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Brain tissue oxygen monitoring identifies cortical hypoxia and thalamic hyperoxia after experimental pediatric cardiac arrest

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Abstract

Background—Optimization of cerebral oxygenation after pediatric cardiac arrest (CA) may reduce neurological damage associated with the post-CA syndrome. We hypothesized that important alterations in regional partial pressure of brain tissue oxygen (PbO_2) occur after resuscitation from CA and that clinically relevant interventions such as hyperoxia and blood pressure augmentation would influence PbO_2.

Methods—Cortical and thalamic PbO_2 were monitored in immature rats subjected to asphyxial CA (9 or 12 min asphyxia) and sham-operated rats using oxygen sensors.

Results—Thalamus and cortex showed similar baseline PbO_2. Post-resuscitation there was early and sustained cortical hypoxia in an insult-duration fashion. In contrast, thalamic PbO_2 initially increased four-fold, and afterwards returned to baseline values. PbO_2 was FiO_2-dependent, and the response to oxygen was more pronounced after a 9 min vs. 12 min CA. After a 12 min CA, PbO_2 was modestly affected by blood pressure augmentation using epinephrine in the thalamus but not cortex.

Conclusion—After asphyxial pediatric CA, there is marked regional variability of cerebral oxygenation. Cortical hypoxia is pronounced and appears early, while thalamic hyperoxia is followed by normoxia. Compromised PbO_2 in the cortex may represent a relevant and clinically measurable therapeutic target aimed at improving neurological outcome after pediatric CA.

Introduction

Hypoxic ischemic brain injury affects 53-76% of children successfully resuscitated from cardiac arrest (CA) (1). Brain tissue hypoxia, cerebral hypoperfusion and impaired autoregulation in the early post-CA syndrome have potential implications for secondary brain injury in patients successfully resuscitated from CA. The International Liaison

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Committee on Resuscitation emphasized in a recent statement that good neurological outcome is contingent upon optimal post-CA care, and identified important knowledge gaps in optimal oxygen delivery during the initial stages of reperfusion, and optimal cerebral monitoring after CA (2). Early optimization of cerebral oxygen delivery to meet metabolic demands may reduce the neurological damage associated with post-CA brain injury.

After experimental pediatric asphyxial CA, cortical regions have decreased perfusion, while thalamic regions are hyperemic (3). Cortical hypoperfusion observed in our model may be associated with cortical hypoxia. Serial and regional partial pressure of brain tissue oxygen (PbO_2) after experimental asphyxial CA has not been characterized. Multiple studies have demonstrated that after traumatic brain injury (TBI) direct monitoring of PbO_2 is safe and some studies have suggested that targeting specific thresholds for PbO_2 has been associated with improved outcomes compared with historical controls (4-8). Although brain tissue monitoring was included in the treatment guidelines for adult victims of TBI in 2007, PbO_2 monitoring after pediatric CA is not used routinely.

Based on our previous studies of post-resuscitation cerebral perfusion, we hypothesized that important differences in regional PbO_2 would be observed during early post-CA syndrome after experimental asphyxial CA and that clinically relevant interventions such as hyperoxia and blood pressure augmentation would influence PbO_2.

Results

Regional PbO_2 during and after asphyxial CA

Table 1 presents physiological data for the groups of rats that underwent CA. Mean arterial pressure (MAP) increased at 5-10 min post resuscitation, then decreased and was lower than baseline after 30 min post resuscitation. The baseline MAP was lower in the 12 min asphyxial CA groups that underwent thalamic PbO_2 measurements vs. 9 min asphyxial CA that underwent cortical or thalamic PbO_2 measurements (55±2 vs. 67±2 and 72±4 mmHg, respectively, $p<0.05$). $PaCO_2$ was maintained in the normal range at all time points except for an increase to 46±1.6 mm Hg only at 60 min post resuscitation in the 9 min thalamic group. Hemoglobin decreased vs. baseline at 30, 60, and 120 min after 9 and 12 min CA, with no difference between groups at each time point.

Baseline PbO_2 was similar for cortical and thalamic areas. After the onset of asphyxia, PbO_2 decreased to less than 5 mm Hg within 60 s in both regions and all rats. After CPR, we observed a rapid rise in PbO_2 in the thalamus and a more gradual rise in PbO_2 in the cortex.

