

## **EFFECT OF 1% INSPIRED CO<sub>2</sub> DURING HEAD-DOWN TILT ON OCULAR STRUCTURES, CEREBRAL BLOOD FLOW, AND VISUAL ACUITY IN HEALTHY HUMAN SUBJECTS**

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### **BACKGROUND**

The cephalad fluid shift induced by microgravity has been hypothesized to elevate intracranial pressure (ICP) and contribute to the development of the visual impairment/intracranial pressure (VIIP) syndrome experienced by many astronauts during and after long-duration space flight. In addition, elevated ambient partial pressure of carbon dioxide (PCO<sub>2</sub>) on the International Space Station (ISS) has also been hypothesized to contribute to the development of VIIP. We seek to determine if an acute, mild CO<sub>2</sub> exposure, similar to that occurring on the ISS, combined with the cephalad fluid shift induced by head-down tilt will induce ophthalmic and ICP changes consistent with the VIIP syndrome.

### **HYPOTHESIS**

We hypothesize that breathing 1% CO<sub>2</sub> during 6° head-down tilt for 1 hr will increase optic nerve sheath diameter (ONSD), intraocular pressure (IOP), choroidal blood volume, and ICP, but not change visual acuity relative to levels of these variables in the seated or the head-down tilt position without elevated CO<sub>2</sub>. We also hypothesize that the magnitude of the response to CO<sub>2</sub> may be affected by genetics, specifically polymorphisms of the one-carbon metabolism pathway that has been documented to be associated with VIIP incidence.

### **METHODS**

Four of eight healthy adult male subjects (30 yrs, range: 25-35) have participated in a single visit to the Cardiovascular and Vision Laboratory at NASA Johnson Space Center. Data collection on the remaining 4 subjects will be completed by December 2015. Subjects completed three 1-hour exposures separated by a 10-min break: (1) seated upright breathing room air; (2) at 6° head-down tilt breathing room air (HDT); and (3) at 6° head-down tilt breathing 1% CO<sub>2</sub>, 21% O<sub>2</sub>, balance N<sub>2</sub> (HDT+CO<sub>2</sub>). The seated exposure was conducted first and the order of the head-down tilt exposures was randomized. For each exposure, subjects breathed through a 2-way non-rebreathing facemask open to room air or connected to a breathing reservoir containing the CO<sub>2</sub> gas mixture and end-tidal CO<sub>2</sub> was continuously measured. Doppler ultrasound was used to measure blood flow in the head, neck, and eye. IOP was measured using the Icare Pro rebound tonometer. Noninvasive ICP (nICP) estimates were obtained using the non-invasive intracranial pressure framework, a novel algorithm modelling the morphology of the transcranial Doppler ultrasound waveform of the middle cerebral artery blood flow velocity, arterial blood pressure waveform, and ECG. Spectral-domain optical coherence tomography was used to obtain images of the choroid, retina, and optic disc. Near visual acuity was assessed using commercially-available Early Treatment Diabetic Retinopathy Study charts. A blood sample was obtained for analysis of one-carbon pathway biochemistry and five single nucleotide polymorphisms.

### **RESULTS**

As expected, HDT increased end-tidal PCO<sub>2</sub> (P<sub>ET</sub>CO<sub>2</sub>) compared to seated, but the addition of 1% CO<sub>2</sub> during HDT only increased P<sub>ET</sub>CO<sub>2</sub> another 1.5 mm Hg to 41.0 mm Hg. Compared to seated, nICP, ONSD, and retinal artery blood flow velocity were greater during HDT and HDT+CO<sub>2</sub>; the two HDT positions did not appear different from each other. IOP, macular thickness, retinal nerve fiber layer thickness, choroid thickness, axial length, and visual acuity were not different between exposures. Compared to seated, only 1 out of 24 CO<sub>2</sub> exposure symptoms (drowsiness) increased slightly during both head-down tilt exposures, likely reflecting duration of the study as there was no difference between HDT and HDT+CO<sub>2</sub>. Analysis of blood samples for 1-C metabolites is ongoing.

### **CONCLUSIONS**

Data reduction on the remaining 4 subjects will be completed by March 2016, after which statistical analysis can be completed using all subjects. Currently the subtle changes observed in our preliminary data from a low number of subjects prevents definitive conclusions regarding the magnitude of physiological changes that occur due to mild

hypercapnic exposure during HDT. Thus far, mild hypercapnia for 1 hr in the HDT position does not appear to replicate VIIP symptoms such as choroidal folds, optic disc edema, or decreased visual acuity.