Fiscal Year:	FY 2021	**Task Last Updated:**	FY 03/05/2021
PI Name:	Marshall-Goebel, Karina Ph.D.		
Project Title:	Venous Congestion Countermeasure Study		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **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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Comments:	New affiliation as of spring 2022: NASA Johnson Space Center; Human Physiology, Performance, Protection & Operations (H-3PO) Laboratory New affiliation as of fall 2018: KBR/NASA Johnson Space Center, Cardiovascular and Vision Laboratory, Houston; previously at Massachusetts General Hospital		
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	02/17/2020	**End Date:**	12/05/2020
No. of Post Docs:	5	**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:	Stenger, Michael	**Contact Phone:**	281-483-1311
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 12/5/2020 (from 9/30/2020) per PI (Ed., 7/17/20)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Laurie, Steven Ph.D. (KBR/NASA Johnson Space Center) Lee, Stuart Ph.D. (KBR/NASA Johnson Space Center) Macias, Brandon Ph.D. (NASA Johnson Space Center) Ebert, Doug Ph.D. (KBR/NASA Johnson Space Center) Kramer, Larry M.D. (University of Texas Health Science Center of Houston) Levine, Benjamin M.D. (University of Texas Southwestern Medical Center, Dallas) Hargens, Alan Ph.D. (University of California San Diego) Petersen, Lonnie M.D., Ph.D. (University of California San Diego) Petersen, Casper M.D. (University of California San Diego) Young, Millenia Ph.D. (NASA Johnson Space Center)		
Grant/Contract No.:	Directed Research		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	NOTE: Continuation of "Venous Congestion Countermeasure Study--PI Stenger" with new Principal Investigator Dr. Karina Marshall-Goebel, beginning February 17, 2020. The chronic headward fluid shift induced by weightlessness is hypothesized to be the instigating factor for the development of ocular structural and functional changes that develop during long-duration spaceflight. Efforts to determine a possible countermeasure (CM) in ground-based studies have focused on reversing the headward fluid shift using a variety of mechanical approaches, including lower body negative pressure (LBNP), veno-constrictive thigh cuffs (VTC), and reducing intrathoracic pressure during inspiration using an impedance threshold device (ITD). However, a final CM has not been implemented during spaceflight, in part because it is unknown which single or combination of CMs will be most efficacious at reversing the headward fluid shift. Measurements of internal jugular vein cross sectional area and pressure (IJVA and IJVP, respectively) collected on Earth in subjects in the 15° head-down tilt (HDT) position indicate that LBNP, VTC, or ITD partially reverse the headward fluid shift to values similar to the supine position, but no single CM successfully reversed the headward fluid shift during HDT to levels observed during upright posture. Moreover, it is critical to determine how best to provide sustained relief of the headward fluid shift. The purpose of this project is to determine if individual CMs or a combination of CMs can effectively reduce the headward fluid shift induced by supine posture and to determine the effectiveness of prolonged use of a CM during sleep. Specific Aims: 1. Determine if a single or combination of mechanical countermeasures, including LBNP, VTC, and breathing through an ITD, will acutely reverse a seated-to-supine posture headward fluid shift and sustain it for up to 45 min. Outcomes will include noninvasive measures of ICP, IJVA, IJVP, choroid thickness, and intraocular pressure. 2. Determine if the most effective CM(s) to reverse vascular outcomes in SA#1 also reverses the cerebral spinal fluid (CSF) shift by quantifying intraventricular volumes using magnetic resonance imaging (MRI). 3. Determine if up to 8 hours of daily LBNP during sleep can prevent the headward fluid shift-induced changes during 3 days of head-down tilt bedrest. Research Methods: Direct intracranial pressure (ICP) measured during parabolic flight [Lawley et al., J Physiol, 595:2115-27, 2017] and preliminary noninvasive measures of ICP collected during long-duration spaceflight (Fluid Shifts Study) suggest ICP during weightlessness is similar to or below the supine position in a 1g environment; IJVA and IJVP measured during spaceflight are also similar to values measured in the supine posture on Earth. These data suggest use of the supine posture on Earth is a more appropriate posture for CM evaluation so as to not confound their effectiveness due to the hydrostatic column which still exists in ground-based studies. To accomplish Aim #1 we will evaluate the effectiveness of candidate CMs to reverse the headward fluid shift imposed by moving from the seated to the supine posture. Ten subjects will participate in 3 visits to the NASA Johnson Space Center (JSC) Cardiovascular and Vision Laboratory. Each day subjects will be studied in the seated and supine position (baseline) and in the supine position during and after the application of each CM separately (Day 1: LBNP, VTC, ITD, randomized order) or CM combinations (Days 2 and 3: LBNP+VTC, LBNP+ITD, VTC+ITD, and LBNP+ITD+VTC). Each data collection phase begins with 5 minutes of stabilization, followed by ocular and vascular ultrasound imaging, IJVP, noninvasive ICP measurements, bilateral IOP (intraocular pressure) measurement, and OCT imaging. All measurements are repeated during each phase. After application of single CMs, measurements will continue during the 45-min post-CM phase. For combination CMs, the primary CM (LBNP or ITD) is applied for 45 min followed by the secondary CM (VTC, ITD, or VTC+ITD). This will allow us to determine if sequestering fluid in the lower body using an “active” CM, like LBNP, can be maintained using more “passive” methods, such as VTC or ITD. Operationally these “passive” CMs have the advantage of allowing crewmembers to move freely throughout the vehicle and perform other tasks without being restrained by a CM device. Thus, we will determine how best to sustain the effects of the acute application of CMs. To accomplish Aim 2, co-investigators from the University of California San Diego and UT (University of Texas) Health Science Center in Houston will use MRI to determine the impact of countermeasures employed in Aim 1 have on cerebral spinal fluid volume and flow. Subjects will complete testing in the supine position with and without CMs, and total CSF volume and flow will be quantified. To accomplish Aim 3, co-investigators at UT Southwestern will develop an LBNP device that can be worn for 8 hours during sleep and test this CM throughout a 3-day bedrest study. Preliminary data demonstrate that 3 days of HDT (without raising the head on a pillow which immediately lowers ICP) leads to thickening of the choroid. Acute application of 20 mmHg LBNP lowers ICP values towards the upright posture, and daily use of 20 mmHg LBNP for 8 hours while awake prevents the choroidal expansion. Outcome variables for this aim will include choroidal volume, hemodynamic monitoring during sleep, systemic and cerebral hemodynamics using comprehensive ultrasound and transcranial Doppler, non-invasive cardiac output, and blood and plasma volume.