Figure 1a illustrates cortical PbO_2 after resuscitation from 9 and 12 min asphyxial CA. After 9 min asphyxial CA, mean cortical PbO_2 was similar to baseline at 5, 10, and 15 min (64±22, 39±8, and 33±6 mm Hg at 5, 10 and 15 min, respectively), and then lower than baseline from 30 min (19±4 mm Hg) to 120 min (25±5 mm Hg) post-resuscitation. After 12 min asphyxial CA, cortical PbO_2 was similar to baseline at 5-15 min (43±18, 25±7 and 25±6 mm Hg), and then lower than baseline from 30 min (15±4 mm Hg) to 120 min (9±2 mm Hg) post-resuscitation (Figure 1a). Cortical PbO_2 was lower in rats subjected to 12 min asphyxial CA vs. 9 min asphyxial CA at 120 min post-resuscitation ($p<0.05$).

Figure 1b illustrates thalamic PbO_2 after resuscitation from 9 and 12 min asphyxial CA. After both 9 and 12 min asphyxial CA, thalamic PbO_2 was markedly increased vs. baseline at 5 min (281±25 vs. 66±16.3, and 256±45 vs. 63±6 mm Hg, $p<0.05$ after 9 and 12 min asphyxia, respectively) and remained elevated at 10 min after resuscitation (151±23 and 217±50 mm Hg, $p<0.05$ vs. baseline after 9 and 12 min asphyxia, respectively). After the initial increase, thalamic PbO_2 decreased towards baseline for the duration of monitoring, and remained well above 20 mm Hg.

Post-CA response of PbO_2 to supplemental oxygen

The response to supplemental oxygen was evaluated at 120 min after resuscitation from 9 or 12 min CA. At 120 min after resuscitation the rats receive a fraction of inspired oxygen (FiO_2) =0.5 in our model. At that time point we decreased the FiO_2 to 0.21 and gradually increased the FiO_2 to 1.0. Decreasing the FiO_2 to 0.21 at 120 min after CA resulted in arterial hypoxemia (Transcutaneous oxygen saturation, $SatO_2$=83±3%, PaO_2=46.2±4.2 mmHg). At an FiO_2 of 0.21, cortical PbO_2 was 16±2 and 5±2 mm Hg after 9 and 12 min asphyxial CA, respectively, while thalamic PbO_2 was 19±5 and 30±3 after 9 and 12 min asphyxial CA, respectively (Figure 2).

Cortical and thalamic PbO_2 and $SatO_2$ values for individual FiO_2 concentrations are shown in Figure 2. Increasing FiO_2 from 0.21 to 0.3 resolved the observed hypoxemia and increased the $SatO_2$ above 95% in all rats. Further increases in FiO_2 increased $SatO_2$ to 99-100%. Under these conditions, cortical and thalamic PbO_2 had different responses to increased FiO_2. Cortical PbO_2 after 9 min of asphyxia increased progressively with supplemental oxygen from FiO_2=0.21 to FiO_2=0.4 ($p<0.05$). Further increase in FiO_2 to 0.5 and 1 did not result in further increase in cortical PbO_2 after 9 min of asphyxia. After 12 min of asphyxia, cortical PbO_2 values were 7.1±3 and 8.3±3 mm Hg at FiO_2=0.3 and 0.4, respectively ($p=0.3$ and 0.2, FiO_2=0.3 and 0.4 vs. FiO_2=0.21, respectively). PbO_2 was slightly increased at FiO_2=0.5 and 1 (PbO_2=10.5±8 mm Hg, $p<0.05$ for FiO_2=0.5 vs. FiO_2=0.21).

Thalamic PbO_2 gradually increased with increases in supplemental oxygen after both 9 and 12 min of asphyxia (Figure 2).

Post-CA response of PbO_2 to epinephrine infusion

To determine whether low cortical PbO_2 levels after 12 min asphyxial CA were related to low MAP, we administered epinephrine to increase MAP at 120 min after CA. A 2 mcg kg^{-1} min^{-1} epinephrine infusion increased MAP from 47±3.7 to 66.6±6.8 mm Hg (baseline MAP), and further infusion of epinephrine to 20 mcg kg^{-1} min^{-1} increased MAP to 82.3±5.8 mmHg (above baseline MAP). Cortical PbO_2 did not increase with epinephrine infusion (Figure 3). Conversely, thalamic PbO_2 did increase during high dose epinephrine infusion ($p<0.05$, epinephrine 20 mcg kg^{-1} min^{-1} vs. before epinephrine infusion, Figure 3). In sham rats treated with epinephrine infusion we observed a similar pattern of PbO_2 response: no increase in cortical PbO_2 and increase in thalamic PbO_2 at 4, 10, and 20 mcg kg^{-1} min^{-1} (data not shown).

