Fiscal Year:	FY 2020	**Task Last Updated:**	FY 11/20/2020
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
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No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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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:	none		
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.:			
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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:	Within this reporting period we have completed data collection, including pre/in/post-flight data collection on all 13 subjects for this experiment. Dr. Mark Haacke's group was added to the team in 2019 in order to enhance analytical capabilities for 3T MRI data. Dr. Haacke and his team have unique specialization in the analysis of susceptibility-weighted imaging (SWI) data from brain MRI protocols, as well as other vascular aspects of MRI protocols. Therefore, emphasis in the recent period was put on the analysis of SWI and Time-of-Flight (TOF) venography data collected as part of the 3T MRI protocol from the head and neck. Preliminary analysis of large neck vessels is complete; further analysis on this and other objectives is underway. The resultant data are verified and organized for statistical analysis, and reviewed periodically as more progress is made. This subset of data was reviewed in detail on 11/13/2020 at the Fluid Shifts Workshop (internal to FS investigators) as a status presentation. The team at large acknowledged the scientific value of the data derived so far. Dr. David Kemp continues to provide invaluable otoacoustic emission (OAE) expertise, streamlining and refining OAE analysis methods. We have focused our analysis on transient evoked OAE (TEOAE) phase shifts, which are highly systematic in response to posture change and lower body negative pressure during ground testing. OAE results indicate that overall, oval window tension (a surrogate for intracranial pressure) is not significantly elevated during space flight. Preliminary analysis has been completed on all data collected to date. Data collected as a part of this project were included in two presentations at the 2020 Human Research Program Investigators' Workshop in Galveston, TX. In addition, a crew report was completed to highlight individual results from that crewmembers' participation in this study. Partial results from this investigation were made available as part of a publication in JAMA Network which described a venous thrombosis in a crewmember during space flight, resulting in a number of news requests and media coverage. Bibliography: Marshall-Goebel K, Laurie SS, Alferova IV, Arbeille P, Auñón-Chancellor SM, Ebert DJ, Lee SMC, Macias BR, Martin DS, Pattarini JM, Ploutz-Snyder R, Ribeiro LC, Tarver WJ, Dulchavsky SA, Hargens AR, Stenger MB. Assessment of Jugular Venous Blood Flow Stasis and Thrombosis During Spaceflight. JAMA Netw Open. 2019 Nov 1;2(11):e1915011. doi: 10.1001/jamanetworkopen.2019.15011. PMID: 31722025 Abstracts: M. B. Stenger, A. R. Hargens, S. A. Dulchavsky, P. Arbeille, R. W. Danielson, D. J. Ebert, S. S. Laurie, S. Johnston, S. M. C. Lee, J. Liu, B. Macias, D. S. Martin, L. Minkoff, R. Ploutz-Snyder, L. C. Ribeiro, A. Sargsyan, and S. M. Smith. Fluid Shifts. Human Research Program Investigators Workshop. Galveston, TX, January 2020. Related abstracts: D. Kemp, D. Ebert, R. Danielson, K. Marshall-Goebel, B. Macias, and M. Stenger. Use of Otoacoustic Phase Change to Evaluate Countermeasures for Spaceflight-associated Neuro-ocular Syndrome. Human Research Program Investigators Workshop. Galveston, TX, January 2020.
Bibliography Type:	Description: (Last Updated: 03/14/2025)
Articles in Peer-reviewed Journals	Marshall-Goebel K, Laurie SS, Alferova IV, Arbeille P, Auñón-Chancellor SM, Ebert DJ, Lee SMC, Macias BR, Martin DS, Pattarini JM, Ploutz-Snyder R, Ribeiro LC, Tarver WJ, Dulchavsky SA, Hargens AR, Stenger MB. "Assessment of jugular venous blood flow stasis and thrombosis during spaceflight." JAMA Netw Open. 2019 Nov 1;2(11):e1915011. https://doi.org/10.1001/jamanetworkopen.2019.15011 ; PMID: 31722025; PMCID: PMC6902784 , Nov-2019