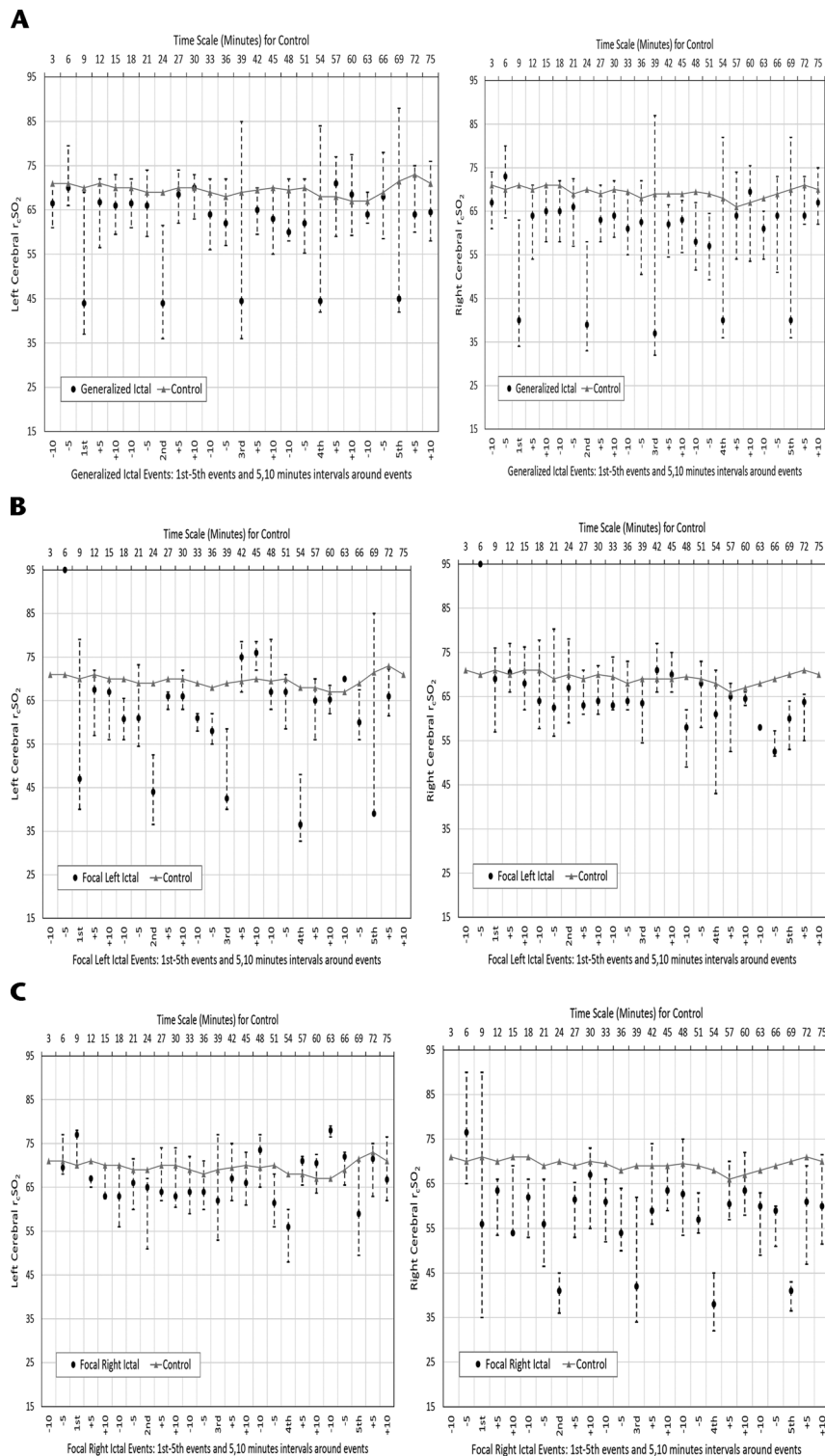
From 2012 to 2016, there were 185 PED patients (59.4% were male) with seizure activity (548 seizure events), simultaneous and continuous hemispheric r<sub>c</sub>SO<sub>2</sub> monitoring duration of 167.6 minutes (101.4, 210.3 minutes) (Table 1B). There were 115 control patients with 52.6% males, and their r<sub>c</sub>SO<sub>2</sub> monitoring duration was 87.6 minutes (71, 105.3 minutes). The seizure patients'

**TABLE 1D.** Comparison of the Left and Right Seizure Event r<sub>c</sub>SO<sub>2</sub> Readings by Overall Age and by Age Grouping (<1, 1–2, 2–5, >5 Years)

Overall Ages: Left r <sub>c</sub> SO <sub>2</sub> (P = 0.36), Right r <sub>c</sub> SO <sub>2</sub> (P = 0.83)	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	P
<1 y (n = 53)	45.7 (45.1, 56.1)	43.4 (38.8, 52.6)	0.15
1–2 y (n = 37)	46 (43.8, 55.9)	43.2 (39.6, 52.0)	0.17
2–5 y (n = 63)	46.7 (40.1, 59.8)	43.3 (38.0, 55.2)	0.19
>5 y (n = 32)	44.3 (32.8, 55.1)	41.5 (37.9, 51.6)	0.37

median age was 2.13 years (0.84, 4.1 years), and the control subjects' median age was 5.17 years (1.9, 9.4 years) (*P* < 0.0001). With no age-specific hemispheric r<sub>c</sub>SO<sub>2</sub> readings, these statistical

age differences did not affect the hemispheric seizure r<sub>c</sub>SO<sub>2</sub> analysis. In the seizure group, 167 patients had 334 generalized seizure events, 106 patients had 214 focal seizure events (48 patients had



**FIGURE 1.** A–C, Left and right cerebral r<sub>c</sub>SO<sub>2</sub> for generalized clinically evident seizure events versus control. Median (●) and interquartile range; 5-minute surrounding intervals are as follows: –10 (10 to 5 minutes prior to start of seizure event), –5 (5 to 0 minutes prior to start of seizure event), +5 (0–5 minutes after ending of seizure event), +10 (5–10 minutes after ending of seizure event). A–C, Left and right cerebral all r<sub>c</sub>SO<sub>2</sub>: A, clinically evident general seizure; B, clinically evident left focal seizure; C, clinically evident right focal seizure.

68 left-sided focal seizure activity, and 75 patients had 146 right-sided focal seizure activity).