Discussion

To our knowledge, this is the first study reporting direct measurements of PbO_2 in a model of pediatric asphyxial CA. Our data suggest important region- and insult duration-dependent alterations in PbO_2 after CA. Cortical PbO_2 was reduced in the first two hours after resuscitation, especially after longer insults, reaching thresholds consistent with cerebral ischemia (9). In distinct contrast, thalamic PbO_2 was markedly increased initially after CA, and then returned to baseline. PbO_2 response to supplemental oxygen was also insult duration and region dependent.

PbO_2 reflects the local oxygen concentration in brain tissue, and serves as a marker of the balance between regional oxygen supply and consumption. It is influenced by cerebral blood flow (CBF), MAP, PaO_2, hemoglobin concentration, and factors affecting diffusion of oxygen in brain (10). In clinical studies, PbO_2 values less than 10 mm Hg are associated with higher risk for ischemic brain injury (11, 12) and with unfavorable outcome after TBI (8). Similar threshold values have not been reported in either experimental or clinical CA.

Post-CA cortical hypoxia in this study reached levels that are below the accepted PbO_2 ischemic thresholds of 20 (5) or even 10 mm Hg in humans (8, 11). Human data demonstrated ongoing ischemia and anaerobic metabolism in the cortex during the first 10 h and up to 40 h after CA (13, 14). Similar to our study, in an experimental model of global cerebral ischemia produced by neck tourniquet in adult primates, PbO_2 was region dependent with cortical hypoxia starting at 1 h post ischemia (15). Conversely, upon resuscitation from neonatal hypoxia with brief (1 min) CA, Linner et al. observed initial cortical hyperoxia followed by return to baseline levels in newborn piglets (16). This is consistent with the hypothesis that PbO_2 changes are insult-duration dependent, with shorter durations of CA producing less hypoxia, similar to our previously described insult-duration dependency of CBF post CA (3). Age-related differences or species differences could also be involved. If this observation translates to children resuscitated from out-of-hospital CA, where the duration of no-flow is most often unknown, PbO_2 could have potential utility in insult-duration stratification and prognostication.

Our data suggest that PbO_2 parallels CBF in our model. Post-CA cortical hypoxia mirrors the cortical hypoperfusion we previously observed, while thalamic hyperoxia parallels thalamic hyperemia (3). Isoflurane, shown to preferentially increase subcortical CBF (17-20), increased thalamic PbO_2 in our sham rats while having no effect on cortical PbO_2 (pilot data, not shown). The association between PbO_2 and CBF was also reported in non-injured rats (21) and models of global ischemia (22). These observations suggest that continuous PbO_2 monitoring may be used as a surrogate marker for cerebral perfusion early after CA.

Supplemental oxygen increased thalamic and cortical PbO_2, with a more robust effect after 9 vs. 12 min CA. It was previously reported that the response of PbO_2 to hyperoxia is diminished in pathological compared with normal tissue (23-25), and increased supplemental oxygen does not correspond to an improvement in brain oxygen delivery in areas with severely reduced CBF (26). We previously reported that CBF is decreased in

cortex, more pronounced after prolonged insults, and increased in thalamus after CA in our model (3). Our findings are in accordance with the hypothesis that raising FiO_2 in the injured brain yields an increase in PbO_2 but is highly dependent on adequate CBF. These observations suggest that interventions targeted to increase PbO_2 after long durations of CA should primarily focus on increasing CBF. Further studies of strategies to increase cortical PbO_2 via blood flow promoting vasodilatatory agents are warranted. Possible CBF promoting strategies include: endothelin receptor antagonists (27), nitrite (28), or inhibition of 20-HETE (29), among other therapies. In our study, conditions of mild arterial hypoxemia, on the contrary, resulted in lower PbO_2 in shams and post-CA, suggesting that arterial hypoxemia should be avoided post-CA.

Increasing MAP using epinephrine infusion after long insults did not significantly increase cortical PbO_2, although it increased thalamic PbO_2 at high doses only. This suggests that nonspecific interventions such as MAP augmentation may not be sufficient to increase PbO_2 in areas of cerebral hypoxia after CA. Our results also indicate that epinephrine could compromise cerebral microcirculatory flow after CA, similar to its effects in a piglet model of CA where despite increase in cerebral perfusion pressure after epinephrine infusion, microcirculatory blood flow decreased (30). As epinephrine is frequently used clinically post resuscitation from CA to stabilize hemodynamic parameters, it would be important to determine if other strategies to raise MAP might be able to improve PbO_2 and microcirculatory flow. While MAP was measured during the epinephrine infusion, measurement of the intracranial pressure to assess the cerebral perfusion pressure could have given us additional information regarding the cerebrovascular effect of epinephrine.

