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Global and regional differences in cerebral blood flow after asphyxial versus ventricular fibrillation cardiac arrest in rats using ASL-MRI

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Abstract

Both ventricular fibrillation cardiac arrest (VFCA) and asphyxial cardiac arrest (ACA) are frequent causes of CA. However, only isolated reports compared cerebral blood flow (CBF) reperfusion patterns after different types of CA, and even fewer reports used methods that allow serial and regional assessment of CBF. We hypothesized that the reperfusion patterns of CBF will differ between individual types of experimental CA. In a prospective block-randomized study, fentanyl-anesthetized adult rats were subjected to 8 min VFCA or ACA. Rats were then resuscitated with epinephrine, bicarbonate, manual chest compressions and mechanical ventilation. After the return of spontaneous circulation, CBF was then serially assessed via arterial spin-labeling magnetic resonance imaging (ASL-MRI) in cortex, thalamus, hippocampus and amygdala/piriform complex over 1 h resuscitation time (RT). Both ACA and VFCA produced significant temporal and regional differences in CBF. All regions in both models showed significant changes over time ($p < 0.01$), with early hyperperfusion and delayed hypoperfusion. ACA resulted in early hyperperfusion in cortex and thalamus (both $p < 0.05$ vs. amygdala/piriform complex). In contrast, VFCA induced early hyperperfusion only in cortex ($p < 0.05$ vs. other

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regions). Hyperperfusion was prolonged after ACA, peaking at 7 min RT (RT7; 199% vs. BL, Baseline, in cortex and 201% in thalamus, $p < 0.05$), then returning close to BL at ~ RT15. In contrast, VFCA model induced mild hyperemia, peaking at RT7, (141% vs. BL in cortex). Both ACA and VFCA showed delayed hypoperfusion (ACA, ~30% below BL in hippocampus and amygdala/piriform complex, $p < 0.05$; VFCA, 34–41% below BL in hippocampus and amygdala/piriform complex, $p < 0.05$). In conclusion, both ACA and VFCA in adult rats produced significant regional and temporal differences in CBF. In ACA, hyperperfusion was most pronounced in cortex and thalamus. In VFCA, the changes were more modest, with hyperperfusion seen only in cortex. Both insults resulted in delayed hypoperfusion in all regions. Both early hyperperfusion and delayed hypoperfusion may be important therapeutic targets.

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Keywords

cardiac arrest; resuscitation; cerebral blood flow; magnetic resonance imaging; brain

INTRODUCTION

Cardiac arrest (CA) is associated with high mortality and morbidity.[1] In non-traumatic CA, common causes are ventricular fibrillation cardiac arrest (VFCA) and asphyxial cardiac arrest (ACA). In adults, the proportion of persons with an initially shockable rhythm (i.e., VF or pulseless ventricular tachycardia) was 24–35%.[2, 3] ACA is the most common etiology of non-traumatic CA in pediatric patients [4] and important in adults, comprising 5.7% of out-of-hospital CA.[5]

Key factors determining the outcome after CA are duration of ischemia, and amelioration of reperfusion-induced injury. The most vulnerable organ to ischemia is brain. Cerebral blood flow (CBF) changes following resuscitation have become the focus of extensive research aimed at improving neurological outcome. Several prior studies investigated the CBF pattern after CA based on the hypothesis that a no-reflow phenomenon after reperfusion may exist.[6, 7] The early experiments used global brain ischemia models that did not include CA. The advances in technologies allowed developing models that included CA. Reperfusion patterns after CA in adult animals have been reported from both ACA[8–11] and VFCA[12–17] models. However, only isolated reports compared CBF reperfusion patterns after different types of CA, and even fewer reports used methods that allow serial and regional assessment of CBF. The seminal paper by Vaagenes et al. published in *Resuscitation* in 1997 explored neurologic outcomes and neurohistopathologic damage after ACA vs. VFCA in dogs. They reported that the functional brain damage caused by VFCA of 10 min is similar to that caused by ACA of 7 min, but that ACA results in greater morphologic brain damage. However, that study did not assess CBF.[18]

In this study we examined if two different insults, namely VFCA and ACA in adult rats, may result in different spatial and temporal patterns of cerebral blood flow (CBF), using arterial spin labeling (ASL) magnetic resonance imaging (MRI). The overall goal was to

characterize regional CBF following resuscitation after CA and to identify potential therapeutic targets for specific types of CA.

