Fiscal Year:	FY 2023	**Task Last Updated:**	FY 02/01/2023
PI Name:	Strangman, Gary E Ph.D.		
Project Title:	Brain-Related Assessments for Investigating the Neurophysiology of SANS (BRAIN-SANS)		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
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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Zip Code:	02129-2020	**Congressional District:**	7
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2018-2019 HERO 80JSC018N0001-SANS: Spaceflight Associated Neuro-ocular Syndrome Countermeasures. Appendix C
Start Date:	04/01/2020	**End Date:**	03/31/2024
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmire, Alexandra	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 03/31/2024 per NSSC information (Ed., 4/14/23)		
Key Personnel Changes/Previous PI:	October 2023 Update: Per the PI, Dr. Stijn Thoolen has left the project (Ed., 10/12/23). We are adding Dr. Stijn Thoolen, MD (Massachusetts General Hospital) as a Co-I at this time, given his medical training. Dr. Thoolen has been added to the list of Co-Investigators on the project.		
COI Name (Institution):	Bershad, Eric M.D. (Baylor College of Medicine, Inc.) Ivkovic, Vladimir Ph.D. (Massachusetts General Hospital) Zhang, Quan Ph.D. (Massachusetts General Hospital) Jimmy, Wu (Baylor College of Medicine, Inc.)		
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Task Description:	Spaceflight Associated Neuro-ocular Syndrome (SANS) remains an important and unmitigated risk to long-duration spaceflight. Current hypotheses suggest that the lack of gravity leads to fluid shifting towards the head, resulting in congestion and/or elevated pressures in the cranial, vascular, and/or lymphatic compartments. NASA is conducting 30-day head-down tilt (HDT) experiments to test SANS countermeasures at the :envihab facility in Cologne, Germany. We propose to provide numerous key measurements in support of these planned 30-day missions. We will focus in particular on providing a toolkit for detailed neurophysiological and fluid shift assessment and monitoring suitable for measuring both SANS- and countermeasure-related changes. These tools will be designed to complement the standard ocular measures used for SANS diagnosis and monitoring (e.g., optical coherence tomography (OCT), ocular ultrasound (US), fundoscopy, visual acuity). Our proposed measures will include: • Relative intracranial pressure (ICP) measurements via distortion product otoacoustic emissions (distortion product otoacoustic emissions: DPOAE). • Blood volume shifts along the body axis via near-infrared spectroscopy (NIRS). • Intracranial blood inflow and outflow, via internal jugular vein (IJV) and carotid artery (CA) ultrasound cross-sectional imaging and Doppler. • Cerebral pulsatility assessment, per our parabolic flight and SPACE-COT (Studying Physiological and Anatomical Cerebral Effects of CO2 and Tilt) :envihab NIRS study. • Blood pressure at the level of the head via local, cuffless superficial temporal artery tonometry. • Sagittal sinus blood volume imaging and monitoring using diffuse optical tomography (DOT). • Cerebral edema assessment based on H2O concentration imaging, similar to that used in previous altitude sickness studies. • Cerebral electrical activity, via electroencephalogram (EEG) measurements. • Dynamic cerebral autoregulation (CAR) assessment during countermeasure (CM) challenges, which can be derived from the NIRS signals used in the above measurements. Our tools will be made fully compatible with the planned SANS countermeasures, as well as with those of other teams proposing specific CMs. Along with the measures, we will provide the necessary expertise and analysis to quantify physiological changes associated with SANS countermeasures deployed during the 30-day HDT campaigns at :envihab. Our specific aims are as follows: Aim 1: Develop an integrated collection of hardware to support multiple simultaneous, continuous brain monitoring/imaging capabilities, and ensure the hardware and measurements are fully compatible with all countermeasures deployed during the :envihab missions. Aim 2: Characterize and quantify individual subjects' physiological responses to each planned condition, including comparative assessment of SANS countermeasures. Aim 3: Relate neurophysiological changes over the 30-day HDT—both with and without SANS-CMs—to cognitive and operational performance, sleep, mood, and ocular measures. This will include the Cognition battery, psychological/mood surveys, and a suite of ocular measures (OCT, fundoscopy). We will obtain as many measures as possible through data sharing and investigate the relationship of our neurophysiological measures to each of these outcome assessments. Jointly, the planned measures and Aims will enable NASA to quantitatively evaluate and compare the (neuro)physiological changes and fluid shifts associated with HDT and SANS countermeasures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our work will involve developing a detailed toolbox of measures for assessing brain physiology. These technologies will be compatible with the planned SANS countermeasures, and hence could be deployed in multiple other settings on Earth, ranging from intensive care units to exercise settings. The detailed and simultaneous monitoring of numerous cerebral physiology variables is expected to provide new insights into how the brain responds to various types of interventions. As such, the data could provide insights into how the body--and brain in particular--responds to pre-syncope, bedrest, exercise, fluid shifts, and sequestration of blood in the extremities. All of these have implications in medicine here on Earth.