We chose to study the effect on PbO_2 of two clinically relevant and frequently used therapies during post-CA syndrome: oxygen and epinephrine. Other clinical strategies to augment PbO_2, such as blood transfusion, administration of pentobarbital or controlled hypoventilation, not studied here, might have some utility.

We found some degree of variability of PbO_2 in our study, both in shams and injured rats. This variability was observed in other studies (15) and is consistent with data showing that cortical PbO_2 varies with as much as 20 mm Hg depending on the cortical area and layers of the somatosensory cortex (31). Likewise, hippocampal PbO_2 varies within different areas (32). Our data suggest, however, that marked reductions of PbO_2 in the cortex are observed after CA and represent a potential therapeutic target for post-resuscitation approaches designed to raise PbO_2.

The ratio of PbO_2/PaO_2 followed the same pattern as PbO_2 (data not shown), confirming the region specific variability to PbO_2 in response to CA is not a function of changes in FiO_2. We found some variability in our physiological data. The thalamic group with lower MAP (12 min asphyxial CA) had a similar PbO_2 tracing with the 9 min thalamic group, and thus MAP values were unlikely to have affected our results. We also observed a decrease in hemoglobin of 0.9-1.5 mg/dl over time in all groups, with no difference between groups. In our model we observe a similar decrease in hemoglobin in sham rats with no change in PbO_2, suggesting that this degree of decrease in hemoglobin does not affect PbO_2 in sham or injured rats.

Relevant to the current study, in previous studies we did not observe sex-based differences in post-arrest CBF (3), although we did observe a sex-based difference in response to a specific treatment (polynitroxyl albumin) (33). As one aspect of the current study was to evaluate PbO_2 as a potential surrogate for continuous CBF measurements after CA, we chose to limit the experiments to males. Future studies utilizing PbO_2, particularly those evaluating treatments, should include males and females.

In this model of pediatric asphyxial CA selective neuronal death in cortex, thalamus, hippocampus and cerebellum is seen, along with behavioral deficits (34, 35). However, the relationship between cortical PbO_2 and histopathological and functional outcome in our model remains to be determined. The threshold for cortical hypoxia that produces neuronal injury may even be lower than 10 mm Hg and remains uncertain. Age-related differences in the PbO_2 threshold for hypoxia after CA also remain undefined. An intriguing hypothesis is that post-ischemic thalamic hyperoxia might also be detrimental. Further experiments in our model assessing the PbO_2 threshold and whether goal directed PbO_2 therapy improves outcome are warranted.

In conclusion, PbO_2 after asphyxial CA in immature rats is region-dependent: there is cortical hypoxia but early thalamic hyperoxia. These findings mimic the pattern of CBF in this model, suggesting that PbO_2 is representative of oxygen delivery and CBF. Increasing supplemental oxygen improves cortical hypoxia. If our model translates to the human condition, these data suggest a possible utility for PbO_2 monitoring after CA in children. Further studies in this model are warranted to assess if goal directed therapy targeting cerebral oxygenation improves outcome after experimental pediatric asphyxial CA.

Materials and methods

Studies were approved by the Institutional Animal Care and Use Committee at the University of Pittsburgh and the care and handling of the animals were in accord with the National Institutes of Health (Bethesda, MD) guidelines. We used male postnatal day 16-18 Sprague-Dawley rats (30-46 g, n=56). We measured PbO_2 after CA in cortex and thalamus in separate groups of rats after asphyxial CA and the response of PbO_2 to hyperoxia or MAP augmentation after CA.

Anesthesia and surgery

Rats were initially anesthetized with 3% isoflurane/50% N_2O/balance O_2 in a Plexiglas chamber until unconscious and then their tracheas were intubated with an 18-gauge catheter. Mechanical ventilation was started and ventilatory rates and tidal volumes were adjusted to maintain $PaCO_2$ at 35-45 mm Hg. Femoral arterial and venous catheters (PE 10) were inserted to monitor MAP and infuse medications. During surgery, anesthesia was maintained with 1.5% isoflurane/50% N_2O/balance O_2. Isoflurane was discontinued after the placement of arterial and venous catheters and anesthesia was maintained with fentanyl as described below. MAP and heart rate were continuously monitored. Rectal temperature was maintained at 37°C via a heated water blanket.

