Fiscal Year:	FY 2019	**Task Last Updated:**	FY 09/30/2019
PI Name:	Laurie, Steven Ph.D.		
Project Title:	Integrative Physiology of VIIP: Cardiopulmonary, Sleep, and Cognitive Function Assessment During Hypercapnic Bed Rest		
Division Name:	Human Research		
Program/Discipline:			
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) **Immune**:Risk of Adverse Health Event Due to Altered Immune Response (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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PI Organization Type:	NASA CENTER	**Phone:**	281-244-0029
Organization Name:	KBR/NASA Johnson Space Center		
PI Address 1:	Cardiovascular and Vision Laboratory		
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City:	Houston	**State:**	TX
Zip Code:	77058-2749	**Congressional District:**	36
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-MIXEDTOPICS. Appendix E: Behavioral Health & Human Health Countermeasures Topics
Start Date:	04/01/2016	**End Date:**	09/30/2019
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:	2	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Extended to 9/30/2019 per PI (Ed., 1/7/2019) NOTE: Extended to 9/30/2018 per JSC HHC element info (Ed., 2/5/18)		
Key Personnel Changes/Previous PI:			

COI Name (Institution):	Hu, Xiao Ph.D. (University of California, San Francisco) Lathan, Corrinna Ph.D. (AnthroTronix, Inc.) Lee, Stuart Ph.D. (KBRwyle/NASA Johnson Space Center) Lovering, Andrew Ph.D. (University of Oregon) Martin, David M.S. (KBRwyle./NASA Johnson Space Center) Stenger, Michael Ph.D. (NASA Johnson Space Center) Young, Millennia Ph.D. (NASA Johnson Space Center) Smith, Scott M Ph.D. (NASA Johnson Space Center) Zwart, Sara Ph.D. (University of Texas Medical Branch/NASA Johnson Space Center)
Grant/Contract No.:	Internal Project
Performance Goal No.:	
Performance Goal Text:	
Task Description:	As of 2016, ~40% of crew members completing long-duration spaceflight missions have developed ocular structural or functional changes that characterize the Spaceflight Associated Neuro-ocular Syndrome (SANS) (formerly, Visual Impairment, Intracranial Pressure syndrome (VIIP)), yet no ground-based analogs have successfully replicated these symptoms. Carbon dioxide (CO2) is elevated on the International Space Station (ISS) and has been hypothesized to contribute to the development of SANS, which may explain why previous ground-based analog studies which have not included elevated CO2 levels in the ambient air have not successfully replicated SANS. The research outlined in this grant proposal seeks to link physiological changes that occur during exposure to chronic hypercapnia (elevated carbon dioxide, 0.5% CO2 inspired) similar to that occurring on ISS, in subjects undergoing the spaceflight analog of 6° head-down tilt bed rest, with changes associated with the SANS syndrome and decrements in cognition, sleep quality, and circadian alignment. Optical coherence tomography, intraocular pressure, cerebral and ocular blood flow, and sensitivity to carbon dioxide will be used to assess the development of SANS and determine the relationship between physiological changes associated with hypercapnic bed rest and SANS symptoms. Cognitive function will be assessed using two tools: the Cognition battery currently being tested on ISS crew members, and the Digital Automated Neurobehavioral Assessment, the only FDA-cleared computerized cognitive assessment tool that has been validated in thousands of active military personnel. The Philips Respironics Alice PDx Sleep System will be used to assess sleep quality and core body temperature will be measured to determine circadian misalignment. This research proposal addresses multiple risks within NASA's Integrated Research Plan, including determining if this unique ground-based analog can simulate SANS, and if the mild hypercapnic environment represents a threat to behavioral health and performance, sleep quality, and normal circadian rhythm.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Research conducted as part of this experiment was unique to the International Space Station environment due to the elevated ambient CO2. However, understanding the role of a chronic headward fluid shift on ocular pathology will provide new insight into mechanisms of ocular diseases on Earth.