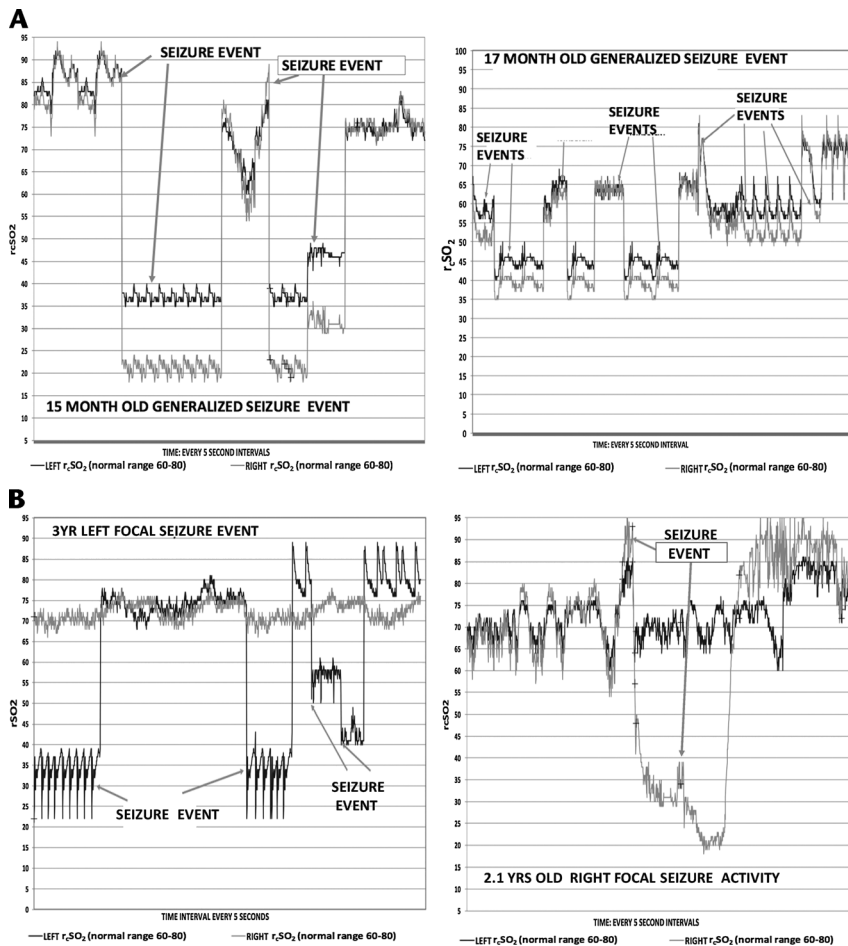
Seizure patients' PED EMR diagnoses were new-onset seizure activities, generalized seizure, left focal seizure, right focal seizure, complex febrile seizure, simple febrile seizure, partial complex seizure, and convulsive status epilepticus. No seizure or control patients had a diagnosis of stroke or cerebral pathology on head computed tomography or magnetic resonance imaging scan. The control patients' final diagnoses were seizure, new-onset seizure, and simple and complex febrile seizures. No patient had positive bacterial or viral meningitis. For study and control patients, the PED EMR recorded no hypoxic periods, intubations, bradycardia events, abnormal electrolytes, hypoglycemia, or positive toxicology screen in either group.

The patients' seizure duration demonstrated no statistical significance between the groups ( $P = 0.13$ ) (Table 1B). The relative left and right  $r_cSO_2$  first 15% relative changes (showing earliest significant  $r_cSO_2$  time change before the start of seizure) from 5 minutes before seizure to the seizure start for generalized, left focal and right focal, are shown in Table 1B. Comparing hemispheric  $r_cSO_2$  reading for all seizures (generalized and focal), a strong significance for lower hemispheric  $r_cSO_2$  readings during seizure events compared with the pre-seizure and post-seizure readings was noted ( $P < 0.001$ ) (Table 1C). For patients with multiple

seizure events (generalized and focal), comparing their first to last seizure events' first 10-minute seizure  $r_cSO_2$  readings showed no statistical difference (left,  $P = 0.37$ ; right,  $P = 0.18$ ) (Table 1C). The various age parameters were not significant (Table 1D).

Figures 1A to C represent the time plots for generalized and left and right focal seizures hemispheric  $r_cSO_2$  seizure compared with controls. Figures 2A and B represent individual generalized and left and right focal seizure patients' graphic representations of their hemispheric  $r_cSO_2$  readings.

In the seizure event time analysis, for the seizure and control patients, the pre-seizure hemispheric and interhemispheric  $r_cSO_2$  readings demonstrated no statistical significance (Table 2). For the during-seizure event, in the seizure and control patients' hemispheric  $r_cSO_2$  readings, the generalized and focal during-seizure  $r_cSO_2$  readings were significantly lower or higher ( $P < 0.0001$ ) than controls and focal during-seizure  $r_cSO_2$  readings. Comparing the post-seizure hemispheric and interhemispheric  $r_cSO_2$  readings between seizure and control patients, there was statistical significance, but clinically both groups'  $r_cSO_2$  readings were within the normal  $r_cSO_2$  reading range (Table 2). Comparing the multiple seizure events (as independent events) during the seizure hemispheric  $r_cSO_2$  readings with that of control patients, there was a strong discordance between the groups with lower median hemispheric seizure  $r_cSO_2$  reading occurrence ( $P < 0.0001$ ) (Table 2).



**FIGURE 2.** A, Fifteen-month and 17-month-old patients with clinically evident generalized seizures (seizure event) with left and right  $r_cSO_2$  graph with clinically evident seizure (events and nonseizure events time graph). B, Left, A 3-year-old with clinically evident left focal seizure with left and right  $r_cSO_2$  graph with clinically evident seizure events and nonseizure events time graph. B, Right, A 2.1-year-old patient with clinically evident right focal seizure with left and right  $r_cSO_2$  graph with clinically evident seizure events and nonseizure events time graph.