PbO_2 electrode placement

The head was stabilized in a stereotaxic instrument using ear bars. A small burr hole (2 mm) was drilled in the skull 2 mm lateral and 3.3 mm posterior to bregma. PbO_2 was measured continuously using a Clark type tissue electrode (Ox-50, Unisense, Denmark) inserted at either a depth of 1 mm for cortical PbO_2 measurements or at a depth of 6 mm for thalamic PbO_2 measurements. We chose to measure PbO_2 in the cortex and thalamus because these are brain regions with the lowest or highest post-resuscitation CBF, respectively, in our previous report (3). The location of the electrode in cortex or thalamus was verified in brain sections after injection of Evans Blue at the conclusion of the experiment. Brain temperature was continuously monitored with an intraparenchymal sensor. Three groups (cortical 9 and 12 min, thalamic 9 min groups) had mean brain temperatures between 36.2 and 36.9. Due to an experimental oversight, the thalamic 12 min group did not have brain temperature monitored; however the body temperature, which parallels brain temperature in our model, was maintained constant in this group. Baseline parameters for MAP, PaO_2, pH, $PaCO_2$ and PbO_2 were obtained immediately before the asphyxial insult.

PbO_2 measurements in shams under different anesthetic conditions

In pilot experiments we determined the effects of two anesthetics: isoflurane and fentanyl on cortical and thalamic PbO_2 in sham rats. Cortical PbO_2 was measured in one group, and thalamic PbO_2 in the other (n=8, 4/group). Each group initially was anesthetized with isoflurane and PbO_2 was measured after a 10 min stabilization period. Isoflurane was then discontinued and a fentanyl infusion at 50 μg kg^{-1} h^{-1} was started. The rats were observed for 30 min prior to measuring the PbO_2 to assure wash out of isoflurane. Cortical PbO_2 values were similar using isoflurane or fentanyl anesthesia. Thalamic PbO_2 were higher using isoflurane vs. fentanyl anesthesia (109±32% increase in thalamic PbO_2 using isoflurane vs. fentanyl, $p<0.05$). Therefore, in all CA experiments, anesthesia was maintained with fentanyl infusion to minimize effects of anesthesia on PbO_2.

Asphyxial cardiac arrest

We used an established asphyxial CA protocol (3). Rats received intravenous fentanyl infusion at 50 μg $kg^{-1}h^{-1}$ to provide anesthesia and vecuronium infusion at 5 mg $kg^{-1}h^{-1}$ to induce neuromuscular blockade. We used fentanyl as the anesthetic agent during the CA experiments because it is clinically relevant and unlike the inhaled anesthetics, it does not affect CBF (19). The FiO_2 was reduced from 0.5 to 0.21 for 1 min before asphyxia to avoid preinsult hyperoxygenation. The tracheal tube was disconnected from the ventilator for 9 or 12 min. Resuscitation was started by reconnecting the ventilator and reinstituting mechanical ventilation at an FiO_2 of 1.0. Epinephrine (0.005 mg kg^{-1}) and sodium bicarbonate (1 mEq kg^{-1}) were administered intravenously, followed by manual chest compressions until return of spontaneous circulation. The fentanyl infusion was restarted 30 min after resuscitation at the pre-arrest infusion rate. At 30 min after resuscitation, FiO_2 was decreased to 0.5. This oxygenation sequence during CPR and post-resuscitation is consistent with common clinical practice at our institution. Arterial blood gas measurements were obtained at the time of arterial catheter insertion, at 30 and 60 min after CA and at the end of the experiment, and the ventilatory rates and tidal volumes were adjusted to a target of

$PaCO_2$ of 35-45 mm Hg. Transcutaneous oxygen saturation ($SatO_2$) was measured continuously with a pulse oximeter (MouseOx, Starr Life Sciences).

PbO_2 measurements during and after CA

In separate groups of rats, cortical or thalamic PbO_2 were measured continuously before, during, and after 9 or 12 min asphyxial CA (n= 6/group for thalamic PbO_2 measurements and n=12/group for cortical PbO_2 measurements). PbO_2 was recorded for analysis at baseline, and at the following time points post-resuscitation: 5, 10, 15, 30, 60, and 120 min. At the completion of 120 min post- resuscitation period, these rats underwent PbO_2 measurements to assess the response to supplemental oxygen or epinephrine as described below.