Task Progress:	The data outlined in this report were collected at the Institute for Aerospace Medicine at the German Aerospace Center (DLR) :envihab facility at an altitude of ~50 meters as part of the "VIIP and Psychological :envihab Research (VaPER)" bedrest campaign. Data collection occurred from October 2 through December 4, 2017. Twelve subjects (six female) consented to participate in this study, but one female subject dropped out after the start of data collection. Data from the remaining 11 subjects are presented here. The novel approach to this study compared to previous head-down tilt bed rest (HDTBR) studies was to more closely match the International Space Station (ISS) environment. To do this, two modifications were implemented that differed from previous HDTBR studies. First, this study included a 3.8 mmHg (0.5%) CO2 environment (3.8 mmHg) in the ambient air during the 30 days of HDTBR. During the pre- and post-HDTBR period subjects were exposed to normal indoor CO2 levels. The mild elevation in ambient CO2 levels was made possible because of the unique climate control capabilities of the DLR :envihab facility that allows for elevated CO2 levels to be maintained throughout the entire module the subjects lived in, including the 12 individual bedrooms used by subjects. Second, previous head-down tilt bed rest (HDTBR) studies have allowed subjects to use a pillow during the day and at night which lifts the head out of the HDTBR position relative to the rest of their body. Additionally, subjects were previously allowed to raise their head and upper body onto an elbow to eat during meals. In the current study subjects were not allowed use of a traditional pillow during HDTBR, nor were they allowed to lift their head and upper body during meals. A custom head-support was developed for use during side-sleeping, which some subjects chose to use. As a result, these subjects maintained a strict head-down tilt posture throughout the duration of the study, more accurately mimicking the chronic nature of the headward fluid shift that occurs on ISS. Currently, an astronaut is diagnosed with SANS if they develop optic disc edema based on fundoscopic images revealing a Frisèn Scale grade 1 or higher. However, additional ocular structural changes including choroidal and/or retinal folds, cotton wool spots, hyperopic shifts, and globe flattening have also been documented in astronauts and are being tracked as metrics related to SANS by Flight Medicine. In this study, we documented for the first time the development of optic disc edema in 5 of 11 subjects, but did not identify any choroidal or retinal folds or cotton wool spots. We did not conduct MRI imaging to determine if globe flattening developed. Cycloplegic refraction was not conducted so we do not have an objective assessment of refractive error change, but there were no changes in corrected visual acuity. Data collection and analysis are complete. Three manuscripts have been published in peer reviewed journals, with additional manuscripts currently being drafted for submission.
Bibliography Type:	Description: (Last Updated: 05/05/2023)

Abstracts for Journals and Proceedings	Laurie SS, Macias BR, Lee SMC, Stenger MB. "VaPER: Linking PCO2 to physiology." Presented at the NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. Abstracts. NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. , Jan-2019
Abstracts for Journals and Proceedings	Christian K, Petitti C, Ortega-Schwartz K, Penrose S, Schallerer A, Lovering A, Laurie S. "Assessment of Sleep and Circadian Rhythm During Hypercapnic 6-degree Head-Down Tilt Bed Rest." Presented at American College of Sports Medicine Northwest Chapter, Annual Meeting, Bend, OR, February 2018. American College of Sports Medicine Northwest Chapter, Annual Meeting, Bend, OR, February 2018. , Feb-2018
Abstracts for Journals and Proceedings	Kysar J, Christian K, Olson T, Laurie SS, Lovering AT. "Breath-by-Breath: Effect of mild hypercapnic bedrest on ventilatory chemosensitivity to carbon dioxide." Presented at American College of Sports Medicine Northwest Chapter, Annual Meeting, Bend, OR, February 2018. American College of Sports Medicine Northwest Chapter, Annual Meeting, Bend, OR, February 2018. , Feb-2018
Articles in Peer-reviewed Journals	Laurie SS, Macias BR, Dunn JT, Young M, Stern C, Lee SMC, Stenger MB. "Optic disc edema after 30 days of strict head-down tilt bed rest." Ophthalmology. 2019 Mar;126(3):467-8. Epub 2018 Oct 9. https://doi.org/10.1016/j.ophtha.2018.09.042 ; PubMed PMID: 30308219 , Mar-2019
Articles in Peer-reviewed Journals	Zwart SR, Laurie SS, Chen JJ, Macias BR, Lee SMC, Stenger MB, Grantham B, Carey K, Young M, Smith SM. "Association of genetics and B vitamin status with the magnitude of optic disc edema during 30-day strict head-down tilt bed rest." JAMA Ophthalmol. 2019;137(10):1195-200. Epub 2019 Aug 15. https://doi.org/10.1001/jamaophthalmol.2019.3124 ; PubMed PMID: 31415055; PubMed Central PMCID: PMC6696878 , Oct-2019
Articles in Peer-reviewed Journals	Laurie SS, Christian K, Kysar J, Lee SMC, Lovering AT, Macias BR, Moestl S, Sies W, Mulder E, Young M, Stenger MB. "Unchanged cerebrovascular CO2 reactivity and hypercapnic ventilatory response during strict head-down tilt bed rest in a mild hypercapnic environment." J Physiol. 2020 Jun;598(12):2491-505. https://doi.org/10.1113/JP279383 ; PMID: 32196672 , Jun-2020
Dissertations and Theses	Christian KH. "VaPER: The Development of Spaceflight Associated Neuro-ocular Syndrome (SANS): sans sufficient sleep?" Master's Thesis, University of Oregon, Eugene, OR, August 2018. , Aug-2018