Rationale for HRP Directed Research:	Insufficient time for solicitation to meet accelerated schedule of work to understand etiology and develop targeted countermeasures for Spaceflight Associated Neuro-ocular Syndrome.
Research Impact/Earth Benefits:	

Task Progress:	Spaceflight associated neuro-ocular syndrome (SANS) is hypothesized to be caused by a weightlessness-induced headward fluid shift in the vascular and cerebrospinal fluid systems. The venous congestion countermeasure study was a three part, multi-site study with the overarching goal of assessing mechanical fluid shift countermeasures in ground based analog settings. Part I of the study, conducted at the NASA Johnson Space Center Cardiovascular and Vision Laboratory, tested 3 mechanical countermeasures (lower body negative pressure [LBNP], veno-constrictive thigh cuffs [VTC], and impedance threshold device [ITD] resistive inspiratory breathing), individually and in combination, to reduce a posture-induced headward fluid shift that is similar in magnitude to the headward fluid shift that occurs during spaceflight. We also aimed to determine if sustaining one or more of the passive, compact countermeasures (VTC and/or ITD) after use of combined countermeasures with LBNP would maintain the footward fluid shift. Ten healthy subjects participated in this cross-over design study; testing occurred on 3 separate days within a 3 week period. On each day, cardiovascular, ocular, and noninvasive ICP measurements were taken in the seated and supine positions (baseline) and in the supine position during countermeasure application and recovery phase. On day 1, subjects were tested during individual countermeasure application (LBNP, VTC, and ITD; randomized order) and after cessation of the countermeasure to determine the recovery of physiological variables. On days 2 and 3, subjects underwent four combined countermeasure conditions (LBNP+VTC, LBNP+ITD, ITD+VTC, and LBNP+ITD+VTC), with two combined countermeasure conditions on each day in a randomized order. After each combined countermeasure data collection, one or more of the passive countermeasures (VTC and/or ITD) were maintained, and another set of measurements were taken. Part II of the study, conducted at the University of Texas Health Science Center at Houston, tested the effects of LBNP (the most effective countermeasure as determined by Part I) on intracranial volumetrics, brain perfusion, as well as blood and CSF flow dynamics using quantitative MRI. Nine healthy subjects participated in this study; subjects underwent MRI measures in the supine posture (baseline) and in the supine posture with low-level LBNP in a randomized order. Total imaging time for each subject was approximately 2 hours. Part III of the study, conducted at University of Texas Southwestern Institute for Exercise and Environmental Medicine and Zale Lipshy University Hospital, tested 8 hour nightly use of LBNP during bedrest. Ten healthy subjects participated in the randomized cross-over design study of 3-day supine bedrest, with and without nightly 8 hours of LBNP (randomized order). Subjects underwent baseline measures in the seated and supine postures, and thereafter measures were repeated each day of the bedrest study at 8 AM and 8 PM. During the LBNP portion of the study, subjects were placed in a next generation prototype airtight sleeping bag, sealed at the iliac crest, from 10 PM to 6 AM. The chamber was designed such that participants could lie on their back, side, or front. Throughout the entire bed rest protocol, participants were monitored to ensure strict adherence to bedrest. Data analysis is complete for all parts of the study.
Bibliography Type:	Description: (Last Updated: 04/15/2024)
Abstracts for Journals and Proceedings	Kramer L, Hasan K, Macias B, Goebel-Marshall K, Laurie S, Gabr R, Hirzallah M, Kamali A, Petersen C, Chaudhary L, Petersen L, Hargens A. "Venous Congestion Countermeasure Study: Quantitative MRI Results with LBNP." Oral presentation at the 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Abstracts for Journals and Proceedings	Dias K, Hearon C Jr, Babu G, MacNamara J, Marshall J, Leidner J, Silva E, Campain J, Peters K, Levine B. "Lower Body Negative Pressure during Sleep Safely Attenuates Choroid Engorgement Associated with Simulated Microgravity." Oral presentation at the 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Abstracts for Journals and Proceedings	Dias K, Hearon C Jr, MacNamara J, Marshall J, Leidner J, Peters K, Babu G, Levine B. "Can Nightly Prolonged Lower Body Negative Pressure Preserve Plasma Volume during Simulated Microgravity?" Poster presentation at the 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
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Abstracts for Journals and Proceedings	Ebert D, Kemp D, Danielson R, Marshall-Goebel K, Macias B, Stenger M. "Use of Otoacoustic Emissions to Evaluate Countermeasures for Spaceflight-Associated Neuro-Ocular Syndrome." Poster presentation at the 2020 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 27-30, 2020. Abstracts. 2020 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 27-30, 2020. , Jan-2020
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