Diffuse Correlation Spectroscopy Measures of Cerebral Blood Flow During Graded Hypoxia in Neonatal Piglets

Danielle S. Shoshany[1], Shadi Malaeb[2], Randolph Sinahon[1], Mert Deniz Polat[1], Meltem Izzetoglu[3], Patricia A. Shewokis[4,1], Kurtulus Izzetoglu[1]

[1] Drexel University School of Biomedical Engineering, Science and Health Systems
[2] Department of Pediatrics, St. Christopher's Hospital for Children, Drexel University College of Medicine
[3] Villanova University Department of Electrical and Computer Engineering
[4] Drexel University College of Nursing and Health Professions

Introduction: Hypoxic-ischemic brain injury occurs when the brain receives inadequate oxygen to meet its metabolic needs. Due to its high metabolic demand, the brain is very sensitive to changes in cerebral blood flow (CBF) and compensatory mechanisms are employed to preserve adequate cerebral perfusion. In response to hypoxemia, chemoreceptors in the carotid bodies transmit information regarding decreased arterial oxygen to the medulla oblongata, resulting in increased sympathetic activity, which cause increases in cardiac output and vasoconstriction of peripheral vessels to divert blood flow towards vital organs (e.g., brain and heart). Diffuse correlation spectroscopy (DCS) is a novel, noninvasive optical technique used to quantify a blood flow index (BFI). The DCS probe consists of a coherent 785nm near-infrared light which diffuses through the tissue and is reflected to the device's detectors by moving red blood cells (RBCs) within the cerebral microvasculature. Within the device itself, the amount of light that is received by the detector at a given time is autocorrelated with a time-shifted version of itself. A BFI reflective of CBF is then derived by fitting an analytical model to these experimentally derived autocorrelations. Our objective is to assess the ability of DCS to measure CBF during different stages of hypoxic shock.

Methods: DCS measurements of CBF, near-infrared spectroscopy (NIRS) measures of cerebral hemoglobin concentrations, ECG measures of heart rate (HR), and amplitude integrated EEG (aEEG) were recorded continuously from anesthetized, ventilated, and instrumented Yorkshire piglets between 3-5 days old. Blood pressure (SBP) was manually recorded every 15 minutes in all animals. The animals included in this analysis were assigned either the protocol for hypoxia-induced brain injury (n=10) or sham-control (n=6). Animals assigned to the hypoxia cohort underwent a gradual reduction in the fraction of inspired oxygen (FiO2) they received (i.e., 28%, 21%, 15%, 11%, 8%, 6(a)%, 6(b)%, and 6(c)% FiO2). We used surgically placed intracranial Laser Doppler flowmetry (LDF) as a verification technique for DCS-derived BFI in a subset of hypoxia animals (n=2). Averages of DCS-derived BFI (cm2/s) and LDF-derived blood perfusion units (BPU) were taken at each level of FiO2. LDF-derived BPU and DCS-derived BFI were divided by their respective averages at 21% FiO2 to obtain relative BPU (rBPU) and relative BFI (rBFI). A Pearson's correlation coefficient was calculated between the means of rBPU and rBFI at each level of FiO2. Upper and lower normative thresholds were derived for each parameter at normoxic baseline. Arterial blood gases and cerebral lactate were also measured. A linear mixed effects model was used to fit the data for each dependent measure and post hoc pairwise comparison testing was used to make comparisons between and within experimental cohorts. P-values < 0.05 were considered significant.

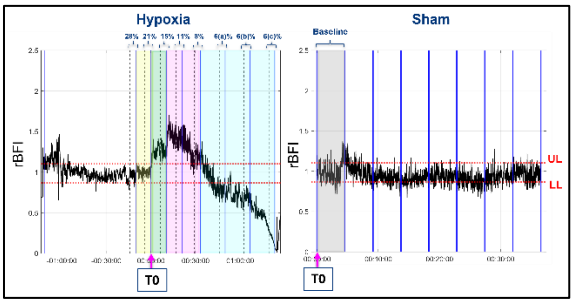

Figure 1. rBFI from representative hypoxia and sham animals.

Results: We observed acceleration in the DCS signal during mild hypoxia followed by deceleration in severe hypoxia. There was a significant, strong, positive correlation between rBFI and rBPU ($r(10) = 0.86$, $p < 0.001$). In hypoxia animals, there was an increase in NIRS-derived deoxygenated and a decrease in oxygenated hemoglobin with reductions in FiO2 as expected. We observed that rBFI increased from 21% during 11% FiO2 and decreased during 6% FiO2 ($p < 0.05$), and HR increased from 21% during 11% FiO2, then decreased during 6% FiO2 ($p < 0.05$) when compared to both sham animals and 21% normoxic baseline. Both SBP and aEEG decreased from 21% during 6% FiO2 ($p < 0.05$). Hypoxia also resulted in significant metabolic acidosis, and cerebral lactic acidosis ($p < 0.05$).

Conclusions: The results demonstrate that DCS-derived BFI can be used to assess hemodynamic response of the cerebral microvasculature during hypoxic injury. Also, changes in DCS-derived BFI could represent acceleration and deceleration of CBF that occurs during progression from compensated to uncompensated shock from hypoxia. Our findings also suggest that DCS has the potential to be a reliable, noninvasive optical tool to monitor cerebral hemodynamics during hypoxia.

Acknowledgements: This work was supported by The Office of the Assistant Secretary of Defense for Health Affairs through the Combat Readiness – Medical Research Program, under award number W81XWH-20-1-0899. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the Department of Defense or the U.S. Government. The authors would like to acknowledge and thank Dr. Leonid Zubkov for DCS system deployment, Dr. Sinan Tuzer, Dr. John Grothusen and Mrs. Juan Du for supporting data collection and technical assistance with the experiments.