Fiscal Year:	FY 2024	**Task Last Updated:**	FY 03/07/2024
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		
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Space Biology Special Category:	None		
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Zip Code:	02129-2020	**Congressional District:**	7
Comments:			
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmire, Alexandra	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 03/31/2025 per NSSC information (Ed., 4/4/24) 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.

Task Progress:	SANS-CM Study at DLR's Envihab Facility 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 4 The 4th year of this project started shortly after Campaign 3 had completed and before Campaign 4 began (in May 2023). Activities that were completed or will be completed by the end of the 4th year of the project are as follows: Initiation and Completion of Campaign 4: BRAIN-SANS data collection for C4 was started on 5/5/2023 and completed on 7/1/2023. Per most prior campaigns, this involved data collection on 12 participants. As per prior reports, we performed data quality control assessments in semi-real time during data collection periods to help optimize the quality of the data that was being collected, as well as to make ongoing adjustments when changes affecting quality appeared. We collected 99.7% of all expected files in Campaign 4. Summary of All BRAIN-SANS Data: Overall, data collection went very well, with 6,615 of 6,780 expected data files—or 97.6% of all data files—accounted for. The minor amount of missing data arose from one subject dropout, and device faults or running behind schedule which prevented full data completion. Ongoing Data Processing: Data preprocessing was underway as of the last report and has been significantly ramped up in the past year. Distortion product otoacoustic emissions (DPOAE) preprocessing (by Dr. Voss) is 95% complete overall, with a poster presented at the 2024 Human Research Program Investigators' Workshop (HRP IWS). Ultrasound imaging/flow data (handled by Dr. Bershad) is approximately 60% complete. Cognition data analysis (Dr. Basner) is approximately 80% complete. NIRS (NINscan and Oxiplex) preprocessing is approximately 70% complete at this time. NIRS results detailing the effects of countermeasures on blood sequestration along the body axis were presented at the 2024 HRP IWS. Data processing remains a high-priority task, and we are currently seeking to engage interns and affiliates to help with the wealth of data (and data types) that require analysis. Preliminary Results on Countermeasures: To summarize the NIRS results presented at HRP IWS 2024, there was a small shift of blood volume towards the head in the control condition, likely because at BDC (when subjects are ambulatory) the participants had only been head-down for <1 hr at the point of measurement. Transitioning to upright seated lead to no change in blood in the head or chest, substantial increases in the thigh, and large increases in the calf. The lower body negative pressure (LBNP) condition significantly reduced the blood volume in the chest and significantly increased blood volume in both the thigh and calf, to equal extents. This might be expected given the geometry of the LBMP vacuum chamber (compressing around the chest and applying uniform vacuum to both the upper and lower leg). Finally, the Exercise+VTC condition led to no significant changes in chest blood volume (trend towards decreases) but greatly increased the blood in both the thigh and calf. This was sustained through the exercise period, the 30-minute "gap" (when some loss of blood in the legs was anticipated), and increased further when the VTC was tightened. The effect size for Exercise+VTC was larger than seated, which was unexpected. These results are still being finalized. The remainder of year 4 will involve completing quality control assessments for Campaigns 3 and 4, completion of the DPOAE analysis, completion of the Cognition data analysis, continued analysis of the ultrasound data, and finalizing unified code for preprocessing all NIRS and physiological data. The upcoming year will be devoted to final analyses and manuscript preparation and submission. SUMMARY Year 4 was a success, with the completion of all data collection with a very low rate of data loss. The large volume of data will take time to preprocess and analyze and, given the shift in the last DLR campaigns from the original schedule, we will be requesting a no-cost extension to continue the analysis and interpretation work in the upcoming year.
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 J, Bershad E, Strangman G. "(2024) BRAIN-SANS: Brain-related assessments for investigating the neurophysiology of SANS - 2024 update." 2024 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 13-16, 2024. Abstracts. 2024 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 13-16, 2024. , Feb-2024
Abstracts for Journals and Proceedings	Voss S, Thoolen S, Moestl S, Frett T, Strangman G. "BRAIN-SANS: What do DPOAEs tell us about intracranial pressure changes during experiments designed to understand SANS?" 2024 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 13-16, 2024. Abstracts. 2024 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 13-16, 2024. , Feb-2024