Post-CA response of PbO_2 to supplemental oxygen

We assessed cortical and thalamic PbO_2 responses to a gradual increase in FiO_2 from 0.21 to 1.0 (FiO_2= 0.21, 0.3, 0.4, 0.5, and 1.0) at 120 min after resuscitation from 9 or 12 min asphyxial CA (n=6/group/region). According to our asphyxial CA protocol, rats receive FiO_2= 1 at resuscitation and during the first 30 min post-resuscitation. From 30-120 min after resuscitation the rats receive an FiO_2=0.5. At 120 min after resuscitation we decreased the FiO_2 to 0.21, and then gradually increased the FiO_2 as above. At each FiO_2 we recorded the transcutaneous oxygen saturation ($SatO_2$), PbO_2, and MAP after a 10 min stabilization period for PbO_2.

Post-CA response of PbO_2 to epinephrine

We assessed the post-CA cortical and thalamic PbO_2 response to an increase in MAP initially to baseline values, followed by MAP increase above baseline (n=6/group). At 120 min after 12 min asphyxia, we increased MAP via infusion of epinephrine. We started at a dose of 2 mcg kg^{-1} min^{-1} to achieve MAP equal to baseline, and then increased the infusion to 4, 10, and 20 mcg kg^{-1} min^{-1} (3, 36) while the FiO_2 was maintained at 0.5. We administered the same infusion of epinephrine to sham rats (n=6/group) and measured PbO_2.

Statistical Analysis

Data were analyzed with the statistical software Systat, Sigmastat 11.2 (Systat Software, Inc., Chicago, IL). Data were expressed as mean ± SEM. A $p < 0.05$ was considered significant. We used repeated measures ANOVA with Student-Newman Keuls post-hoc test to compare MAP, $PaCO_2$, PaO_2, pH, and PbO_2 values at each time point and within each group over time. For data that failed equal variance and normality we ranked the data and afterwards performed repeated measures ANOVA.

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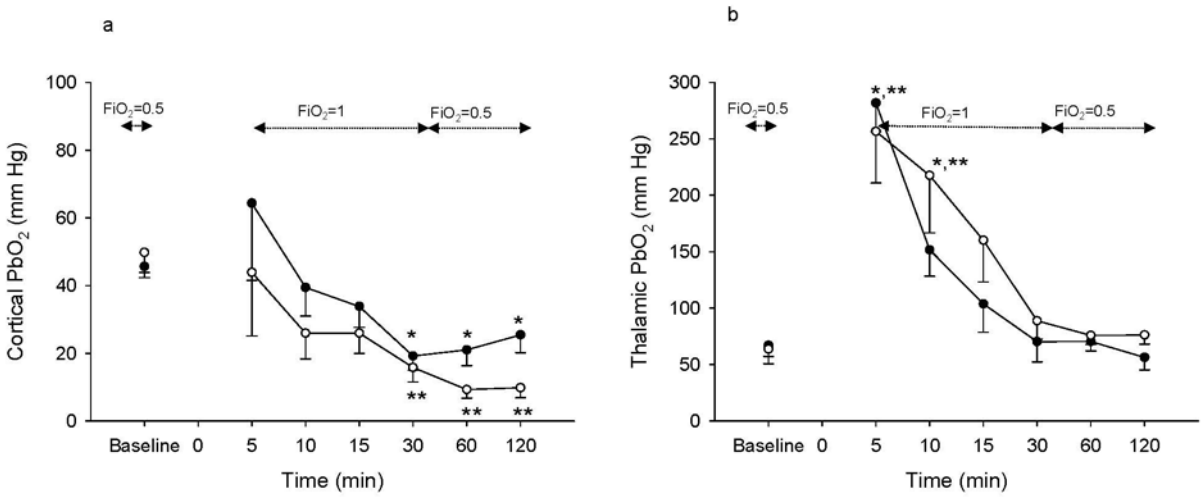

Figure 1.

Cortical (a) and thalamic (b) PbO_2 at baseline and after resuscitation from 9 and 12 min of asphyxia. Time 0 represents the time of CA. Black circles represent 9 min CA group, and white circles represent 12 min CA group. n= 6/group for thalamic PbO_2 measurements and n=12/group for cortical PbO_2 measurements. (*p<0.05 vs. baseline for 9 min insult, **p<0.05 vs. baseline for 12 min insult).