MATERIALS AND METHODS

Adult male Sprague-Dawley rats (n = 43) 10 to 15 weeks old were used for this study. With the Institutional Animal Care and Use Committee approval, rats were obtained from Hilltop Lab Animals (Scottsdale, PA) and allowed to acclimate for at least three days with access to food and water ad libitum. Rats were anesthetized with 4% isoflurane (1:1 O₂/N₂O), intubated with 14 G uncuffed cannula (Becton Dickinson, Sandy, UT), and mechanically ventilated (Harvard Ventilator 683, Harvard Rodent Apparatus, South Natick, MA) with FiO₂ 0.5 to maintain normocapnia. Isoflurane 2% was used for maintenance of anesthesia. Using asepsis, the left femoral artery (PE90) and bilateral femoral veins (PE60) were cannulated via surgical cutdowns to allow monitoring and drug administration. Electrocardiogram, respiratory rate, and arterial pressure were continuously monitored and recorded. After completion of surgical procedures, isoflurane was discontinued. To both mimic clinical care and eliminate effects of volatile anesthetics on CBF, total intravenous anesthesia was induced by fentanyl (10 mcg), followed by a continuous infusion (50 mcg/kg/h), as described earlier.[19] Neuromuscular blockade was induced with cisatracurium (0.4 mg) followed by a continuous infusion (2 mg/h) to prevent motion artifacts and spontaneous breathing. A 10 min isoflurane washout period with FiO₂ 0.21 under fentanyl/cisatracurium anesthesia was allowed to eliminate isoflurane. Rats were then block-randomized (n=4/block) into three groups.

Baseline regional CBF data were obtained from separate a group of rats studied concurrently and subjected to the same anesthesia protocol and instrumentation (n=8).

In the ACA model (n=12), CA was induced by disconnecting the rats from the ventilator for 8 min. After this period, rats were resuscitated with epinephrine, sodium bicarbonate, mechanical ventilation (FiO₂ 1.0), and chest compressions until a return of spontaneous circulation (ROSC) was achieved.

In the VFCA model (n=23), CA was induced by electrical stimulation via external electrodes by a 1-minute impulse of 12 V/50 Hz alternating current and ensured by ECG readings and reduction in mean arterial pressure (MAP). If spontaneous defibrillation occurred, additional 15 s impulses were delivered. After 8 min, resuscitation efforts were started, including mechanical ventilation with baseline parameters except FiO₂ 1.0, chest compressions and intravenous administration of resuscitative drugs. In the ACA group, epinephrine (10 mcg/kg) and sodium bicarbonate (1 mEq/kg) were administered. In the VFCA group, epinephrine 20 mcg/kg at the start of resuscitation and 10 mcg/kg at 1 min resuscitation time (RT) were given. Sodium bicarbonate (1 mEq/kg) was administered at the start of resuscitation. These procedures represent the standard approach used in the respective models, as described previously.[20, 21] At 2 min RT, external defibrillation was performed via an esophageal vs. mid-chest external electrode (10 J) and repeated every min up to 5 min RT if necessary. If ROSC was not achieved at 5 min RT resuscitation was terminated for futility.

Body temperature was maintained at 37 ± 0.5 °C using warm air. During each MRI study, ECG, MAP, heart rate (HR) and rectal temperature were monitored. Arterial blood samples were taken at baseline after preparation phase on isoflurane anesthesia (BL1), after isoflurane wash-out phase on fentanyl anesthesia (BL2) prior to CA, and at 5 min, 30 min, 45 min and 60 min RT to evaluate blood gases, electrolytes and hematocrit. MAP was maintained at $\pm 20\%$ of baseline (BL) values with the use of epinephrine if needed. The rats were sacrificed at 60 min RT with isoflurane overdose and KCl-induced CA.

CBF was assessed globally (in the entire hemisphere) and in four separate regions of interest (ROIs) – cortex, thalamus, hippocampus and amygdala/piriform complex - that have been described earlier.[22] Please see the Supplemental File 1 for the delineation of the ROIs and Supplemental File 2 for detailed description of the ASL MRI methods. In brief, MRI studies were performed on a 4.7-Tesla, 40 cm bore Bruker Biospec system, equipped with a 12 cm diameter shielded gradient insert. A two coil system was used, a 72 mm volume coil and an actively-decoupled 4-channel array coil. Continuous ASL was used to quantify CBF.[23] Intra-subject variability for naïve rats was between 2–5%.

