Title: NNeMo (Neonatal Neuromonitor): A non-invasive optical device for continuous monitoring of cerebral blood flow and energy metabolism in the developing brain

Trainee Name: Ajay Rajaram

Supervisor(s): Dr. Keith St. Lawrence and Dr. Mamadou Diop

Structured Abstract:

Introduction. The human brain relies almost exclusively on oxidative metabolism, having very limited energy storage, and is therefore susceptible to injury related to impaired cerebral blood flow (CBF). This is particularly evident in preterm infants as the underdeveloped vascular system in the immature brain can lead to poor CBF control. For example, cerebral autoregulation – the ability to maintain CBF despite changes in blood pressure – is known to be impaired in this age group [1]. However, the impact of cerebrovascular dysfunction on the coupling of CBF to cerebral energy metabolism in the developing brain is unknown due to a lack of adequate technologies for assessing these measures in such a fragile population. This study outlines the development of a unique neuromonitor for the neonatal intensive care unit (NICU) to measure CBF and energy metabolism. Metabolic measures were the cerebral metabolic rate of oxygen (CMRO2) and the oxidation state of cytochrome c oxidase (oxCCO) – the final electron acceptor in the electron transport chain and a direct marker of oxidative metabolism [2]. A demonstration of the system’s ability to track changes in these metabolic markers was conducted in a porcine model.

Methods. The neonatal neuromonitor (NNeMo) combines broadband near-infrared spectroscopy (B-NIRS) to measure cerebral tissue saturation (StO2) and oxCCO with diffuse correlation spectroscopy (DCS) to provide continuous CBF monitoring. The combination of these systems was achieved using a multiplexing shuttering system capable of continuous quantification of StO2, CBF, oxCCO, and CMRO2 with a temporal resolution of 6 seconds. In four newborn piglets, cerebral energy metabolism was altered by (i) injections of an anesthetic (propofol 1.6 mg/kg) and (ii) occluding the common carotid arteries to induce transient ischemia (10-min), leading to CBF-driven changes in metabolism.

Results. Propofol injections resulted in a reduction of all parameters (CBF: 9%, StO2: 5%, CMRO2: 6%, and oxCCO: 0.3μM) while vascular occlusion produced larger decreases (CBF: 72%, StO2: 35%, CMRO2: 60%, and oxCCO: 1μM, at their respective nadirs). A temporal delay in oxCCO was observed compared to the CBF and CMRO2 responses.

Conclusions. Combination of B-NIRS with DCS provides a unique monitoring approach to study the coupling of CBF and metabolism in the developing brain. When manipulating metabolism directly (anesthetic) and through vascular occlusion, expected reductions in CBF and metabolic markers were observed; however, the temporal differences in CMRO2 and oxCCO responses requires further investigation. The immediate aim is to translate the developed system to the NICU to assess if flow/metabolic monitoring will provide clinicians with greater sensitivity to changes in cerebral hemodynamics that precede preterm brain injury.