Fiscal Year:	FY 2022	**Task Last Updated:**	FY 01/29/2022
PI Name:	Seidler, Rachael D. Ph.D.		
Project Title:	Recovery Timeline of Spaceflight-Induced Central Nervous System Changes		
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) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (2) **EVA**:Risk of Mission Impacting Injury and Compromised Performance and Long-Term Health Effects due to EVA Operations (3) **SANS**:Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS) (4) **Sensorimotor**:Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	NOTE: PI moved to University of Florida in July 2017; previous affiliation was University of Michigan.		
Project Type:	Ground	**Solicitation / Funding Source:**	2019-2020 HERO 80JSC019N0001-HHCBPSR, OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D
Start Date:	03/30/2021	**End Date:**	03/31/2029
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**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 03/31/2029 per L. Juliette/JSC (Ed., 5/3/22).		
Key Personnel Changes/Previous PI:	March 2022 Report: Babette Brumback, Ph.D., CoInvestigator, has retired from the University of Florida and is no longer with the project.		
COI Name (Institution):	Wood, Scott Ph.D. (NASA Johnson Space Center)		
Grant/Contract No.:	80NSSC21K0813		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Our group has reported an upward shift of the brain within the skull following spaceflight, which results in apparent reduced gray matter volume in inferior and frontal brain regions, and apparent increased volume in superior and posterior regions, as measured by magnetic resonance imaging (MRI). Another recent paper that we have published reports free water (fluid in the ventricles and extracellular space) changes in the brain with spaceflight, and degradation of sensory and motor white matter pathways (Pasternak O et al., "Spaceflight-Associated Brain White Matter Microstructural Changes and Intracranial Fluid Redistribution." JAMA Neurol. 2019 Apr 1;76(4):412-419. https:// . PMID: 30673793; PMCID: PMC6459132). Some of these measures show recovery to preflight levels by six months postflight, whereas others do not. For example, in two crewmembers who spent ~12 months in space, free water recovers only 75% by six months postflight. We have also observed increases in ventricular volume with spaceflight, ranging from 5 – 35% across astronauts. These changes exhibit little recovery by six months postflight, raising the possibility that these effects persist for prolonged durations. The brain's glial lymphatic (or 'glymphatic') pathway was identified in humans in just the past few years. It has been suggested that "ocular glymphatic" and cerebral lymphatic dysfunction may contribute to optic disc edema in astronauts, which is one sign of Spaceflight Associated Neuro-ocular Syndrome (SANS). SANS affects up to 50% of long-duration astronauts and poses significant health concerns. Many of these glymphatic vessels are found at the top of the brain and in the human extravascular visual system. Thus, the fluid and brain positional shifts that occur in microgravity may slow the rate of clearance of substances through this system. We are currently testing the impact of elevated CO2 on glymphatic clearance supported by an Office of Naval Research (ONR) grant (awarded to Kernagis and Seidler). The long-term health and functional consequences of these spaceflight-induced brain changes remain unknown, but our preliminary data suggest little recovery of fluid shifts that occur with one year in space when measured six months after return. Thus, we propose the following aims in response to Topic 3 of 80JSC019N0001-HHCBPSR: Aim 1) Determine the recovery timeline of spaceflight-induced ocular changes (e.g., signs of SANS such as optic disc edema) and changes in brain structure, function, and fluid shifts, measuring out to five years postflight. Aim 1a will comprise prospective assessments, while Aim 1b will leverage follow up testing on crewmembers who participated in our Neuromapping flight study and those crewmembers who have existing retrospective pre and postflight MRI scans. Aim 2) Examine longitudinal data for markers of long term health consequences and determine their association with persistent, spaceflight-induced ocular / brain changes. This project will elucidate the persistence of spaceflight-induced ocular and brain changes, as well as quantify their association with long-term health. Determining this is critically important as we extend the duration and distance of human space travel in the near future.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This project has the potential to benefit life on Earth by leading to a greater understanding of central nervous system plasticity.
Task Progress:	INTRODUCTION Spaceflight-associated neuro-ocular syndrome (SANS) describes structural and functional alterations of the eye that develop in many astronauts during long-duration spaceflight missions (>6 month). Understanding the consequences of the structural and functional changes to the eye and brain that endure long after return from spaceflight is essential for future exploration-class spaceflight missions. PURPOSE The primary purpose of this project is to quantify long-term changes in ocular and brain structure that remain or develop long after spaceflight and to determine the functional consequences of those changes. Specifically, we will characterize the recovery and long-term structural and functional alterations to the eye and brain for 5 years following 6-month spaceflight missions. We will also characterize the structural and functional changes to the eye and brain, including cognitive changes, in crewmembers who have participated in past missions, calling them back several years after their most recent flights. METHODS Advanced techniques will be used to study the eyes and brains of astronauts. For one set of experiments, preflight, inflight, and 5 years of postflight results from astronauts (n = 10) who have participated in =6-month missions will be compared to those from age and sex-matched non-astronaut control subjects (n=13). In a second set of experiments, outcomes from astronauts who had previously participated in =6-month missions (n=30) will be compared to control subjects that do not have standard duration spaceflight experience (n=30). In addition to characterizing the effects observed for individual variables, all data collected during the study will be analyzed using an integrative approach to identify relationships across ocular measures, brain measures, individual crewmembers, and time. Ocular structure and function will be evaluated using MRI and 3D structural analysis, optical coherence tomography (OCT), angiography, electroretinography (ERG), visual field analysis, pneumotonometry (intraocular pressure), visual field analysis, optical biometry, and dynamic vessel analysis. In collaboration with the integrated project team, MRI will be used to assess brain structural changes, and functional MRI (fMRI) and a series of cognitive batteries will be used to evaluate brain function. To better understand the neurophysiological mechanisms underlying anticipated changes, biomarkers associated with specific structural and functional brain alterations will be measured in blood samples. To complement the research measures, medically relevant test results already collected by the Space Medicine Operations Division will be shared. PROGRESS DURING THIS REPORTING PERIOD This project is being combined with the work of three other Principal Investigators (PIs) who responded to the same solicitation with independent proposals. During this reporting period, the protocols and aims from all four PIs are being integrated into a revised integrated proposal that will be delivered to NASA Human Health Countermeasures (HHC) and NASA Human Factors and Behavioral Performance (HFBP) Element scientists in early 2022. To reach this goal, the research team determined how to combine MRI sessions from multiple PIs, identified and removed overlapping procedures, and made substantial progress towards having a single, integrated budget.
Bibliography Type:	Description: (Last Updated: 03/18/2025)

Abstracts for Journals and Proceedings	Issabekov G, Wood S, Pasternak O, Kernagis D, Iliff J, Rane S, Seidler R. "Recovery timeline of spaceflight-induced central nervous system changes." 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. , Feb-2022