	Background Spaceflight-associated neuro-ocular syndrome (SANS) is an unsolved risk for astronauts on long-duration missions. When diagnosed from Frisen grade papilledema on fundoscopy, some 10 of 68 astronauts have exhibited SANS, although related ocular findings are more common (e.g., acquired hyperopia, globe flattening, choroidal folds, retinal fiber nerve layer thickening), and current estimates are closer to a 75% prevalence of SANS in astronauts on 6-month missions. Unexpectedly, SANS signs do not always spontaneously resolve upon return to Earth gravity. While the cause of SANS is unknown, the hyperopia, globe flattening, and choroidal folds—coupled with typically normal or slightly elevated intraocular pressure (IOP)—suggests that intracranial pressure (ICP) may be elevated as compared to average Earth levels. Various pathophysiological mechanisms have been proposed for SANS, with particular suspicions regarding cephalad fluid shifts. SANS Countermeasures Most hypotheses regarding SANS involve headward fluid shifts as a factor, and various proposed SANS countermeasures (CMs)—including lower-body negative pressure (LBNP), veno-constrictive thigh cuffs (VTC), inspiratory resistance threshold devices (ITD), and artificial gravity (AG)—all involve "mechanical" redistribution of body fluids away from the head. Understanding the relative benefits of such CMs calls for assessments of perfusion and fluid flow into, within, and out of the cranium not only for potentially assessing and monitoring SANS but also to help quantify and compare the effect sizes of various CMs. SANS-CM Study at DLR's Envihab Facility

Task Progress:	To address the lack of SANS CMs, NASA negotiated a plan with the German Aerospace Center's :envihab facility to conduct 30-day head-down tilt (HDT) bedrest studies—the SANS-CM study. This effort currently includes 4 study arms: 1. 6o HDT bedrest alone (Reference) 2. 6o HDT bedrest plus two 3-hour periods per day seated upright (Seated CM) 3. 6o HDT bedrest plus two 3-hour periods per day of LBNP (LBNP CM) 4. 6o HDT bedrest plus one ~1-hour period of exercise followed by 6 hours of VTC (Exercise CM) This last arm was changed from 1hr exercise+2hr VTC, completed twice per day. Each arm will consist of n=12 subjects and different investigators will be involved in different portions of the overall SANS-CM study. BRAIN-SANS Contribution This BRAIN-SANS project seeks to provide a wide range of brain-related measures for all subjects in all study arms. These include changes in (i) intracranial pressure (ICP), (ii) blood flow in/out of the brain, (iii) cerebral blood flow velocity, (iv) brain perfusion and oxygenation, (v) blood distribution along the body axis, (vi) intracranial pulsatility, (vii) sagittal sinus imaging of potential venous congestion, (viii) intracranial water concentration, (ix) functional brain activation, (x) electrical brain activity, as well as (xi) cognitive performance data (Cognition). We also plan to compare these measures with measures from other groups, including ocular measures, mood and sleep, 1-carbon single nucleotide polymorphisms, and MRI. ACHIEVEMENTS IN YEAR 3 We completed Campaigns 1 and 2 during year 2 of the project. During the 3rd year of project, we conducted the following major tasks: Campaign 2: Data acquisition (and troubleshooting as needed) was completed for the entirety of Campaign 2, from January-March 2022. A total of 1,542 data files (out of a nominally expected 1,656 data files) were collected for a 93.1% data collection rate. This was lower than in year 1, consequent to one subject that had to be removed from the study (n=11 completers in Campaign 2). Excluding this subject, the data collection rate was 98.5%. Quality control assessments for all C1 and C2 datasets were conducted during and immediately after the respective campaign. Dry runs: Full-up dry runs were conducted with DLR personnel to adapt our integrated toolbox of devices for use during the exercise countermeasure activities. Finalizing protocols: Consequent to the dry runs, we finalized all protocols for the control (HDT-only) and exercise+VTC arms of the study. This included tilt-testing for calibration, orthostatic tilt testing, rest measurements, and measurements during onset, maintenance and offset of countermeasures. Preparation for and Initiation of Campaign 3: Experimental procedures for Campaign 3, including a 50/50 mix of control and exercise+VTC subjects, began January 23, 2023, and will continue until March 27, 2023. Preparations included adapting our toolbox to be robust to use during the exercise periods, delivering all needed hardware and materials to DLR for startup, and having an on-site presence for the initiation and BDC testing for Campaign 3. All data is evaluated for missing or erroneous data points, noise, and overall usability for analysis on a daily basis during the data collection period. SUMMARY Campaigns 1 and 2 (starting in year 2 and ending in year 3) proceeded well after substantial virtual and on-site dry-run procedures. Additional dry runs were conducted after the 9-month hiatus in the study at DLR to help ensure Campaigns 3 and 4 proceed smoothly as well. Data collection success rates have been high to date and are expected to be similarly successful in Campaigns 3 and 4. We are currently on track to complete Campaign 3 data collection by early March 2023 and complete Campaign 4 data collection by June 2023. At that point, final data processing and analysis will begin in earnest.
Bibliography Type:	Description: (Last Updated: 02/05/2025)
Abstracts for Journals and Proceedings	Thoolen S, Zhang Q, Ivkovic V, Voss S, Moestl S, Frett T, Tank J, Wu, Bershad EM, Strangman GE. "Brain-sans: brain-related assessments for investigating the neurophysiology of sans – 2023 update." 2023 NASA Human Research Program Investigators' Worshop, Galveston, TX, Feb 7-9, 2023. Abstracts. 2023 NASA Human Research Program Investigators' Worshop, Galveston, TX, Feb 7-9, 2023. , Feb-2023