Statistical methods

Biochemical and physiologic values between groups were compared using Student's t-test. CBF data were analyzed by repeated measures analysis of variance (RMNOVA) with post-hoc Tukey's test to assess differences over time and between groups. Paired-sample t-test was used to compare values during RT phase vs. respective BL2 timepoint. IBM SPSS Version 21 was used. $P < 0.05$ was considered statistically significant.

RESULTS

Cardiac arrest

The induction of asphyxia in the ACA group led to a gradual decrease in MAP secondary to hypoxemia, resulting in pulseless electrical activity or asystole. MAP decreased to <20 mmHg after 259 ± 59 s, and CA occurred at 297 ± 58 sec.

In contrast, the induction of VF in the VFCA model resulted in an immediate decrease in MAP. ECG showed asystole at the end of 8 min VFCA in all rats.

Resuscitation

All rats in the ACA achieved ROSC. In the VFCA group, 8 out of 23 rats did not achieve ROSC and 3 rats were out of protocol from technical reasons. These rats were excluded from further analyses, thus 12 rats were included in the final analysis in the VFCA group.

Mean CPR time required to achieve ROSC was significantly longer after VFCA than after ACA. Resuscitation resulted in ROSC after 34 ± 2 s RT in the ACA group vs. 141 ± 31 s RT in the VFCA group ($p < 0.001$). All rats in the ACA group were successfully resuscitated. Two rats in the VFCA group required 2 shocks. After ROSC, rats subjected to VFCA required more epinephrine than rats after ACA (32 ± 15 mcg vs. 9 ± 12 mcg; $p = 0.001$).

The baselines hemodynamic and biochemical values did not differ between groups. Both insults resulted in significant derangements in physiologic values documenting the severity of both insults but also highlighting the differences. There were no differences between pH in the ACA vs. VFCA groups at RT5 (7.08 ± 0.07 vs. 7.04 ± 0.12 , $p=0.27$), but ACA resulted in higher $p\text{CO}_2$ (63 ± 10 vs. 53 ± 14 mmHg). Base excess was pronounced in both groups at RT5 (less than -10 mEq/L in both groups) but the differences did not reach statistical significance. The metabolic acidosis was, however, sustained at RT30 only in the VFCA group, as documented by the more pronounced base excess and lower pH at that timepoint. Significant hemoconcentration was observed in both groups at RT30. Both groups achieved near-normal physiologic values at RT60. There were no differences in the rectal temperature between groups. (Table 1)

CBF

There were no differences between left and right hemispheres. The data are displayed for left hemisphere only.

Eight min of asphyxia in the ACA group vs. 8 min VFCA produced significant temporal and regional differences in CBF (Figure 1). There was global hyperperfusion at RT7 in both groups, although it was more modest in the VFCA animals (167% vs. 115% compared to BL for ACA and VFCA rats respectively), followed by a return to BL and mild hypoperfusion (Figure 2). Regions that demonstrated the greatest differences between the two models were the cortex and thalamus (Figure 3A & 3B). Hyperperfusion was prolonged in the ACA model, peaking at RT7 (199% compared to BL values for the cortex (3A) and 201% for the thalamus (3B), $p<0.05$), then returning close to BL at $\sim$ RT15. In contrast, rats in the VFCA model experienced mild hyperemia, peaking at RT7, (141% compared to BL values for the cortex (3A) and no thalamic hyperemia (3B)).

There was a sustained decrease in CBF which resulted in VFCA rats showing significant cortical hypoperfusion at RT22 and continuing until the end of the experiment. CBF in other regions such as the hippocampus (3C) and the amygdala/piriform complex (3D) showed similar patterns in both models. There was early hyperemia, again more modest in the VFCA model, followed by significant hypoperfusion for both the ACA model (31% below BL values for the hippocampus and 30% for the amygdala/piriform complex, $p<0.05$) and the VFCA insult (34% below BL values for the hippocampus and 41% for the amygdala/piriform complex, $p<0.05$).

