Development of Non-invasive Method for Cerebrovascular Regulation Assessment

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Introduction: Mechanisms of mild traumatic brain injury (mTBI), or concussion, are poorly understood, and non-invasive, accurate devices for early mTBI detection are lacking. Real-time identification of cerebral blood flow (CBF) dysregulation may aid in early mTBI detection. Hypercapnia is known to produce cerebrovascular vasodilation, and CO₂-inhalation-based hypercapnic breathing challenges have been used to study cardiovascular and respiratory dynamics. Near infrared spectroscopy (NIRS) has been used to monitor cerebrovascular function during surgery and ventilation, and cerebral bioimpedance coupled with continuous blood pressure recordings has been used to monitor CBF. These three techniques are not known to have been previously combined to use CO₂-inhalation-based hypercapnic breathing challenges as a tool to simulate CBF dysregulation and to monitor the CBF autoregulatory response using NIRS and bioimpedance. A breathing circuit for the selective administration of CO₂-compressed air mixtures was designed and tested in order to assess CBF regulatory responses to hypercapnia in healthy young adults using this combination of non-invasive methods and real-time sensors.

Materials and Methods: The study had Florida Institute of Technology (FIT) Institutional Research Board approval. Honeywell North 5500 series half-mask respirators were modified with in-house 3D printed connectors to securely fit two lengths of continuous positive airway pressure (CPAP) tubing and serve as the basis of the breathing circuit. Hypercapnic challenges were delivered by inserting a plug into the room air side of the breathing circuit, switching the inhalation source to a CO₂-compressed air mixed gas cylinder connected to a SCUBA regulator adjusted to free-float conditions. After a 5 or 10 minute baseline period, 1 to 3 hypercapnic challenges of 5 or 10 minutes duration were delivered in each study, for a total of 89 challenges in 33 studies on 26 healthy student subjects. The room air end of the breathing circuit was unplugged after each hypercapnic challenge for 5 or 10 minute recovery periods. Throughout the duration of each study, regional cerebral oxygen saturation (rSO₂, %) was monitored with a Nonin Equanox Advance 7600 and 8004CA NIRS sensor, partial pressure of end tidal CO₂ (PCO₂, mmHg) and respiration rate were monitored with a Smiths Medical Capnocheck II 8400, vital signs were monitored with a Bionet BM3, and bioimpedance was monitored with a UFI RESP1 impedance pneumograph and the signal digitized with a DATAQ DI-155.

Figure 1. Subject fully connected to breathing and monitoring circuit.

Results and Discussion: Disruption of the Equanox Advance 7600 data output connection (rSO₂) excluded 7 challenges from further analysis, and a total of 82 challenges in 31 studies were analyzed in detail. Change in PCO₂ (ΔPCO₂) during CO₂ inhalation provided a measure of the degree of hypercapnic challenge. Change in rSO₂ (ΔrSO₂) during hypercapnia was positively correlated to ΔPCO₂ ($R^2 = 0.40$). The mean response ± standard error in ΔPCO₂ and ΔrSO₂ were 6.39 ± 0.52 mm Hg and 2.22 ± 0.30 % respectively. In the 5 subjects studied for intra-subject reproducibility assessment, the mean inter-day ΔPCO₂ change was 1.52 mm Hg, and mean inter-day ΔrSO₂ change was 1.62%. Individual analysis of vital signs (respiration and heart rate and variance) and bioimpedance changes in each of the 31 studies was required to identify the combined measured response to hypercapnia in each study.

Conclusions: The combined monitoring of vital signs, bioimpedance, and changes in rSO₂ can detect periods of hypercapnia, which alter CBF, better than rSO₂ alone. Algorithms will be developed to relate ΔrSO₂ and vital sign changes and trends during hypercapnia to enable non-invasive detection of CBF dysregulation, which may be a marker of mTBI. The non-invasive method of cerebrovascular regulation assessment will be extended to study concussed and non-concussed athletes at FIT and combined with cognitive data through a partnership with the Psychology Department and Athletic Program.

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