Fiscal Year:	FY 2022	**Task Last Updated:**	FY 12/01/2022
PI Name:	Dulchavsky, Scott A. M.D., Ph.D.		
Project Title:	Fluid Shifts		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (2) **SANS**:Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	48202-2608	**Congressional District:**	13
Comments:			
Project Type:	Flight	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	05/16/2013	**End Date:**	01/31/2022
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Brocato, Becky	**Contact Phone:**	
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Flight Program:	ISS		
Flight Assignment:	NOTE: Extended to 1/31/2022 per NSSC information (Ed., 2/16/21) NOTE: Extended to 1/31/2021 per NSSC information (Ed., 10/16/18)		
Key Personnel Changes/Previous PI:	December 2022 Report NOTE: This study was merged with investigations from Dr. Alan Hargens (Fluid distribution before, during and after prolonged space flight) and Dr. Michael Stenger (Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance) resulting in a comprehensive study titled “Fluid Shifts Before, During and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment” (short title: Fluid Shifts). As a result of the combination, the team of CoInvestigators changed. CoInvestigators for this study have included: Philippe Arbeille, MD (François-Rabelais University, Tours, France) Doug Ebert, PhD (KBR/NASA Johnson Space Center) Stuart Lee, PhD (KBR/NASA Johnson Space Center) Brandon Macias, PhD (NASA Johnson Space Center) David Martin, MS (Wyle Integrated Science and Engineering Group) Ashot Sargsyan, MD (KBR/NASA Johnson Space Center) Scott Smith, PhD (NASA Johnson Space Center) Michael Stenger, PhD (NASA Johnson Space Center) Sara Zwart, PhD (NASA Johnson Space Center) (Ed., 1/5/23)		
COI Name (Institution):	Ebert, Douglas Ph.D. (KBR/NASA Johnson Space Center) Sargsyan, Ashot M.D. (KBR/NASA Johnson Space Center)		

Grant/Contract No.:	NNX13AK30G
Performance Goal No.:	
Performance Goal Text:	
Task Description:	Editor's Note (7/11/2013): NOTE THIS IS A CONTINUATION OF FUNDING FOR NNX13AB42G (Microgravity Associated Compartmental Equilibration (MACE)) WITH THE SAME PRINCIPAL INVESTIGATOR, Dr. Scott Dulchavsky. Fifty percent of American astronauts have developed ocular refraction change after long duration space flight on the International Space Station (ISS). Recent findings have also included structural changes of the eye (papilledema, globe flattening, choroidal folds) and the optic nerve (sheath dilatation, tortuosity, and kinking), as well as imaging signs and lumbar puncture data indicative of elevated intracranial pressure (ICP). While short duration space flight is also characterized by vision disturbances, these are generally transient and do not appear to have lasting impacts on the structure or function of the eye. Changes in vision, eye, and adnexa morphology are hypothesized to be the result of space flight-induced cephalad fluid shifts and transiently elevated intracranial pressure. This hypothesis, however, has not been systematically tested. In earlier anecdotal publications, ICP elevation in long-duration space flight has been inferred but without association with structural or functional changes of the eye. Furthermore, while fluid shifts and compartmentalization during short-duration space flight (Space Shuttle missions) have been studied, the fluid distribution patterns and their effects on intracranial pressure or the structure and function of the sensory organs in the course of long-duration space flight are not well known. Several ISS crewmembers have reported consistent worsening of nasal congestion and associated symptoms in late afternoon hours, necessitating topical and systemic decongestant use. Although several explanations have been entertained, food (salt) and water intake are likely to have provoked these symptoms through postprandial modification of fluid balance or increase in the circulating volume that manifests in the most susceptible individuals. The purpose of the proposed work is to objectively characterize the changes in fluid distribution, including intra/extracellular and intra/extravascular fluid shifts, by applying advanced non-invasive assessment technologies before, during, and after long duration space flight. Additionally, we will examine the relationship between the type and magnitude of the fluid shift with any effects on eye morphology and vision disturbances, intraocular pressure (IOP), and measures of intracranial pressure. Further, we seek to determine whether the magnitude of fluid shifts during space flight, as well as the above effects of those shifts can be predicted based upon crewmember baseline data and responses to acute head-down tilt tests performed before launch. Finally, we propose to evaluate the effect of lower body negative pressure (LBNP) on the above parameters. To our knowledge, this is the first attempt to systematically determine the impact of the fluid distribution in microgravity on a comprehensive set of structural and functional measures including, but not limited to, those related to intracranial pressure, vision, morphology of the eye and its adnexa, and the vascular systems of the head and neck, during and after long duration space flight. The study design and methodology are based on the extensive relevant experience of the Investigators, including many successful ground-based, space flight analogue, and space flight projects and investigations. Primary Hypothesis Prolonged microgravity-induced, headward volume, and pressure shifts promote elevation of intracranial pressure and result in alterations in crewmembers' vision. Specific Aims Specific Aim I: To characterize fluid distribution and compartmentalization before, during, and after long-duration space flight. Hypothesis 1: Fluid distribution measured by dilution techniques will reflect a headward fluid shift and an intra- to extra-vascular fluid shift during space flight, returning to pre-flight condition after landing. Hypothesis 2: Regional headward fluid shifts in-flight are documented by increased cephalad venous dimensions (jugular veins) and flow characteristics, skin and soft tissue thickness. Hypothesis 3: Fluid re-distribution towards the eye (detected in choroid, retina, and optic nerve head using ultrasonography and optical coherence tomography), and in arteries supplying ocular vascular beds, contributes to vision alterations. Hypothesis 4: Splanchnic venous congestion (detected by portal vein size) contributes to headward volume shift, but is not in communication with the veins of head and neck. Thus, there should be a different level of venous congestion in these two compartments. Specific Aim II: To correlate in-flight alterations of eye structure, ocular vascular parameters, and vision with headward fluid shifts, vascular dimensions, and flow patterns. Hypothesis 5: Space flight-induced fluid shifts will have an upregulating effect on ICP and will alter ocular refraction / visual acuity. These changes will vary in magnitude and respectively, in their resolution pattern after space flight. Hypothesis 6: In-flight ICP-related measures, IOP (intraocular pressure), venous and arterial morphometric and flow characteristics, vascular resistance of ocular vascular beds, and optic nerve anatomy will trend towards normal-gravity levels temporarily during and residually after fluid sequestration (LBNP) interventions. Specific Aim III: To determine systemic and ocular factors of individual susceptibility to the development of ICP elevation and/or vision alterations. Hypothesis 7: Subjects with greater fluid shifts (as measured by the ultrasound method in Aim 1) during pre-flight testing will experience greater fluid shifts in-flight and will be more susceptible to flight-induced vision alterations. Hypothesis 8: Subjects who are resistant to the reversal of in-flight symptoms and physiological status through the application of LBNP will be more susceptible to persistent flight-induced vision alterations.

