Fiscal Year:	FY 2024	**Task Last Updated:**	FY 12/23/2023
PI Name:	Seidler, Rachael D. Ph.D.		
Project Title:	Effect of Head-Down Tilt +/- CO_2 on Human Glymphatic Function		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	None		
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:**	2020 HERO 80JSC020N0001-FLAGSHIP, OMNIBUS1 Human Research Program: Crew Health Appendix A; Omnibus1-Appendix B
Start Date:	01/06/2023	**End Date:**	08/31/2024
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
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 08/31/2024 per M. Stenger/NASA HHC Element Scientist and C. Ribeiro/NASA HHC (Ed., 1/12/24)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Richmond, Sutton Ph.D. (University of Florida, Gainesville) Roy, Arkaprava Ph.D. (University of Florida, Gainesville)		
Grant/Contract No.:	80NSSC23K0365		
Performance Goal No.:			
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Task Description:	Spaceflight Associated Neuro-ocular Syndrome (SANS) is a potentially mission-limiting condition for astronauts, yet its underlying pathophysiology is poorly understood. It has been proposed that impairment of the glymphatic system in response to fluid shift or venous congestion could be an underlying cause of SANS. However, there have been no studies to date evaluating human glymphatic function in response to simulated microgravity. While our team is currently evaluating the effect of elevated carbon dioxide (CO_2) on human glymphatic function (awards from NASA and the Office of Naval Research), we have yet to evaluate the spaceflight-relevant combination of CO_2 and simulated microgravity. (Ed. Note: See related Grant #80NSSC17K0021--PI: Seidler). The latter can be achieved via 6° head-down tilt (HDT), simulating the headward fluid shifts of microgravity. Here, we propose to conduct glymphatic magnetic resonance imaging (MRI) in human subjects over a span of several hours while they are either supine or lying on a 6° foam wedge with head-down tilt. They will also be breathing elevated CO_2 to better mimic the conditions on the International Space Station. We will measure the effects of HDT positioning on human glymphatic function (Aim 1) and the combined effects of breathing elevated CO_2 and HDT on human glymphatic function (Aim 2). Thus, we will quantify the acute effects HDT with and without elevated CO_2.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This project is examining the effects of elevated CO_2 combined with and without head down tilt on the brain's waste clearance system (glymphatic system). Understanding the impact that elevated CO_2 has on this process may inform environmental health.
Task Progress:	Spaceflight-Associated Neuro-Ocular Syndrome (SANS) describes a constellation of ocular structural changes exhibited by ~33% of astronauts returning from long duration-spaceflights [1, 2]. These changes include optic disc edema, choroidal folding, globe flattening, and hyperopic refractive error shifts. The etiological mechanisms behind SANS remain insufficiently understood; it is thought to be linked to headward fluid shifts, increased intracranial pressure, altered glymphatic drainage, hypercapnia-related volume and pressure disturbances, and a number of other potential mechanisms [1]. Traveling beyond the confines of Earth's atmosphere is accompanied by various health stressors such as microgravity, ionizing radiation, and disrupted circadian rhythms [3]; insight into the various complex interactions of these induced stressors on brain fluid dynamics, glymphatic exchange, and brain health is necessary to develop effective SANS countermeasures. The glymphatic system functions to distribute solutes and clear waste from the brain via cerebrospinal fluid (CSF) circulation and interstitial fluid flow along its perivascular spaces. Glymphatic clearance has been implicated as a key determinant of brain health, acting to remove or redistribute metabolic products, inflammatory and immune-mediated molecules, as well as additional solutes for disposal [4]. Glymphatic dysfunction may cause the failure of interstitial solute clearance or derangement of cranial fluid dynamics resulting from the mismatch between CSF influx and interstitial fluid efflux, with negative impacts on brain homeostasis. It is not known at this point how the environmental stressors of microgravity exposure impact glymphatic function. In the proposed study, we will investigate the individual and combined effects of simulated microgravity and hypercapnia on human glymphatic function. Using acute head-down tilt (HDT) bedrest and exposure to elevated CO_2, this study will be a critical first step toward understanding the potential interactions of microgravity and elevated CO_2 on perivascular glymphatic function and brain health. Progress to Date We identified a vendor for an MRI-safe foam wedge to place participants in the head-down tilt position. We acquired it and have conducted pilot testing to ensure that it does not create signal distortion in the MRI environment. We also confirmed that it is tolerable for participants to remain head-down tilt on the wedge for the duration of the testing day (approximately eight hours). We are currently in process of recruiting participants and collecting data in the head-down tilt position with and without elevated CO_2.
Bibliography Type:	Description: (Last Updated: 01/24/2024)