**TABLE 2.** Seizure Versus Control Patients' Hemispheric (Left and Right) r<sub>c</sub>SO<sub>2</sub> Readings With Corresponding Comparison Time Analysis: Control Patients' r<sub>c</sub>SO<sub>2</sub> Versus PED Seizure r<sub>c</sub>SO<sub>2</sub> Readings at Various Time Intervals Analysis

n <sub>1</sub> = Patients	PED Seizure Events Median				Control (Nonseizure Activity) Median				Seizure vs Control P		
	n <sub>1</sub>	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	Difference	n <sub>1</sub>	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	Difference	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	Difference
	10 min Before first seizures	22	66.5 (61, 70.5)	67 (61, 74)	-1 (-2, 2)	115	71 (69, 76)	72 (67, 77)	0 (-2, 3)	0.05	0.06
5 min Before first seizures	40	70 (66.5, 80.5)	73.5 (64.3, 80)	0 (-2.8, 3)	115	71 (69, 76)	70 (65.5, 76)	2 (-2, 4)	0.96	1	0.95
During first seizures	171	46 (43, 80)	45 (35, 78)	5 (0, 9)	115	71 (69, 76)	70 (66, 76)	2 (-1, 4)	<0.0001	<0.0001	0.24
During second seizures	146	47 (39, 66)	41 (34.5, 70)	5 (-3, 14)	115	71 (68, 76.5)	71 (66, 76)	1 (-2, 4.5)	<0.0001	<0.0001	0.08
During third seizures	87	50 (42, 80)	43 (34, 84)	5 (-1, 17)	104	73 (69, 77.5)	72 (68.5, 76)	2 (-1, 4)	<0.0001	<0.0001	0.27
During fourth seizures	42	48 (43, 60)	40 (36, 58)	6 (1.5, 15)	58	70 (68.5, 77)	70 (65, 76)	2 (-1, 6)	<0.0001	<0.0001	0.06
During all seizures (n = 185 patients)	548	47 (41, 77)	41.5 (35, 74)	5 (-1, 15)	420	71 (68.5, 77)	71 (66, 76)	2 (-1, 4)	<0.0001	<0.0001	<0.0001
5 min After last seizure <sup>+</sup>	171	69 (63, 74)	66 (62, 72)	2 (0, 4)	115	72 (68, 76)	68 (67, 77.5)	2 (-1, 4)	0.002	0.002	1
10 min After last seizure*	167	67 (63, 74)	66 (62, 74)	1 (-2, 3)	115	70 (68, 76)	70 (66, 75)	2 (-1, 4)	0.002	0.2	0.67

\*Statistically significant but not clinically because of an accepted 5% difference between hemispheric r<sub>c</sub>SO<sub>2</sub> readings.<sup>13-15,23-27</sup>

Time interval analysis parameters: (1) 10 to 0<sup>1</sup> minutes before the documented start of the seizure event; (2) 5 to 0<sup>1</sup> minutes before the seizure event; (3) during the seizure event (total duration of the seizure event); (4) 0<sup>2</sup> to 5 minutes after the documented end of the seizure event; (5) 0<sup>2</sup> to 10 minutes after the end of seizure event. Further time analysis for patients with only 1 clinically evident seizure event, 2 seizure events, 3 seizure events, four seizure events, and for all clinically evident seizure events: <sup>1</sup>(0 = before the start of seizure event), <sup>2</sup>(0 = before the start of seizure event).

Patients with multiple seizures all had significant postictal times between repetitive seizure intervals, generalized, 20 minutes (11, 27 minutes); left focal seizures, 22 minutes (13, 28 minutes); and right focal seizure, 22 minutes (16, 25 minutes). These multiple seizure types were either repetitive focal seizures, generalized progressing to focal seizures, or repetitive generalized seizures. All multiple-seizures patients had appropriate PED seizure protocol adherence.

For the various seizure time parameter analysis in the generalized and focal seizures by their hemispheric r<sub>c</sub>SO<sub>2</sub> readings and initial abnormal r<sub>c</sub>SO<sub>2</sub> readings (<60% and >80%), the pre-seizure, seizure, and post-seizure r<sub>c</sub>SO<sub>2</sub> readings for the all generalized and focal seizures showed that during seizure r<sub>c</sub>SO<sub>2</sub> readings had a stronger significant difference compared with the pre-seizure and post-seizure r<sub>c</sub>SO<sub>2</sub> reading times (P < 0.0001) and not the pre-seizure to post-seizure times (P = 0.99) (Tables 3A, 3B, and 3C).

Focal ipsilateral seizure r<sub>c</sub>SO<sub>2</sub> readings compared with generalized ipsilateral r<sub>c</sub>SO<sub>2</sub> readings showed no statistical difference (Table 4A). Simultaneously, the focal contralateral r<sub>c</sub>SO<sub>2</sub> readings were statistically higher than the corresponding generalized seizure r<sub>c</sub>SO<sub>2</sub> (P < 0.0001) (Table 4A). The focal ipsilateral r<sub>c</sub>SO<sub>2</sub> readings had either a lower r<sub>c</sub>SO<sub>2</sub> reading compared with the contralateral r<sub>c</sub>SO<sub>2</sub> with a wide interhemispheric difference and were statistically significant (P < 0.0001) (Table 4B). For left to right focal seizure r<sub>c</sub>SO<sub>2</sub> reading comparison, right focal seizure r<sub>c</sub>SO<sub>2</sub> readings were significantly less than the left focal seizure r<sub>c</sub>SO<sub>2</sub> readings (P < 0.0001) (Table 4A and 4B). With increasing focal seizure frequency, these focal seizure r<sub>c</sub>SO<sub>2</sub> reading findings were consistent with persistent correlation to the focal seizure side (P < 0.0001) (Table 4B). The focal interhemispheric r<sub>c</sub>SO<sub>2</sub> reading discordances, whether single or multiple seizures, were consistently wide (P < 0.0001) (Table 4B). Comparing the overall left focal contralateral (right) r<sub>c</sub>SO<sub>2</sub> readings median r<sub>c</sub>SO<sub>2</sub> 64 (57.7, 77.7) to the corresponding control's (right) r<sub>c</sub>SO<sub>2</sub> readings 70 (64.0, 76.0) there was no median difference detected (P = 0.15). Whereas the right focal contralateral r<sub>c</sub>SO<sub>2</sub> side (left) r<sub>c</sub>SO<sub>2</sub> 64 (56, 70) median compared to the control's (left) side r<sub>c</sub>SO<sub>2</sub> 70 (65, 75) had a significant difference (P < 0.001).