All regions in both models showed a significant changes over time ($p<0.01$). Comparing the same regions between ACA and VFCA, thalamus, amygdala/piriform complex and hippocampus all showed significant differences ($p<0.001$, $p=0.027$ and $p=0.004$, respectively). These differences were driven mostly by the initial hyperemic phase, more pronounced in the ACA group. In contrast, although there were differences in CBF in cortex between ACA and VFCA group in the initial phase that showed more pronounced hyperemia in the ACA group, the delayed hypoperfusion phase was almost identical in both groups and the overall comparison of CBF in cortex thus did not reach statistical significance ($p=0.148$).

In the ACA group, there was an overall difference between regions over time ($p=0.003$). On individual region analysis, there was difference over time between cortex and amygdala/piriform complex ($p=0.013$) and between thalamus and amygdala/piriform complex ($p=0.007$). Other comparisons did not reach statistical significance. (Figure 4)

In the VFCA model, there was a significant difference between regions over time ($p=0.005$). This difference was driven by early hyperperfusion in the cortex that was significantly different vs. thalamus ($p=0.008$), amygdala/piriform complex ($p=0.015$) or hippocampus, respectively ($p=0.039$). The comparisons between other regions were not statistically significant. (Figure 5)

DISCUSSION

CBF after CA has been previously evaluated in multiple experimental models and species. However, to the best of our knowledge, a direct comparison of CBF between ACA and VFCA models on a regional level in a single study has not been carried out yet. Thus, we compared early post-resuscitation CBF patterns in clinically relevant rat models of ACA vs. VFCA.

We documented that significant temporal and regional differences exist not only between ACA and VFCA, but also between individual regions in each model. ACA, but not VFCA resulted in a global transient early hyperperfusion. Regional CBF was characterized by early hyperperfusion in all studied regions in the ACA model, with most pronounced increases in cortex and thalamus, both reaching two-fold increase in peak CBF compared to baseline. In contrast, only the cortex showed mild hyperperfusion in the VFCA model. In contrast, CBF was significantly decreased in the delayed phase (15–60 min) despite an adequate blood pressure in both groups across the regions.

Earlier explorations of CBF after global ischemia insults used the four-vessel occlusion model using vessel ligation,[6, 24] CSF obstruction or neck tourniquet;[25] models that may not result in complete cessation of CBF and/or that failed to produce ischemia to the brain stem.[26] Our models induced whole body ischemia rather than isolated global brain ischemia, increasing their clinical relevance.

It is important to acknowledge that although the insult time was identical (8 min) in both models, there are several important features that set these models apart. First, VF resulted in CA almost immediately, with abrupt cessation of perfusing rhythm. In contrast, asphyxia resulted in gradual decrease in MAP, reaching levels < 20 mmHg in 4 min and 19 s, and CA in ~ 5 min, resulting in ~ 3 min no-flow time, compared to 8 min no-flow time in VFCA group. Second, the resuscitation protocols were different in each group, based on previous experiments by us and others. Resuscitation was significantly shorter in the ACA group than in VFCA group. Both insults resulted in similar derangements in acid-base balance, as documented by the extremely low pH and base excess at RT5, which were corrected more rapidly in the ACA group. Epinephrine requirements were higher during resuscitation and after ROSC in rats subjected to VFCA. This suggests that ACA resulted in significantly lesser impairment of postresuscitation myocardial function, as corroborated by others.[27]

Third, a prolonged period of low-flow during CPR may independently affect the CBF pattern, as documented earlier. In the report by Xu et al. in a rat model of ACA, the impact of short vs. long periods of resuscitation on CBF were compared – and a shorter resuscitation time was associated with higher CBF early in reperfusion.[28] Ristagno et al. reported in the VFCA model cortical CBF restoration to 40% of BL value during CPR, with full restoration over 3 min after ROSC.[29] Taken together, this could argue for a milder insult in the ACA group.

Various methods have been employed to investigate CBF.[9, 14, 16, 17, 30, 31] We have used ASL-MRI, a validated method that has been used in several prior studies in CA.[10, 28, 32]

In our study we used fentanyl anesthesia without volatile anesthetic agents that are known to increase CBF. Using ASL-MRI, we have previously established that fentanyl anesthesia provides homogenous CBF and has the least effect on CBF in normal rats.[33]

We have documented an early transient hyperemic period lasting ~15 min, followed by a delayed hypoperfusion phase (~30% below BL in both ACA and VFCA models) despite adequate MAP. Our observations are consistent with previously published findings.