	Hypothesis 9: Propensity towards more severe changes in-flight and the more indolent postflight resolution pattern will correlate with a range of individual characteristics of the crewmembers, such as anatomical and microanatomical and physiological features and potentially, hitherto unsuspected factors. NOTE: This study was merged with investigations from Dr. Alan Hargens (Fluid distribution before, during and after prolonged space flight) and Dr. Michael Stenger (Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance) resulting in a comprehensive study titled “Fluid Shifts Before, During and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment” (short title: Fluid Shifts).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Current means of measuring increased intracranial pressure require an invasive monitoring system with skilled medical personnel. The techniques outlined in this proposal, if verified, would provide a rapid, accurate, non-invasive, and scalable solution to measure increases in intracranial pressure for a number of critical medical conditions. These studies will also provide physiological insight to the mechanisms of fluid shifts and their relationship to intracranial pressure. This information could be relevant to terrestrial disorders of intracranial pressure such as idiopathic intracranial hypertension (IIH).
Task Progress:	The Fluid Shifts flight study was funded starting in 2012 and was a result of the combination of three selected grant proposals into a single study (Principal Investigators: Michael Stenger/Cardiovascular and Vision Laboratory NASA Johnson Space Center (JSC); Alan Hargens/University of California-San Diego; and Scott Dulchavsky/Henry Ford Health System). In 2013, the Cardiovascular & Vision Laboratory (CVL) portion of the project budget was rescoped at the request of NASA Human Health Countermeasures (HHC) Element management to increase the grant from 3 years to 7 years. Data collection on 10 subjects began in 2014, and 3 additional subjects were added to the CVL scope of work in 2017. This international investigation included astronauts from NASA, ESA (European Space Agency), and JAXA (Japan Aerospace Exploration Agency), as well as Russian cosmonauts. Due to the change in the role of Michael Stenger within HHC, Steven Laurie has taken on responsibilities as the primary point-of-contact Co-Principal Investigator in his place. The combination of these 3 independent studies, along with required usage of international assets on the International Space Station (ISS), required extraordinary cooperation involving the independent Principal Investigators (PIs) along with international partners. The primary goals of this study were to (1) characterize the fluid shift that occurs during spaceflight, (2) determine if measurements obtained preflight could be used to predict ocular changes during spaceflight, and (3) evaluate the effectiveness of lower body negative pressure (LBNP) during spaceflight to acutely reverse the headward fluid shift. The Fluid Shifts study has greatly enhanced our understanding of numerous aspects of spaceflight physiology and our understanding of SANS (spaceflight-associated neuro-ocular syndrome). • The 12 crewmembers who participated in 52 sessions of lower body negative pressure (25 mmHg) for up to 60 minutes per session tolerated the sessions without needing to terminate a test. • During spaceflight, numerous key outcome measures were similar to values in the seated or supine posture on Earth, and use of LBNP during spaceflight partially reversed some values. Still, none reached values measured in the seated upright posture on Earth. • The effects of LBNP appear to be transmitted to the level of the eye, although the mechanism is unclear. • Noninvasive indicators of intracranial pressure during long-duration spaceflight appear most similar to the seated or supine posture on Earth. Acute use of LBNP during spaceflight did not lower nICP indicators other than OAE (otoacoustic emission) phase at FD 150. Measurements during spaceflight were overall mostly similar to the seated posture on Earth. • Our team identified altered cerebral venous blood flow draining the head and, for the first time, observed a venous thrombus in the left internal jugular vein. • We have advanced our understanding of the effects of spaceflight on ocular morphology based on enhanced analyses of optical coherence tomography (OCT) images. • We corroborated previous findings from brain MRI (magnetic resonance imaging) analyses and demonstrated that there is no association between the change in lateral ventricular volume and magnitude of optic disc edema that develops during spaceflight. • MRI data analysis confirmed the hypothesis of an increased response to HDT (head-down tilt) position in postflight compared to preflight, indicating a physiological change induced by extended microgravity.
Bibliography Type:	Description: (Last Updated: 03/14/2025)
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