For all generalized seizure r<sub>c</sub>SO<sub>2</sub> readings during seizure event times compared between non-seizure event times, a wide median with significant difference was noted (P < 0.0001) (Table 5A). Refining this comparison time by initial abnormal hemispheric r<sub>c</sub>SO<sub>2</sub> readings (<60% or >80%) during seizure times to other times, a wide median with a significant difference occurred (P < 0.0001) (Table 5A). For generalized and focal seizures between pre-seizures and during seizures, their hemispheric delta r<sub>c</sub>SO<sub>2</sub> reading change was for general seizures: left 10 and right 18.5, and left focal 19.8 and right focal 20.3, all demonstrating significant differences (P < 0.0001) (Table 5B). However, the pre-seizure to post-seizure hemispheric delta r<sub>c</sub>SO<sub>2</sub> change demonstrated no significance (P = 0.7) (Table 5B). The delta r<sub>c</sub>SO<sub>2</sub> changes for generalized and focal seizures by initial hemispheric abnormal r<sub>c</sub>SO<sub>2</sub> readings (<60% or >80) demonstrated a wider significant difference (P < 0.0001) (Table 5B). In multiple seizures, similar delta r<sub>c</sub>SO<sub>2</sub> change parameter results demonstrated similar differences (P < 0.0001). (For readers interested in the generalized seizure r<sub>c</sub>SO<sub>2</sub> frequency, analysis for the first, second, and third seizure events is presented in Supplementary Tables 5C, D, E [C, 1 seizure event; D, patient with 2 seizures: second seizure event; and E, patients with 3 seizures, third seizure event, and their statistical analysis], <http://links.lww.com/PEC/A217>).

**DISCUSSION**

This preliminary PED hemispheric cerebral oximetry study during clinically evident generalized and focal seizure activity demonstrates the following findings. Overall, hemispheric during-seizure r<sub>c</sub>SO<sub>2</sub> readings significantly correlated with generalized and focal seizures. In generalized and focal seizure activity, during the seizure, hemispheric r<sub>c</sub>SO<sub>2</sub> readings revealed significant cerebral tissue oxygenation alteration during the seizure (increase or decrease) compared with pre-seizure, and in the post-seizure, it returned to baseline. These findings correlated with prior cerebral oximetry seizure studies.<sup>16-20,24-27</sup> In the generalized and focal seizure patients, during the seizure phase, there were 2 trends noted during the seizure phase: r<sub>c</sub>SO<sub>2</sub> readings of less than 60 or greater than 80%, and with seizures with greater than 80%

**TABLE 3A.** Comparing All Generalized Hemispheric (Left, Right [Using All Generalized Seizure  $r_cSO_2$  Readings as Independent Events]) During the Seizure  $r_cSO_2$  Readings to Various Nonseizure  $r_cSO_2$  Readings Time Intervals by All Their Seizure  $r_cSO_2$  Readings (as Independent Events) and by Their Initial Hemispheric Seizure  $r_cSO_2$  Readings Less Than 60% and Greater Than 80% With Same Time Comparisons

All Generalized Seizure	(1) Generalized Seizure: Left $r_cSO_2$			(2) Generalized Seizure: Right $r_cSO_2$			
	Seizure Period	n	Median (Q1, Q3)	Differences	Median (Q1, Q3)	Differences	P
All	10 to 5 min before	148	66 (60.0, 71.5)	During and 10 to 5 min before	62 (58.0, 73.0)	During and 10 to 5 min before	-20.5
	5 to 0 min before	201	66 (58.5, 74.0)	During and 0-5 min before	64 (61.0, 73.0)	During and 0-5 min before	-18.5
	During seizure	334	44 (36.5, 82.0)	0-5 min after and during	42.5 (62.0, 88.0)	0-5 After - During	21.5
	0-5 min after	306	66 (58.0, 72.0)	5-10 min after and during	64 (62.0, 71.5)	5-10 min after and during	21.5
	5-10 min after	261	66 (60.0, 74.0)	0-5 min after and 0-5 min before	64 (61.0, 71.0)	0-5 min after and 0-5 min before	0
				5-10 min after and 10 to 5 min before		5-10 min after and 10 to 5 min before	2
Both <60 <sup>11-15</sup>	10 to 5 min before	87	63 (56.0, 69.5)	During and 10 to 5 min before	63 (53.0, 68.0)	During and 10 to 5 min before	-27
	5-0 min before	122	62 (55.85, 73.0)	During and 0-5 min before	60.5 (50.0, 71.0)	During and 0-5 min before	-24.5
	During seizure	205	43 (36.0, 44.5)	0-5 min after and during	36 (30.5, 40.0)	0-5 min after and during	27
	0-5 min after	187	64.5 (56.0, 72.5)	5-10 min after and during	63 (49.0, 71.0)	5-10 min after and during	27
	5-10 min after	155	66 (55.0, 74.0)	0-5 min after and 0-5 min before	65 (55.0, 72.0)	0-5 min after and 0-5 min before	2.5
				5-10 min after and 10 to 5 min before		5-10 min after and 10 to 5 min before	2
Both >80 <sup>11-15</sup>	10 to 5 min before	34	67 (64.0, 72.0)	During and 10 to 5 min before	62 (58.0, 73.0)	During and 10 to 5 min before	20.5
	5 to 0 min before	43	68 (65.0, 75.0)	During 0-5 before	64 (61.0, 73.0)	During and 0-5 min before	18.5
	During seizure	88	86 (57.0, 90.0)	0-5 min after and during	82.5 (62.0, 88.0)	0-5 min after and during	-18.5
	0-5 min after	81	67 (64.0, 72.0)	5-10 min after and during	64 (62.0, 71.5)	5-10 min after and during	-18.5
	5-10 min after	74	65.3 (63.0, 74.0)	0-5 min after and 0-5 min before	64 (61.0, 71.0)	0-5 min after and 0-5 min before	0
				5-10 min after and 10 to 5 min before		5-10 min after and 10 to 5 min before	2

Time interval analysis parameters: (1) 10 to 5 minutes before start of the seizure event; (2) 5 to 0 minutes before the seizure event; (3) during the seizure event (total duration of the seizure event); (4) 0 to 5 minutes after the end of the seizure event; (5) 5 to 10 minutes after seizure event cessation: (0 = before the start of seizure event), (0 = before the start of seizure event).