Crumrine and LaManna characterized metabolic changes and CBF after KCl-induced CA in rats (total no-flow time of 11–13 min). An early hyperemic period lasted ~15 min with regional increases of CBF to 230–350%. The hypoperfusion was, however, more pronounced (16–37% of BL CBF) possibly due to the longer insult duration.[34] Similar observations regarding biphasic response of CBF were reported in dogs after CA.[12, 17, 35]

Early post-resuscitation CBF using ASL-MRI was evaluated in rats subjected to CA.[28, 32] A transient early regional hyperemia and delayed hypoperfusion was observed after 4–15 min CA. These observations support our data despite significant differences in the protocols. We avoided isoflurane as a known potent cerebral vasodilator. Also, in that study, CA was induced by the short-acting beta-blocker esmolol. Each of these interventions could have an impact on CBF.

A pronounced hyperemia was observed in the ACA group in our study, as previously reported in multiple global ischemia models.[30, 36–39] The limited hyperemic phase in the VFCA model is surprising since similar pattern has been reported in this insult previously.[37]

While both groups exhibited an early hyperemia, this effect was more pronounced in the ACA group. At RT5, paCO_2 was higher in the ACA group. It could be speculated that higher paCO_2 contributed to this effect since CO_2 is a known cerebral vasodilator. However, this vasodilation effect was not observed in some prior studies focused on CBF after CA. Cerebral vascular reactivity to CO_2 is however variable in the first hours after CA[16, 40, 41] being decreased or abolished in some studies but not in others. In one study, no significant correlation was found between post-resuscitation arterial CO_2 level and CBF in

rats subjected to ACA.[28] In contrast, clinical data from CA survivors indicate the CBF response to CO₂ challenge is maintained, at least at 6 h or later after ROSC.[42, 43]

Multiple vasoactive mediators accumulating during ischemia in brain tissue may be implicated in hyperemia, as well as systemic factors such as acidosis and hypertension. Hyperemia was deemed necessary for the tissue recovery from an ischemic insult.[36] While the long-term effects of hyperemia on post-ischemic cellular viability remain unclear, hyperemia did not impair the short-term restoration of cellular energy metabolites after reperfusion.[34]

In the ACA group, cortex and thalamus showed sustained hyperperfusion over other regions, namely amygdala/piriform complex. The rise of CBF in thalamus was earlier than in cortex. This is similar to our data on regional CBF assessed by ASL-MRI after ACA in juvenile (post-natal day 17) rats.[10]

In contrast, the only region that showed early hyperemia in the VFCA model was cortex. The magnitude of increase was rather mild, reaching ~30% vs. baseline.

The reasons for these discordant results with regard to the degree of hyperemia are unclear. Regional reperfusion patterns have not been systematically studied in rats subjected to VFCA due to technical challenges. In a KCl-induced CA in rats, a 230–350% increase in CBF during reperfusion was reported in cortex, hippocampus and striatum. The rate of loss of energy charge was almost identical between cortex, hippocampus and striatum and complete within 5 min of no-flow. Similarly, the restoration was rapid and uniform across regions.[34] A large body of evidence regarding VFCA was gained from large animal models. However, these results should be cautiously applied to rats. Prior studies indicated significant no-reflow after VFCA in cats but not rats.[7, 31] The lack of gyrfication of rat brain was suggested as a plausible explanation,[31] but other mechanisms could play a role.

Differences in regional CBF between models could be produced by abrupt cessation of cardiac output and CBF in the VFCA, contrasting gradual cessation in the ACA model. In a work by Goplerud et al. using piglet ACA model, cortex showed decreased CBF during asphyxia. In contrast, brain stem structures showed vasodilation. Hippocampus and thalamus showed only modest increase of CBF during asphyxia. Those brain regions that had been vasoconstricted during asphyxia were hyperemic during recovery.[9] Further supporting the possibility that VFCA in our current study was a more severe insult is that we previously reported that hyperemia is not seen and is replaced by hypoperfusion in ACA as the duration of the insult is increased.[10] Other possible explanation is that regional differences followed a pattern of neuronal density rather than specific patterns of functionally or biochemically defined regions or of vascular territories.[44]