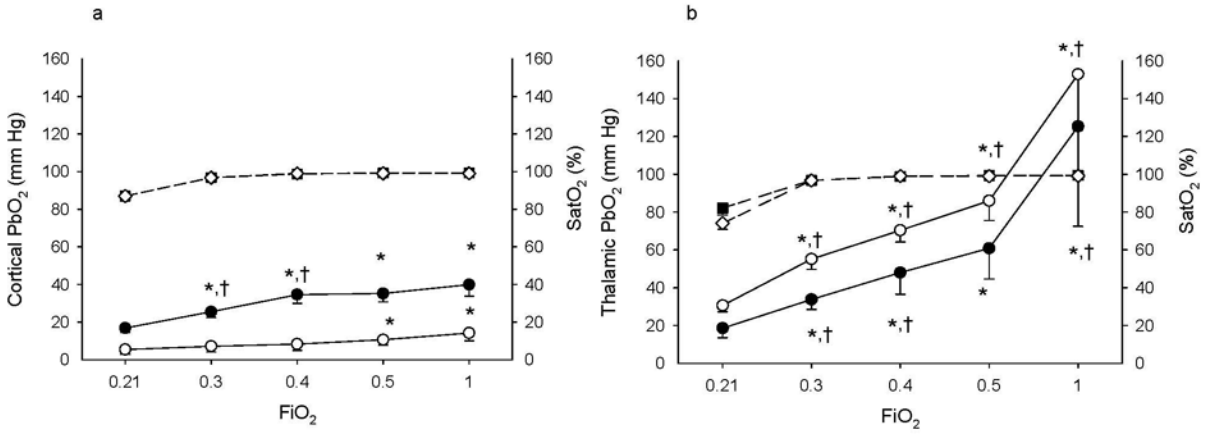

Figure 2.

Cortical (a) and thalamic (b) PbO_2 and Sat O_2 response to increase in FiO_2 from 0.21 to 0.3, 0.4, 0.5, and 1.0 after 9 and 12 min asphyxia. Black circles represent PbO_2 for the 9 min CA group, white circles represent PbO_2 for the 12 min CA group, black squares represent $SatO_2$ for the 9 min CA group, and white diamonds represent $SatO_2$ for the 12 min CA group. n= 6/group/region. (*p<0.05 vs. FiO_2=0.21, $^{\dagger}p$<0.05 vs. previous FiO_2).