**TABLE 3B.** All Left Focal Hemispheric (Left, Right [Using All Left and Right Focal Seizure r<sub>c</sub>SO<sub>2</sub> Readings as Independent Events]) During the Seizure r<sub>c</sub>SO<sub>2</sub> Readings to Various Nonseizure r<sub>c</sub>SO<sub>2</sub> Readings Time Intervals by All Their Seizure r<sub>c</sub>SO<sub>2</sub> Readings (as Independent Events) and by Their Initial Hemispheric Seizure r<sub>c</sub>SO<sub>2</sub> Readings of Less Than 60% and Greater Than 80%

All Left Focal Seizure		(1) Focal-Left Seizure: Left r <sub>c</sub> SO <sub>2</sub>			(2) Focal-Left Seizure: Right r <sub>c</sub> SO <sub>2</sub>				
Seizure Period	n	Median	(Q1, Q3)	Differences	P	Median	(Q1, Q3)	Differences	P
All									
10–5 min before	21	62	(57.0, 67.0)	During and 10 to 5 min before	–18	62	(58.0, 74.0)	During and 10 to 5 min before	3
5 to 0 min before	34	61.8	(56.0, 71.0)	During and 0–5 min before	–17.8	64	(56.5, 75.0)	During and 0–5 min before	1
During seizure	68	44	(36.5, 55.5)	0–5 min after and during	22	65	(57.0, 74.5)	0–5 min after and during	1.5
0–5 min after	57	66	(60.0, 72.0)	5–10 min after and during	23	66.5	(62.0, 72.0)	5–10 min after and during	1
5–10 min after	45	67	(62.5, 72.0)	0–5 min after and 0–5 min before	4.2	66	(62.0, 72.0)	0–5 min after and 0–5 min before	1.5
				5–10 min after and 10 to 5 min before	5	0.46		5–10 min after and 10 to 5 min before	4
Left r <sub>c</sub> SO <sub>2</sub> <60 <sup>1–15</sup>	13	59.5	(57.0, 63.0)	During and 10 to 5 min before	–19.5	64	(60.5, 76.5)	During and 10 to 5 min before	1
5 to 0 min before	22	59.8	(55.5, 67.0)	During and 0–5 min before	–19.8	64.5	(58.0, 75.0)	During and 0–5 min before	0.5
During seizure	48	40	(35.0, 45.5)	0–5 After – during	26	65	(57.0, 74.0)	0–5 After – during	1.8
0–5 min after	44	66	(58.8, 72.0)	5–10 min after and during	26	66.8	(62.0, 73.0)	5–10 min after and during	1
5–10 min after	34	66	(60.0, 72.0)	0–5 min after and 0–5 min before	6.2	66	(62.0, 75.0)	0–5 min after and 0–5 min before	1.8
				5–10 min after and 10 to 5 min before	6.5	0.06		5–10 min after and 10 to 5 min before	2
Left r <sub>c</sub> SO <sub>2</sub> >80 <sup>1–15</sup>	3	62	(61.0, 67.0)	During and 10 to 5 min before	25	62	(54.5, 63.0)	During and 10 to 5 min before	4.3
5 to 0 min before	5	65	(56.0, 68.0)	During and 0–5 min before	22	64	(56.5, 65.0)	During and 0–5 min before	2.3
During seizure	12	87	(81.5, 89.0)	0–5 After – during	–17	66.3	(61.0, 71.0)	0–5 min after and during	0.7
0–5 min after	8	70	(69.5, 77.3)	5–10 min after and during	–16	67	(60.5, 70.5)	5–10 min after and during	–1.8
5–10 min after	6	71	(69.0, 72.0)	0–5 min after and 0–5 min before	5	64.5	(62.0, 69.5)	0–5 min after and 0–5 min before	3
				5–10 min after and 10 to 5 min before	9	0.49		5–10 min after and 10 to 5 min before	2.5

Time interval analysis parameters: (1) 10 to 5 minutes before start of the seizure event; (2) 5 to 0<sup>1</sup> minutes before the seizure event; (3) during the seizure event (total duration of the seizure event); (4) 0<sup>2</sup> to 5 minutes after the end of the seizure event; (5) 5 to 10 minutes after seizure event cessation: <sup>1</sup>(0 = before the start of seizure event), <sup>2</sup>(0 = before the start of seizure event).

**TABLE 3C.** All Right Focal Hemispheric (Left, Right [Using All Left and Right Focal Seizure  $r_cSO_2$  Readings by All Their Seizure  $r_cSO_2$  Readings (as Independent Events), and by Their Initial Hemispheric Seizure  $r_cSO_2$  Readings of Less Than 60% and Greater Than 80% With Same Time Comparisons

All Right Focal Seizure		(1) Focal-Right Seizure: Left $r_cSO_2$				(2) Focal-Right Seizure: Right $r_cSO_2$				
Seizure Period	n	Median	(Q1, Q3)	Differences	P	Median	(Q1, Q3)	Differences	P	
All										
10 to 5 min before	64	65	(56.0, 75.8)	During and 10 to 5 min before	0	61.3	(62.0, 66.0)	During and 10 to 5 min before	-20.3	<0.0001
5 to 0 min before	105	66	(60.0, 72.0)	During and 0-5 min before	-1	57	(49.0, 64.0)	During and 5 min before	-16	<0.0001
During seizure	146	65	(43.0, 77.0)	0-5 min after and during	2	41	(35.0, 56.0)	0-5 min after and during	20.5	<0.0001
0-5 min after	133	67	(62.0, 73.0)	5-10 min after and during	-0.5	61.5	(54.0, 67.0)	5-10 min after and during	22.5	<0.0001
5-10 min after	96	64.5	(61.8, 72.5)	0-5 min after and 0-5 min before	1	63.5	(55.0, 69.5)	0-5 min after and 0-5 min before	4.5	0.04
				5-10 min after and 10 to 5 min before	-0.5			5-10 min after and 10 to 5 min before	2.2	0.33
Right $r_cSO_2 < 60^{11-15}$										
10 to 5 min before	45	64	(56.0, 75.0)	During and 10 to 5 min before	-2	57	(49.0, 64.0)	During and 10 to 5 min before	-19	<0.0001
5 to 0 min before	81	66	(61.0, 71.0)	During and 0-5 min before	-4	54	(48.5, 61.0)	During and 5 min before	-16	<0.0001
During seizure	108	62	(52.0, 68.0)	0-5 min after and during	4	38	(34.0, 42.0)	0-5 min after and during	20	<0.0001
0-5 min after	97	66	(62.0, 72.0)	5-10 min after and during	1	58	(51.0, 63.5)	5-10 min after and during	24	<0.0001
5-10 min after	67	63	(61.0, 72.0)	0-5 min after and 0-5 min before	0	62	(55.0, 69.0)	0-5 min after and 0-5 min before	4	0.002
				5-10 min after and 10 to 5 min before	-1			5-10 min after and 10 to 5 min before	5	0.04
Right $r_cSO_2 > 80^{11-15}$										
10 to 5 min before	15	70	(61.0, 77.0)	During and 10 to 5 min before	7	69	(60.0, 80.0)	During and 10 to 5 min before	20	<0.0001
5 to 0 min before	18	65	(60.0, 76.0)	During and 0-5 min before	12	66.5	(58.5, 82.0)	During and 5 min before	22.5	<0.0001
During seizure	30	77	(65.0, 77.0)	0-5 min after and during	-10	89	(88.0, 90.0)	0-5 min after and during	-22.5	<0.0001
0-5 min after	28	67	(64.8, 75.0)	5-10 min after and during	-13	66.5	(65.8, 77.8)	5-10 min after and during	-24	<0.0001
5-10 min after	23	64	(62.0, 76.0)	0-5 min after and 0-5 min before	2	65	(54.0, 79.0)	0-5 min after and 0-5 min before	0	0.99
				5-10 min after and 10 to 5 min before	-6			5-10 min after and 10 to 5 min before	-4	1