The early hyperemia resolved over ~ 15 min and relative hypoperfusion followed. The bi-phasic curve of post-ROSC CBF pattern has been described before and our results correspond to the work of others.[14, 30, 37–39] The exact underlying mechanisms and consequences, however, remain unknown. The reperfusion pattern is a net result of multiple factors, including dysregulation of the vascular tone by agents such as nitric oxide,[45] oxygen radical species,[46] and others. It was also postulated that the perturbations are a

result of vasoconstriction, since blood volume was decreased while mean transit time of blood through the brain was increased.[30] The work of Leonov et al. in a 12.5 min VFCA in dogs observed hypoperfusion between 1–4 h after the insult with impaired oxygen delivery.[12] In contrast, outcome studies showed no correlation between the duration and magnitude of hypoperfusion and long-term neurologic outcome in a canine global ischemia model.[30] It is thus unclear whether the hypoperfusion represents a therapeutic target or represents a self-protective mechanism of the brain to limit the reperfusion injury.[30] This is an area that needs additional investigation using contemporary models of CA and clinically relevant protocols.

Both ACA[47] and VFCA[27] induce myocardial dysfunction that may result in low cardiac output and hypotension which could impact CBF if MAP autoregulation of CBF is disturbed after CA. Administration of vasopressors is needed to achieve ROSC from VFCA in rats.[48] Unfortunately, the use of epinephrine significantly reduced post-resuscitation CBF[49] and increased the severity of myocardial dysfunction and decreased duration of survival after VFCA in rats.[50, 51] Alternative experimental resuscitative agents or methods in lieu of epinephrine may provide similar resuscitative benefits with better long-term neurologic outcome.[52–54] However, epinephrine is well known to confer benefit with regard to ability to achieve ROSC.[55]

In our paradigm, we chose to maintain MAP at the baseline level during the post-resuscitation period using epinephrine. The use of epinephrine in this setting is controversial but clinically relevant. While rats in the ACA group did not require epinephrine support, some rats in the VFCA groups required epinephrine infusion. The optimal hemodynamic management after CA is not yet defined. A combination of induced hypothermia and hypertension after ACA in rats resulted in better neurologic outcome.[56] Both epinephrine and bicarbonate were necessary to achieve ROSC after ACA in rats,[57] but larger doses of epinephrine were detrimental after short durations of ACA.[58, 59] The original report describing no-reflow phenomenon did not treat severe hypotension, possibly contributing to the effect.[6] In our prior study, hemodynamic support with epinephrine to achieve supra-physiologic target MAP values resulted in higher CBF early after ACA in immature rats, [10] arguing against a direct cerebral vasoconstriction response, but supports the possibility that autoregulation is lost.

We did not pursue determining the neurologic or histological outcome in this study. These outcome parameters for our models of ACA[20, 60] and VFCA[61] in rats have been reported previously. Both insults result in acute neurological deficits and significant histological damage that approximates post-ischemic injuries seen in clinical setting, further strengthening the validity of our models.[62]

In summary, despite inherent differences in no-flow time between our clinically relevant ACA and VFCA models, both global ischemic insults resulted in significant derangements in monitored physiologic parameters. Post-resuscitation CBF was characterized by a significant early hyperperfusion in the ACA group only but delayed hypoperfusion in both groups, with significant regional differences. While the underlying mechanisms for these phenomena are yet to be determined, our unique data suggest that both early hyperperfusion

in the ACA paradigm and delayed cerebral hypoperfusion, despite adequate MAP, may be important therapeutic targets for resuscitation following CA. The treatment of CA survivors may need to be tailored to the etiology of CA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Representative CBF maps of rat brains, including baseline and post-resuscitation up to RT60 in both ACA and VFCA groups. CBF, cerebral blood flow; RT, resuscitation time; ACA, asphyxial cardiac arrest; VFCA, ventricular fibrillation cardiac arrest.

Figure 2.

Analysis of the CBF map for the left hemisphere for ACA and VFCA groups, respectively. The bars represent SD. CBF, cerebral blood flow; ACA, asphyxial cardiac arrest; VFCA, ventricular fibrillation cardiac arrest. * $p < 0.05$ ACA vs. respective baseline; # $p < 0.05$ VFCA vs. respective baseline; a, $p < 0.05$ ACA vs. VFCA; b, $p < 0.01$ ACA vs. VFCA.

Figure 3.

