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PI Name:	Strangman, Gary E Ph.D.		
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Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
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Space Biology Special Category:	None		
PI Email:	strang@nmr.mgh.harvard.edu	**Fax:**	FY
PI Organization Type:	NON-PROFIT	**Phone:**	617-724-0662
Organization Name:	Massachusetts General Hospital		
PI Address 1:	Department of Psychiatry		
PI Address 2:	149 13th Street, Suite 2651		
PI Web Page:			
City:	Charlestown	**State:**	MA
Zip Code:	02129-2020	**Congressional District:**	7
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No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmire, Alexandra	**Contact Phone:**	
Contact Email:	alexandra.m.whitmire@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Ed. note - PI addition to Feb 2022 report: Jimmy Wu, of the Baylor College of Medicine, was added to the project due to his expertise in biomedical engineering.		
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 proposing to conduct 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 our 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.

PROJECT OVERVIEW
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). 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 intra-ocular 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 a particular suspicion 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 the German Space Agency (Deutsches Zentrum fur Luft-und Raumfahrt or "DLR") Envihab Facility: To address the lack of SANS CMs, NASA negotiated a plan with the DLR German Aerospace Center's Envihab (: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 two ~1-hour periods of exercise plus an additional 2 hours of VTC (Exercise CM) 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 magnetic resonance imaging (MRI). ACHIEVEMENTS IN YEAR 2 By the end of the 2nd year of this project, we will have completed the following major tasks: Hardware & Supplies Shipping: After COVID-related scheduling delays at DLR, all hardware for our BRAIN-SANS monitoring toolkit—developed in Aim 1—was shipped to the DLR for training and use. Training: All :envihab personnel were trained to use the various toolkit instruments, including NINscan CW-NIRS (continuous wave/near-infrared spectroscopy) systems, the OptiplexTS RF-NIRS system, the Mimosa Acoustics HearID DPOAE (distortion-product otoacoustic emissions) system, and MAICO EasyTymp tympanometer. Dry runs: Full-up dry runs were conducted with DLR personnel to demonstrate the integration of the above devices, as well as how to further integrate the DLR imaging ultrasound, transcranial Doppler (TCD), and finometer devices. Finalizing protocols: The dry runs were used to finalize all protocols, customized to the specific DLR testing environment. This included tilt-testing for calibration, orthostatic tilt testing, rest measurements, and measurements during onset, maintenance, and offset of countermeasures. Campaign 1: Data acquisition (and troubleshooting as needed) was completed for the entirety of Campaign 1, from Sept-Nov 2021. A total of 735 data files (out of a nominally expected 744 data files) were collected, for a 98.8% data collection rate. Quality control assessments for all Campaign 1 datasets were conducted during and immediately after Campaign 1. Campaign 2: Preparations for Campaign 2—which is conceptually a repeat of Campaign 1 involving n=6 additional seated-upright CM subjects plus n=6 LBNP subjects—was initiated in Jan 2022 and is expected to complete in Mar 2022. Initial data collection sessions went smoothly. SUMMARY Despite challenges bought on by COVID-19 from the beginning of our funding, we initiated and completed running n=12 volunteers in Campaign 1 of the SANS-CM study (n=6 using the LBNP CM and n=6 as seated-upright controls). We have also started Campaign 2, with n=6 additional LBNP and n=6 seated-upright participants. We are on-track to complete Campaign 2 as planned. Campaigns 3-4 are currently scheduled to be conducted in the first half of 2023.
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. "BRAIN-SANS: Brain-related assessments for investigating the neurophysiology of SANS." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022 (Abstract # 1133-000156). , Feb-2022