Time interval analysis parameters: (1) 10 to 5 minutes before start of the seizure event; (2) 5 to 0<sup>1</sup> minutes before the seizure event; (3) during the seizure event (total duration of the seizure event); (4) 0<sup>2</sup> to 5 minutes after the end of the seizure event; (5) 5 to 10 minutes after seizure event cessation. <sup>1</sup>(0 = before the start of seizure event), <sup>2</sup>(0 = before the start of seizure event).

**TABLE 4A.** Comparison Analysis of Hemispheric (Left and Right) Seizure r<sub>c</sub>SO<sub>2</sub> Readings Between Generalized Seizure Compared With Left Focal and Right Focal Seizure r<sub>c</sub>SO<sub>2</sub> Readings (n<sup>1</sup> = patients, I = Total Number of Seizure Events) by Their First, Second, Third, and All Seizure Events (as independent events) and the Difference Between General and Focal (left and right) Seizure r<sub>c</sub>SO<sub>2</sub> Readings

	Generalized Seizure	Focal Left Seizure	P	Difference Between Generalized and Left Focal Seizure*	Focal Right Seizure	P	Difference Between Generalized and Right Focal Seizure*
First seizure	n = 139	n = 21		0 (-7, 4)	n = 25		-8 (-17, 1)
Left r <sub>c</sub> SO <sub>2</sub> <sup>1</sup>	44 (37, 69)	47 (40, 79)	0.98		77 (70, 78)	<0.001	
Right r <sub>c</sub> SO <sub>2</sub>	40 (34, 63)	69 (57, 76)	0.001		46 (35, 90)	0.18	
Second seizure	n = 95	n = 24		0 (-4, 5)	n = 41		-1 (-5, 3)
Left r <sub>c</sub> SO <sub>2</sub>	44 (36, 61.5)	44 (36.5, 52.5)	0.96		65 (51, 67)	<0.001	
Right r <sub>c</sub> SO <sub>2</sub>	39 (33, 58)	67 (59, 78)	0.0002				
	41 (36, 45)	0.94					
Third seizure	n = 50	n = 8		2 (-6.5, 30)	n = 43		1.1 (-1.5, 23.7)
Left r <sub>c</sub> SO <sub>2</sub>	44.5 (36, 85)	42.5 (40, 58.5)	0.95		62 (53, 77)	0.14	
Right r <sub>c</sub> SO <sub>2</sub>	37 (32, 87)	63.5 (54.5, 69)	0.24		42 (34, 62)	0.82	
All seizure	n = 334	n = 68		1 (-1, 4)	n = 146		1 (-4, 1)
Left r <sub>c</sub> SO <sub>2</sub>	44 (36.5, 82)	44 (36.5, 55.5)	0.56		65 (53, 77)	<0.001	
Right r <sub>c</sub> SO <sub>2</sub>	39 (34, 80)	65 (56.3, 74.5)	<0.001		41 (35, 56)	0.42	

\*Hodge-Lehman estimate of location shift, 95% confidence interval.

readings decreasing over time.<sup>16-20,24-27</sup> In either left or right focal seizure, hemispheric r<sub>c</sub>SO<sub>2</sub> readings had a strong correlation to the seizure side with a wide interhemispheric discordance r<sub>c</sub>SO<sub>2</sub>. As in similar cerebral oximetry studies, these focal and general seizures' r<sub>c</sub>SO<sub>2</sub> reading changes demonstrate that nonfrontal hemispheric abnormal regional cerebral activity has a dynamic interplay with and can affect the frontal hemispheric cerebral physiology. In all groups, generalized seizures, focal seizures, and controls, upon seizure resolution or postictal phase, the postseizure r<sub>c</sub>SO<sub>2</sub> readings return to pre-seizure r<sub>c</sub>SO<sub>2</sub> readings or normal range, 60% to 80%, demonstrating resolution of the cerebral seizure's abnormal physiology. With increased generalized or focal seizure frequency, there was a persistent strong correlation for the during-seizure r<sub>c</sub>SO<sub>2</sub> reading change compared with pre-seizure and postseizure r<sub>c</sub>SO<sub>2</sub> readings, postseizure r<sub>c</sub>SO<sub>2</sub> readings, and returning to pre-seizure readings across all seizure frequencies. For all the seizure r<sub>c</sub>SO<sub>2</sub> readings, there was a significant r<sub>c</sub>SO<sub>2</sub> reading change by 2 to 3 minutes before the documented clinically

evident seizure start time, demonstrating a hemispheric cerebral physiological change occurrence before clinical evidence. Overall, hemispheric seizure r<sub>c</sub>SO<sub>2</sub> readings highly correlated with clinically evident (generalized or focal) seizures and demonstrate hemispheric cerebral oxygenation and physiology alteration during seizures. Also, by utilizing left and right cerebral oximetry sensors, detection of these unilateral and bilateral hemispheric cerebral physiological alterations was possible.