Regional analyses of the CBF maps for the individual regions of left hemisphere for ACA and VFCA groups, respectively. A, cortex; B, thalamus; C, hippocampus; D, amygdala/piriform complex. The bars represent SD. CBF, cerebral blood flow; ACA, asphyxial cardiac arrest; VFCA, ventricular fibrillation cardiac arrest. * $p < 0.05$ ACA vs. respective baseline; # $p < 0.05$ VFCA vs. respective baseline; a, $p < 0.05$ ACA vs. VFCA; b, $p < 0.01$ ACA vs. VFCA.

Figure 4.

Regional analyses of the CBF maps in ACA group. There was an overall difference between groups ($p=0.003$). a, $p<0.05$ thalamus vs. amygdala/piriform complex; b, $p<0.01$ thalamus vs. amygdala/piriform complex; c, $p<0.05$ cortex vs. amygdala/piriform complex; d, $p<0.01$ cortex vs. amygdala/piriform complex; e, $p<0.05$ thalamus vs. hippocampus. SD bars are omitted to improve clarity of the figure.

Figure 5.

Regional analyses of the CBF maps in VFCA group. There was an overall difference between groups ($p=0.005$). a, $p<0.01$ cortex vs. thalamus; b, $p<0.05$ cortex vs. amygdala/piriform complex; c, $p<0.05$ cortex vs. hippocampus; d, $p<0.01$ cortex vs. amygdala/piriform complex; e, $p<0.01$ cortex vs. hippocampus. SD bars are omitted to improve clarity of the figure.

Table 1

Physiologic and biochemical parameters of the ACA and VFCA groups.

	BL1	BL2	CA8	RT5	RT30	RT45	RT60
HR							
ACA	362±16	361±26	0	381±46 ^a	372±52	380±40	369±54
VFCA	373±26	386±41	0	330±63 [†]	349±45	380±36	403±30
MAP							
ACA	80±8	86±6	8±1	116±39 [†]	92±22	100±27	104±24 [†]
VFCA	78±8	85±9	9±1	133±32 [*]	83±10 [*]	89±10	90±10
pHa							
ACA	7.39±0.08	7.40±0.03		7.08±0.07 [*]	7.32±0.1 ^{b†}	7.33±0.06 [*]	7.33±0.05 ^{a*}
VFCA	7.44±0.04	7.42±0.03		7.04±0.12 [*]	7.14±0.09 [*]	7.33±0.1 [*]	7.39±0.06
paO2							
ACA	366±54	96±13		274±72 [*]	284±97 [*]	293±108 [*]	284±103 [*]
VFCA	369±38	91±18		280±66 [*]	252±80 [*]	247±91 [*]	272±87 [*]
paCO2							
ACA	41±10	38±4		63±10 ^{a*}	40±8 ^b	44±7 [†]	46±5 ^{a*}
VFCA	38±7	38±2		53±14 [*]	49±5 [*]	43±9	41±5
BE							
ACA	-0.4±2.2	-1.1±2.3		-11.4±3.4 [*]	-4.0±2.6 ^{a*}	-1.7±1.4	-0.2±2.1
VFCA	0.9±2.1	0.1±1.9		-14±3.6 [*]	-11.3±4.6 [*]	-0.6±2.6	4.0±3.7
Hct							
ACA	36±3	35±4		36±4	39±5 ^{a*}	38±4 [†]	39±4 [*]
VFCA	38±3	36±3		38±4	43±3 [*]	42±5 [*]	39±4 [†]
Trec							
ACA	36.5±0.6	36.4±0.7	35.9±0.6	36.0±0.5	36.7±0.8	36.6±1.1	36.6±1.7
VFCA	36.4±0.8	36.4±0.7	36.2±0.7	36.1±0.6	36.3±1.2	36.5±1.0	36.8±1.2

BL, baseline; CA, cardiac arrest; RT, resuscitation time; ACA, asphyxial cardiac arrest; VFCA, ventricular fibrillation cardiac arrest; HR, heart rate; MAP, mean arterial pressure; pHa, arterial pH; paO₂, partial arterial pressure of oxygen; paCO₂, partial arterial pressure of carbon dioxide; BE, base excess; Hct, hematocrit; Trec, rectal temperature.

^a p<0.05 vs. VFCA;

^b p<0.01 vs. VFCA;

[†] p<0.05 vs. BL2;

^{*} p<0.01 vs. BL2.