Proteomic Assessment of Fluid Shifts and Association with Visual Impairment and Intracranial Pressure in Twin Astronauts

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BACKGROUND: Astronauts participating in long duration space missions are at an increased risk of physiological disruptions. The development of visual impairment and intracranial pressure (VIIP) syndrome is one of the leading health concerns for crew members on long-duration space missions; microgravity-induced fluid shifts and chronic elevated cabin CO_2 may be contributing factors. By studying physiological and molecular changes in one identical twin during his 1-year ISS mission and his ground-based co-twin, this work extends a current NASA-funded investigation to assess space flight induced "Fluid Shifts" in association with the development of VIIP. This twin study uniquely integrates physiological and -omic signatures to further our understanding of the molecular mechanisms underlying space flight-induced VIIP. We are: (i) conducting longitudinal proteomic assessments of plasma to identify fluid regulation-related molecular pathways altered by long-term space flight; and (ii) integrating physiological and proteomic data with genomic data to understand the genomic mechanism by which these proteomic signatures are regulated.

PURPOSE: We are exploring proteomic signatures and genomic mechanisms underlying space flight-induced VIIP symptoms with the future goal of developing early biomarkers to detect and monitor the progression of VIIP. This study is first to employ a male monozygous twin pair to systematically determine the impact of fluid distribution in microgravity, integrating a comprehensive set of structural and functional measures with proteomic, metabolomic and genomic data. This project has a broader impact on Earth-based clinical areas, such as traumatic brain injury-induced elevations of intracranial pressure, hydrocephalus, and glaucoma.

HYPOTHESIS: We predict that the space-flown twin will experience a space flight-induced alteration in proteins and peptides related to fluid balance, fluid control and brain injury as compared to his pre-flight protein/peptide signatures. Conversely, the trajectory of these protein signatures will remain relatively constant in his ground based co-twin.

METHODS: We are using proteomic and standard immunoelectrophoresis techniques to delineate the change in protein signatures throughout the course of a long duration space flight in relation to the development of VIIP. We are also applying a novel cell-based metaboloic organ system assay ("Organs on a Plate") to address how these circulating biomarkers affect physiological processes at the cellular and organ level which could result in VIIP symptoms. These molecular data will be correlated with physiological measures (eg. extra and intracellular fluid volume, vascular filling/flow patterns, MRI, and Optic Coherence Tomography.

DISCUSSION: Pre- and in-flight data collection is in progress for the space-flown twin, and similar data have been obtained from the ground-based twin. Biosamples will be batch processed when received from ISS after the conclusion of the 1-year mission. Omic and Physiological measures from the twin astronauts will be compared to similar data being collected on twin subjects who participated in simulated microgravity study. bed rest study.