Seizure activity is related to neuronal mitochondrial dysfunction, producing abnormal neuronal cellular metabolism, further mitochondrial damage, tissue hypoxia, persistent neuronal dysfunction, and increased regional cerebral oxygen and glucose consumption all during the seizure event.<sup>1-4,16-20,25-27</sup> A compensatory action is an increase in regional CBF and oxygenation.<sup>16-20,25-27</sup> However, when this increased regional CBF becomes inadequate to meet the seizure's metabolic demand, decreased regional tissue oxygenated hemoglobin occurs.<sup>16-20,25-27</sup> This study's generalized and focal seizure hemispheric r<sub>c</sub>SO<sub>2</sub> readings during single

**TABLE 4B.** Comparison Analysis of Left and Right Seizure r<sub>c</sub>SO<sub>2</sub> Readings Between Left and Right Focal Seizure r<sub>c</sub>SO<sub>2</sub> Readings and Between Hemispheric r<sub>c</sub>SO<sub>2</sub> Reading Side Differences (During Focal Events) (n<sup>1</sup> = Patients, I = Total Number of Seizure Events) by Their First, Second, and Third Seizures and in All focal Seizures' r<sub>c</sub>SO<sub>2</sub> Readings (as Independent Events) and the Differences Between the Focal Seizure r<sub>c</sub>SO<sub>2</sub> Readings

	Focal Left Seizure				Focal Right Seizure			
	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	P	Difference Between r <sub>c</sub> SO <sub>2</sub> Sides	Left r <sub>c</sub> SO <sub>2</sub>	Right r <sub>c</sub> SO <sub>2</sub>	P	Difference Between r <sub>c</sub> SO <sub>2</sub> Sides
First seizure	n <sup>1</sup> = 21, I = 21				n <sup>1</sup> = 25, I = 25			
	47 (40, 79)	69 (57, 76)	<0.001	24.9 (15.9, 27.1)	77 (70, 78)	46 (35, 90)	0.003	25.3 (12.9, 33)
Second seizure	n <sup>1</sup> = 24, I = 24				n <sup>1</sup> = 41, I = 41			
	44 (36.5, 52.5)	67 (59, 78)	<0.001	22 (16.7, 31.9)	66 (51, 67)	41 (36, 45)	<0.001	24.6 (21.0, 28.2)
Third seizure	n <sup>1</sup> = 8, I = 8				n <sup>1</sup> = 43, I = 43			
	42.5 (40, 58.5)	63.5 (54.5, 69)	0.004	19.1 (11, 22)	61.6 (53, 77)	40 (34, 62)	0.001	19.9 (13.7, 28.9)
All seizure	n <sup>1</sup> = 48, I = 68				n <sup>1</sup> = 75, I = 146			
	44 (36.5, 55.5)	65.7 (56.3, 73.3)	0.001	22 (15.8, 31.2)	63.8 (53, 77)	39.9 (35, 56)	<0.001	19.9 (13.2, 30.5)

**TABLE 5A.** Patients With Multiple Generalized Seizures: Comparative Time Analysis of Their Hemispheric (Left and Right) Seizure  $r_cSO_2$  Readings by Time Intervals: All Their Seizure  $r_cSO_2$  Readings (as Independent Events) and by Their Initial Hemispheric Seizure  $r_cSO_2$  Readings of Less Than 60% and Greater Than 80% With Same Time Comparisons

	10 to 5 min Before Seizure		5 to 0 min Before Seizure		During Seizure		0–5 min After Seizure		5–10 min After Seizure		P During, Before, and After Seizure
	n	Median	n	Median	n	Median	n	Median	n	Median	
Left $r_cSO_2$											
All	148	66 (60.0, 71.5)	201	66 (58.5, 74.0)	334	44 (36.5, 82.0)	306	66 (58.0, 72.0)	261	66 (60.0, 74.0)	<0.0001
Left $r_cSO_2 <60$	88	64 (56.0, 69.5)	123	62 (55.5, 73.0)	206	43 (36.0, 44.5)	187	64.5 (56.0, 72.5)	155	66 (55.0, 74.0)	<0.0001
Left $r_cSO_2 >80$	42	67 (62.5, 72.0)	58	68 (65.0, 76.0)	106	87.5 (62.0, 90.0)	98	67 (64.0, 73.0)	87	65 (63.0, 73.0)	<0.0001
Right $r_cSO_2$											
All	148	64 (56.0, 72.0)	201	65 (56.5, 73.0)	334	39 (34.0, 80.0)	306	63 (54.0, 71.0)	261	64 (58.0, 72.0)	<0.0001
Right $r_cSO_2 <60$	89	63 (53.0, 67.5)	124	60.5 (50.0, 71.0)	210	36 (30.0, 40.0)	192	62.8 (50.0, 71.0)	158	64.3 (55.0, 72.0)	<0.0001
Right $r_cSO_2 >80$	42	64.8 (60.0, 73.0)	51	66.5 (62.5, 73.0)	96	82.5 (59.0, 88.0)	88	64.5 (62.0, 71.75)	81	64 (61.0, 71.0)	<0.0001

Time interval analysis parameters: (1) 10 to 5 minutes before start of the seizure event; (2) 5 to 0<sup>1</sup> minutes before the seizure event; (3) during the seizure event (total duration of the seizure event); (4) 0<sup>2</sup> to 5 minutes after the end of the seizure event; (5) 5 to 10 minutes after seizure event cessation: <sup>1</sup>(0 = before the start of seizure event), <sup>2</sup>(0 = before the start of seizure event).

P value = the comparison of the during  $r_cSO_2$  median to the before and after seizure  $r_cSO_2$  median time interval.

or multiple seizure events followed similar patterns.<sup>24–26</sup> From this study, some seizure patients' hemispheric  $r_cSO_2$  readings initially rose to greater than 80% and then declined during their seizure. These seizure  $r_cSO_2$  readings pattern probably reflected that the increased CBF became inadequate for the seizure's metabolic demand, causing a tissue oxygenation deficit as indicated by the lower  $r_cSO_2$  readings.<sup>16–20,25–27</sup>

In left or right focal seizure, compared with generalized seizure events, there were no significant differences between the focal seizure  $r_cSO_2$  readings and the generalized ipsilateral seizure  $r_cSO_2$  readings. In either left or right focal seizure, there were significant interhemispheric  $r_cSO_2$  discordance readings, which was consistent over multiple focal seizure events. This significant focal seizure interhemispheric discordance was significant and like

other pediatric neurological cerebral oximetry findings in strokes, hydrocephalus, epidural, and subdurals.<sup>12–14</sup>

The ED patient's documented seizure times compared with the  $r_cSO_2$  readings did have a high correlation, which could be due to 77% of the patients having clinically evident seizures upon PED presentation. Knowledge of a patient's prior seizure could heighten the PED staff's seizure awareness, leading to quicker seizure interpretation, quicker subsequent seizures detection, and improved seizure documentation.

