MRI Assessment of Regional Cerebral Blood Flow after Asphyxial Cardiac Arrest in Immature Rats: A Preliminary Report

L. M. Foley[1], M. D. Manole[2], T. K. Hitchens[1], H. L. Alexander[2], C. Ho[1], P. M. Kochanek[2], and R. S. Clark[2]

[1]Pittsburgh NMR Center for Biomedical Research, Carnegie Mellon University, Pittsburgh, PA, United States, [2]Safar Center for Resuscitation Research, University of Pittsburgh School of Medicine, Pittsburgh, PA, United States

INTRODUCTION

In the United States, it is estimated that 87% of children that suffer unexpected cardiac arrest do not survive, whilst 50% of survivors suffer an unfavorable neurological outcome [1,2]. It has been suggested that changes in cerebral blood flow (CBF) after cardiac arrest plays an important role in irreversible brain damage. Changes in CBF after cardiac arrest are well documented in adults, and experimental cardiac arrest in adult animals, but not in either children or pediatric models. In infants and children asphyxia is the principle cause of cardiopulmonary arrest, whereas in adults it is mainly a cardiac etiology. Asphyxial cardiac arrest produces a physiologically different arrest, due to the fact that hypoxemia, acidosis, hypercarbia and hypotension precede the arrest.

Our research team has modified an adult model of asphyxial arrest, simulating the pediatric population using postnatal day (PND) 17 rats. This model allows for invasive physiological monitoring and acute resuscitation that closely mimics guidelines used in humans. The aim of this study is to characterize changes in CBF after asphyxial cardiac arrest.

MATERIALS AND METHODS

PND 17 rats (n = 6) 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 during which baseline CBF measurements were obtained. While on neuromuscular blockade asphyxial cardiopulmonary arrest was produced by disconnecting the ventilator from the rats for 8 min. After this period, rats were then resuscitated with epinephrine, sodium bicarbonate, reinitiation of mechanical ventilation, and chest compressions performed until restoration of spontaneous circulation (ROSC) returned. 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.

MR studies were performed on a 7-Tesla, 21cm bore Bruker Biospec system, equipped with a 12 cm diameter shielded gradient insert and a 72 mm volume RF coil. For all imaging experiments, an FOV = 3 cm and slice thickness = 2 mm were used. Maps of T_{1obs} [3] were generated from a three-parameter exponential fit to a series of spin-echo images with variable *TR* (*TR* = 8000, 4300, 2300, 1200, 650, 350, 185, 100 msec, 2 averages, 128 x 70 matrix). Perfusion spin-echo images were acquired in duplicate using the arterial spin-labeling technique [4] (*TR*/*TE* = 2000/10, 20, 30, summation of 3 echoes, 2 averages, 128 x 70 matrix) with labeling applied ± 2.5 cm from the imaging plane. CBF (cerebral blood flow) maps were generated from: $CBF = \lambda \cdot (T_{1obs} \cdot 2\alpha)^{-1} \cdot (M_C - M_L) \cdot (M_C)^{-1}$, where M_C and M_L are the magnetization 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). The spin labeling efficieny (α) [5] was determined in each study with gradient echo images on the carotid arteries and spin-labeling applied at ± 11 mm (*TR*/*TE* = 100/9.6 msec, 45˚ flip angle, 8 averages, 256 x 256 matrix). CBF was quantified for 5 anatomical regions within each hemisphere for baseline measurements as well as 5 min, 10 min, 15 min, 30 min, 1 hr, 1.5 hr, 2 hr, and 2.5 hr post asphyxial arrest.

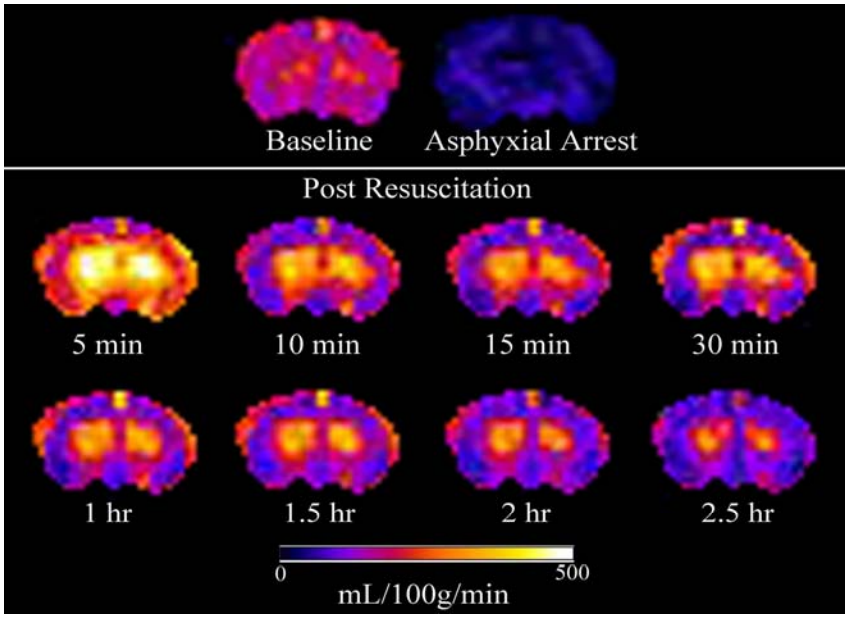

Figure 1: Representative CBF maps of PND 17 rat before, during asphyxial cardiac arrest and up to 2.5 hours after return of spontaneous circulation.

RESULTS AND DISCUSSION

Asphyxial arrest occurred ~1 min after ventilation was discontinued and ROSC was achieved at ~30 sec into the resuscitation. Figure 1 shows that CBF during asphyxial arrest was negligible, as expected. At 5 min after ROSC, CBF was increased significantly above baseline by 20-60%, with the greatest increases in the thalamic and hippocampal areas. After 30 min all animals showed a decline in CBF, which was significant in the amygdala and the cortex. During this period of hypoperfusion, thalamic and hippocampal regions showed better perfusion recovery. Our study shows there is a temporal and regional heterogeneity of CBF after asphyxial cardiac arrest. The temporal pattern observed mimics findings in the adult setting [6]. However, despite a global insult, it is surprising that hyperemia and subsequent hypoperfusion are both regional in nature after ROSC. These results lay the foundation for future studies assessing the relationship between CBF disturbances and histopathology and testing novel therapies specific for pediatric cardiac arrest.

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