Asphyxiation versus Ventricular Fibrillation Cardiac Arrest and the effect on Cerebral Blood Flow using ASL-MRI.

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INTRODUCTION

Cardiopulmonary arrest is associated with high mortality and morbidity. In non-traumatic cardiac arrest, the two of the most prevalent causes are ventricular fibrillation cardiac arrest (VFCA) and asphyxial cardiac arrest (ACA). Key factors after cardiac arrest are ischemia and reperfusion [1]. Previous studies of ACA in developing rats from our group have shown that reperfusion following ischemia has two characteristic phases, early hyperemia and delayed hypoperfusion [2]. Regions in the brain that are affected are the cortex and thalamus, both of which are associated with higher metabolic demands [3].

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), with the aim of tailoring therapies specifically to the type of insults sustained.

MATERIALS AND METHODS

Sprague-Dawley rats (n = 28) 10 to 15 weeks in age were used for this study. Isoflurane (1:1 O_2/N_2O) anesthetized rats were intubated, mechanically ventilated and femoral catheters were inserted. Isoflurane was discontinued and anesthesia was maintained by an infusion of fentanyl and vecuronium. ACA was produced by disconnecting the rats from the ventilator for 8 min. After this period, rats were then resuscitated with epinephrine, sodium bicarbonate, mechanical ventilation, and chest compressions performed until spontaneous circulation returned. For the VFCA model, cardiac arrest was induced by electrical stimulation via external electrodes. After 8 min, resuscitation procedures included mechanical ventilation, closed chest compression and intravenous administration of epinephrine and sodium bicarbonate. At 2 min external defibrillation was carried out via an esophageal and external electrode. Body temperature was maintained at 37 ± 0.5 ˚C using warm air, regulated with a rectal temperature probe. During each MRI study, $PaCO_2$, PaO_2, MABP, HR and rectal temperature were monitored. MABP was maintained at ± 20% of baseline values with the use of epinephrine if needed.

MR studies were performed on a 4.7-Tesla, 40cm 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 [4]. A single shot, SE-EPI sequence with a TR = 2 s, 64 x 64 matrix, FOV = 2.3 cm, 2 s labeling pulse, with labeling applied ± 2 cm from the imaging plane. Maps of T_1 were generated from spin-echo images with variable *TR* (*TR* = 9100, 8500, 7900, 7300, 6700, 6100, 5500, 4900, 4300, 3700, 3100, 2500, 1900, 1300, 700, 100 msec, FOV = 2.3 cm, 4 averages, 64 x 64 matrix). CBF maps were generated with a pixel-wise fit: $CBF = \lambda \cdot (T_{1obs} \cdot 2\alpha)^{-1} \cdot (M_C - M_L) \cdot (M_C)^{-1}$, where M_C and M_L are the pixel intensities from the control and labeled images, respectively. A spatially constant value of 0.9 mL · g^{-1} was assumed for the blood brain partition coefficient for water (λ) and a spin-labeling efficiency (α) of 0.7 was assumed.

RESULTS AND DISCUSSION

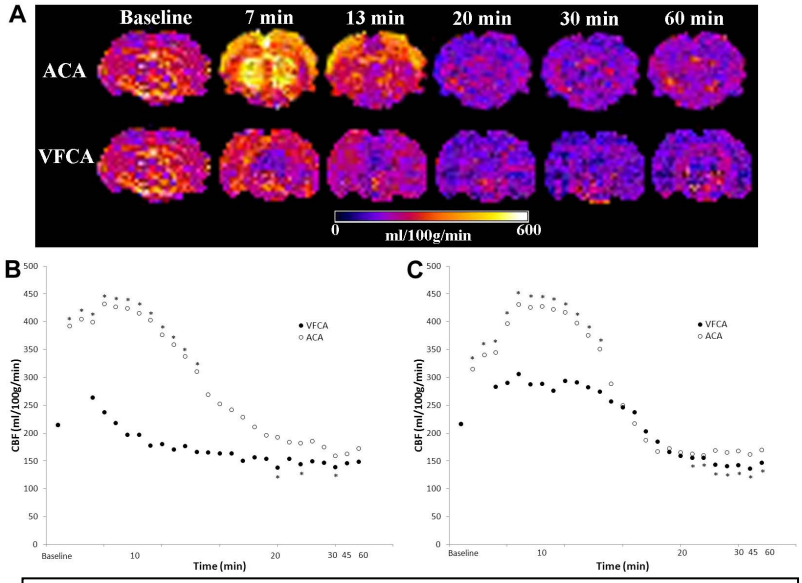

Figure 1: (A) Representative CBF maps of rat brains before and following ACA and VFCA. CBF values for the thalamic (B) and cortical (C) regions of the brain for the VFCA model (closed circles) and the ACA model (open circles). * p<0.05

An 8 min ACA vs. VFCA insult produced regional differences in CBF in adult rats as seen in Figure 1. There was global hyperperfusion 7 min following resuscitation in both groups, although it was more modest in the VFCA animals (167% vs 115% compared to baseline for ACA and VFCA rats respectively), followed by a return to baseline and mild hypoperfusion. Regions that demonstrated the differences between the two models were the thalamus and cortex (Figure 1B & 1C). Hyperperfusion was prolonged in the ACA model, peaking at 7 min (201% compared to baseline values for the thalamus (1B) and 199% for the cortex (1C), p<0.05), then returning close to baseline at about 15 min post resuscitation. In contrast, rats in the VFCA model experienced mild hyperemia, peaking at 7 min post resuscitation, (123% compared to baseline values for the thalamus (1B) and 141% for the cortex (1C)), which was not significant. There was a sustained decrease in CBF which resulted in VFCA rats showing significant cortical hypoperfusion at about 22 min post resuscitation and continuing until the end of the experiment. CBF in other regions such as the hippocampus and the amygdala/piriform cortex 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 (30% below baseline values for the amygdala/piriform cortex and 31% for the hippocampus, p<0.05) and the VFCA insult (41% below baseline values for the amygdala/piriform cortex and 34% for the hippocampus, p<0.05). While the underlying mechanisms for this phenomenon are yet to be determined, and since we don't know if either of these perturbations are deleterious, our unique data suggest that cerebral hypoperfusion, despite adequate MABP, may be an important therapeutic target for resuscitation following VFCA, while early hyperemia may represent a target in ACA.

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