In summary, in the acute setting, once the seizure patient's airway, breathing, circulation, and glycemic state are stabilized, focus should shift to rapid seizure termination and restoring normal cerebral physiology to minimize the abnormal hemispheric cerebral physiology, energy depletion, and neurological injury.<sup>1–4,16–20,23–27</sup>

**TABLE 5B.** Comparative Time Analysis of Delta Difference of Seizure  $r_cSO_2$  Readings in Generalized, Left and Right Focal Hemispheric and Abnormal Seizure (Both  $r_cSO_2 <60$ ,<sup>11–15</sup> Both  $r_cSO_2 <80$ <sup>11–15</sup>)  $r_cSO_2$  Readings (Differences Between Seizure Times) and by Their Initial Hemispheric Seizure  $r_cSO_2$  Readings of Less Than 60% and Greater Than 80% With Same Time Comparisons. Overall: A positive value = increase, negative value = decrease. 1. Generalized seizure event had a  $r_cSO_2$  change of left –9.8, right –10.7. 2. Left focal event had a left  $r_cSO_2$  change of –17.8. 3. Right focal event had a right  $r_cSO_2$  change of –20.3

Seizure Type	Subgroup: $r_cSO_2$ Differences	Left $r_cSO_2$		Right $r_cSO_2$	
		Change	P	Change	P
Generalized seizure	All $r_cSO_2$ : during and before seizures	–12	<0.0001	–18.5	0.002
	During and after seizures	10	<0.0001	11.2	<0.0001
	After and before seizures	–2.5	0.95	–1	0.7
	Both $r_cSO_2 <60$ <sup>11–15</sup>	–21	<0.0001	–24.5	<0.0001
	Both $r_cSO_2 >80$ <sup>11–15</sup>	18	<0.0002	18.5	0.003
Left focal seizure	All $r_cSO_2$ : during and before seizure	–17.8	<0.0001	1	0.99
	During and after seizures	–19.8	<0.0001	1	0.99
	After and before seizures	–4.2	0.6	–2.5	0.99
	Left $r_cSO_2 <60$ <sup>11–15</sup>	–19.8	<0.0001	.5	0.87
	Left $r_cSO_2 >80$ <sup>11–15</sup>	22	0.01	2.3	0.98
Right focal seizure	All $r_cSO_2$ : during and before seizure	–1	0.54	–20.3	<0.0001
	During and after seizures	–2	0.04	–22.5	<0.0001
	After and before seizures	1	0.81	4.5	0.75
	Right $r_cSO_2 <60$ <sup>11–15</sup>	–4	0.98	–19	<0.0001
	Right $r_cSO_2 >80$ <sup>11–15</sup>	7	0.61	22.5	<0.0001

In either generalized or focal seizure, r<sub>c</sub>SO<sub>2</sub> readings correlated with seizure event and demonstrated a consistent decrease or increase, probably reflecting a decrease or increase in regional cerebral oxygen and physiology during the seizure compared with either their pre-seizure or post-seizure time.<sup>16–20,24–27</sup> Post-seizure r<sub>c</sub>SO<sub>2</sub> readings approximated their pre-seizure r<sub>c</sub>SO<sub>2</sub> readings, demonstrating a resolution of the abnormal hemispheric cerebral oxygen and physiology. In the focal seizure events, ipsilateral r<sub>c</sub>SO<sub>2</sub> strongly correlated with the focal seizure side and in the post-seizure phase returned to the pre-seizure readings. This study demonstrates that there is a dynamic hemispheric cerebral physiology change occurring during clinically evident seizure events, and this change may indicate physical neuronal compromise and potential for neuronal injury. These hemispheric frontal lobe r<sub>c</sub>SO<sub>2</sub> readings are dynamic, have an interplay with other cerebral regions, and can be affected by other abnormal regional cerebral activity as shown by focal and generalized seizure r<sub>c</sub>SO<sub>2</sub> readings. From this vast pool of left and right cerebral oximetry readings in the generalized and focal seizures patients, if the hemispheric r<sub>c</sub>SO<sub>2</sub> readings are less than 60% or greater than 80%, or the interhemispheric discordance r<sub>c</sub>SO<sub>2</sub> readings are greater than 10 with no obvious signs of clinically evident seizure for the nonneurologist, further investigation for possible clinical and/or subclinical seizures is warranted. Because seizure recognition is greatly impaired in neonates, pediatric patients, and nonverbal or developmentally challenged patients, cerebral oximetry has shown its potential as an objective neurological assessment tool and possibly decreases misperception of clinically evident seizure recognition. This study should not be interpreted as a replacement for the diagnostic electroencephalogram (EEG) system, but rather as an adjunct acute-setting neurological assessment tool for the health care provider. Cerebral oximetry has shown its potential utilization in neonate and pediatric seizure research as an adjunct assessment tool. Further research is needed to investigate the potential use of hemispheric and interhemispheric discordant r<sub>c</sub>SO<sub>2</sub> readings as a predictive tool for anticonvulsants therapeutic effectiveness especially in pharmacoresistant seizures.

### LIMITATIONS

Documentation and detection of pediatric seizures can have sampling error due to the PED staff's clinically evident seizure recognition experience. Current hemispheric cerebral oximetry probes physically prevent ambulatory EEG forehead probe placement; therefore, correlating clinical seizures to EEG seizures with simultaneous hemispheric r<sub>c</sub>SO<sub>2</sub> readings cannot be accomplished.

### CONCLUSIONS

This PED preliminary hemispheric cerebral oximetry seizure study during clinically evident general and focal seizures showed altered cerebral oximetry r<sub>c</sub>SO<sub>2</sub> readings and significantly correlated with seizures and reflected abnormal seizure cerebral physiology. In generalized seizures, hemispheric r<sub>c</sub>SO<sub>2</sub> readings were either significantly decreased (<60%) or increased (>80%) compared with their pre-seizure and post-seizure readings and nonseizure patients. During focal seizures, ipsilateral r<sub>c</sub>SO<sub>2</sub> readings correlated to the seizure side, and interhemispheric discordance r<sub>c</sub>SO<sub>2</sub> readings differed significantly (>10). Post-seizure r<sub>c</sub>SO<sub>2</sub> readings returned to pre-seizure readings, showing altered cerebral physiology resolution. Overall, cerebral oximetry during generalized and focal seizure r<sub>c</sub>SO<sub>2</sub> readings were less than 60% or greater than 80%, and in focal seizures their interhemispheric r<sub>c</sub>SO<sub>2</sub> discordance was greater than 10, demonstrating its potential pediatric seizure

utility. This PED seizure cerebral oximetry study substantiates further investigation in subclinical seizure detection and anticonvulsant therapeutic effectiveness especially in pharmacoresistant seizures. This study advances cerebral oximetry functionality as an adjunct neurological assessment tool in pediatric neuroresuscitation.

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