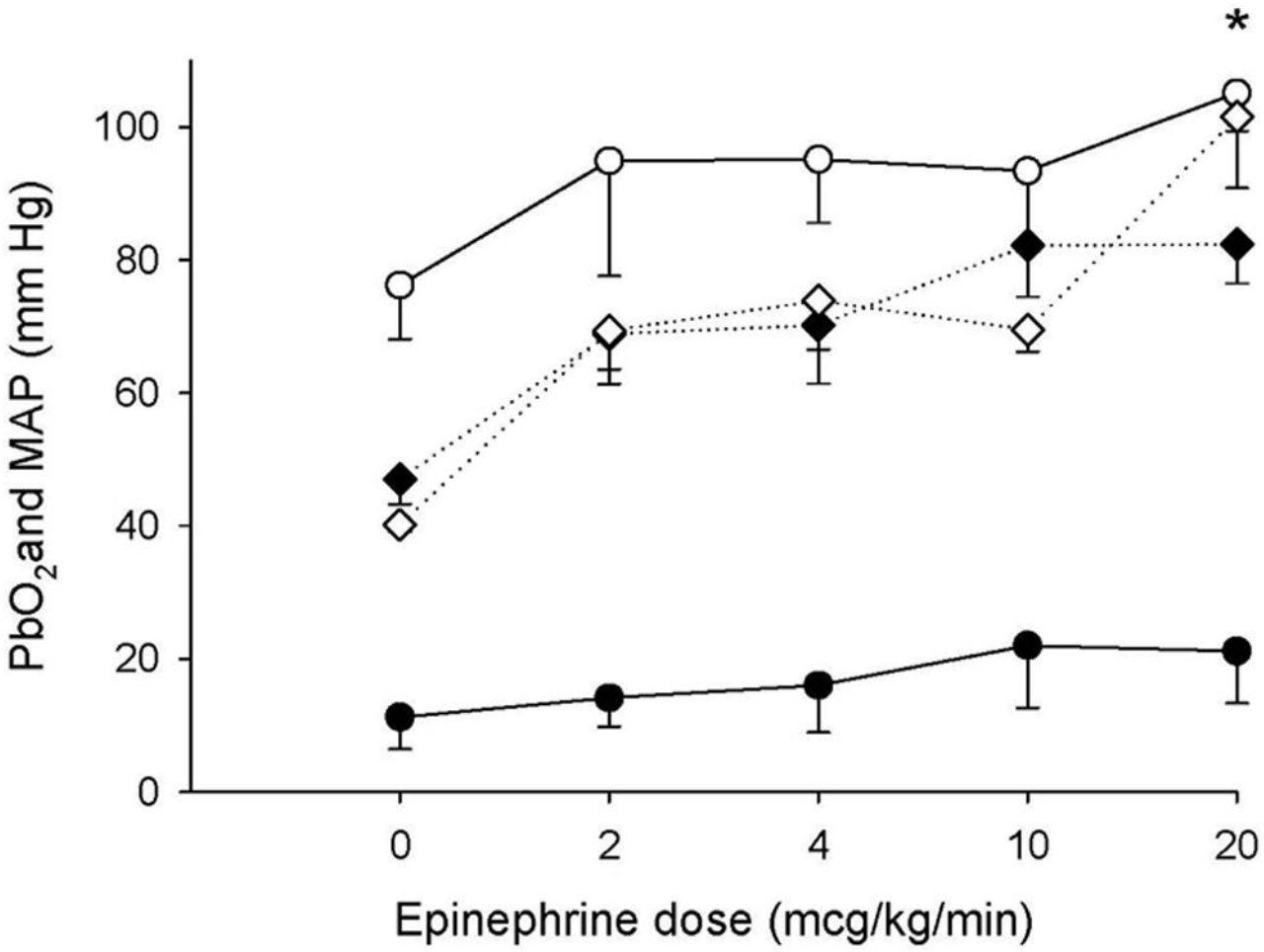

Figure 3.

Cortical PbO_2 at 120 min after resuscitation from CA (12 min asphyxia), before epinephrine (epinephrine dose=0), and after infusion of epinephrine at doses of 2, 4, 10, and 20 mcg kg^{-1} min^{-1}. Black circles represent cortical PbO_2, white circles represent thalamic PbO_2, black diamonds represent MAP for the cortical group, and white diamonds represent MAP for the thalamic group. n= 6/group. (*p<0.05 vs. before epinephrine).

Table 1

MAP, pH, PaO_2, $PaCO_2$, and hemoglobin (Hb) at baseline (immediately before asphyxia) and after asphyxial CA

			Baseline	10 min	30 min	60 min	120 min
Cortex	9 min	MAP	67±2	78±2*	56±2*	52±2*	52±2*
		pH	7.40±0.01	7.29±0.01*	7.46±0.02*	7.47±0.01*	7.44±0.03
		PaO_2	207±11	402±12*	412±10*	183±15*	235±6
		$PaCO_2$	37±1	41±1	36±1	37±1	36±4
		Hb	9.0±0.2	8.9±0.2	8.2±0.2*	8.2±0.5*	8.1±0.3*
	12 min	MAP	65±2	86±3*	55±5*	49±3*	47±3*
		pH	7.39±0.01	7.27±0.02*	7.40±0.01	7.44±0.01	7.39±0.01
		PaO_2	212±3	411±20*	403±1*	266±38	208±5
		$PaCO_2$	36±1	39±3	37±2	37±1	38±1
		Hb	8.7±0.3	8.9±0.3	8.4±0.2*	7.9±0.3*	7.7±0.3*
Thalamus	9 min	MAP	72±4	73±1	58±2*	49±3*	55±2*
		pH	7.36±0.10	7.32±0.10*	7.37±0.10*	7.34±0.10*	7.42±0.10*
		PaO_2	210±7	302±17*	360±7*	204±3	228±7
		$PaCO_2$	37±0.8	39±2.5	39±2.0	46±1.6*	33±2.5
		Hb	10±0.2	9.6±0.7	8.9±0.2	8.0±0.1*	8.5±0.1
	12 min	MAP	55±2	72±4*	42±5*	41±2*	40±1*
		pH	7.35±0.01	7.25±0.02	7.36±0.01	7.39±0.01	7.34±0.01
		PaO_2	192±11	385±36*	375±14*	184±6	207±5
		$PaCO_2$	41±2	40±4	38±1	42±1	44±1
		Hb	9.1±0.1	9.7±0.2*	8.9±0.2	8.1±0.2*	7.7±0.2*

*($p<0.05$ vs. baseline)