**FLUID SHIFTS**

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**INTRODUCTION**

NASA is focusing on long-duration missions on the International Space Station (ISS) and future exploration-class missions beyond low-Earth orbit. Visual acuity changes observed after short-duration missions were largely transient, but more than 50% of ISS astronauts experienced more profound, chronic changes with objective structural and functional findings such as papilledema and choroidal folds. Globe flattening, optic nerve sheath dilation, and optic nerve tortuosity also are apparent. This pattern is referred to as the visual impairment and intracranial pressure (VIIP) syndrome. VIIP signs and symptoms, as well as postflight lumbar puncture data, suggest that elevated intracranial pressure (ICP) may be associated with the spaceflight-induced cephalad fluid shifts, but this hypothesis has not been tested. The purpose of this study is to characterize fluid distribution and compartmentalization associated with long-duration spaceflight, and to correlate these findings with vision changes and other elements of the VIIP syndrome. We also seek to determine whether the magnitude of fluid shifts during spaceflight, as well as the VIIP-related effects of those shifts, is predicted by the crewmember’s preflight conditions and responses to acute hemodynamic manipulations (such as head-down tilt). Lastly, we will evaluate the patterns of fluid distribution in ISS astronauts during acute reversal of fluid shifts through application of lower body negative pressure (LBNP) interventions to characterize and explain general and individual responses.

**METHODS**

We will examine a variety of physiologic variables in 10 long-duration ISS crewmembers using the test conditions and timeline presented in the Figure below. Measures include: (1) fluid compartmentalization (total body water by D₂O, extracellular fluid by NaBr, intracellular fluid by calculation, plasma volume by CO rebreathe, interstitial fluid by calculation); (2) forehead/eyelids, tibia, calcaneus tissue thickness (by ultrasound); (3) vascular dimensions by ultrasound (jugular veins, cerebral and carotid arteries, vertebral arteries and veins, portal vein); (4) vascular dynamics by MRI (head/neck blood flow, cerebrospinal fluid pulsatility); (5) ocular measures (optical coherence tomography, intraocular pressure, 2-dimensional ultrasound including optic nerve sheath diameter, globe flattening, and retina-choroid thickness, Doppler ultrasound of ophthalmic and retinal arteries, and veins); (6) cardiac variables by ultrasound (inferior vena cava, tricuspid flow and tissue Doppler, pulmonic valve, stroke volume, right heart dimensions and function, four-chamber views); and (7) ICP measures ( tympanic membrane displacement, distortion-product otoacoustic emissions, and ICP calculated by MRI). On the ground, acute head-down tilt will induce cephalad fluid shifts, whereas LBNP will oppose these shifts. Controlled Mueller maneuvers will manipulate cardiovascular variables. Through interventions applied before, during, and after flight, we intend to fully evaluate the relationship between fluid shifts and the VIIP syndrome.

**DISCUSSION**

Six crewmembers have consented to participate in this experiment. The first two are currently inflight, with the others in preflight testing and training. The first two subjects are projected to complete testing in 2016 with the entire complement of subjects completed by 2018.