Fiscal Year:	FY 2019	**Task Last Updated:**	FY 02/08/2022
PI Name:	Fuller, Charles A. Ph.D.		
Project Title:	Head-Down Tilt As a Model for Intracranial and Intraocular Pressures, and Retinal Changes during Spaceflight		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
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		
PI Email:	cafuller@ucdavis.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	530-752-2979
Organization Name:	University of California, Davis		
PI Address 1:	Section of Neurobiology, Physiology & Behavior		
PI Address 2:	One Shields Avenue, 196 Briggs Hall		
PI Web Page:			
City:	Davis	**State:**	CA
Zip Code:	95616-5270	**Congressional District:**	3
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	02/01/2013	**End Date:**	03/31/2019
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 3/31/2019 per NSSC information (Ed., 1/7/19) NOTE: End date changed to 12/30/2018 per H. Paul/JSC HRP (Ed., 12/22/17) NOTE: End date changed to 12/31/2017 per NSSC information (Ed., 4/20/2016) NOTE: End date will be 6/30/2017 per R. Brady/JSC HRP (Ed., 11/3/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Hoban-Higgins, Tana Ph.D. (University of California, Davis) Murphy, Christopher Ph.D. (University of California, Davis) Robinson, Edward Ph.D. (University of California, Davis) Gompf, Heinrich Ph.D. (University of California Davis)		
Grant/Contract No.:	NNX13AD94G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	This ground-based program is intended to address the etiology of visual system structural and functional changes observed in astronauts during both inflight and postflight periods. Using the well-documented rat hindlimb suspension (HLS) model, functionally equivalent to human head-down bedrest, we will examine the relationship between cephalic fluid shifts resulting from long-duration G-unloading and the regulation of intracranial and intraocular pressures, as well as the effects these same cephalic fluid shifts have on visual system structure and function. Animals will be chronically instrumented with biotelemetry to continuously measure intracranial pressure. Additionally, regular intraocular pressure measurements will be made by tonometry during long-term exposure to cephalic fluid shifts induced by suspension. MRI images visualizing the visual system morphology will also be collected from HLS and control animals at regular intervals. Retinal morphology and ultrastructure will be examined at specified intervals both during HLS and post-HLS recovery by both ophthalmic examinations and tissue histology evaluation. This program will utilize both male and female subjects in order to examine possible gender differences in these responses. We will also examine the possible contributory factors of aging and elevated atmospheric carbon dioxide (hypercapnia) on to these responses of the visual system. Further, in addition to mimicking the effects of long duration exposure to microgravity through the use of the HLS model, we will examine the responses of our measured outcomes during long-term recovery in the post-HLS period. Collectively, these data will help allow us to develop a model to both understand and predict the etiology of changes in visual structure and function in astronauts exposed to the microgravity of spaceflight and during postflight recovery. In summary, our ultimate goal is to develop a translational mammalian model by which the data generated using this model can facilitate the development of countermeasures to alleviate any visual system decrements arising from exposure to the microgravity spaceflight environment.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This research has the potential to help further our understanding of chronic cephalic fluid shifts on neurological and ophthalmic health. No innovative technologies have been developed during this period.
Task Progress:	FINAL REPORTING [Ed. note February 2022; Compiled from Final Technical Report received November 2021] Hind-limb unloading (HLU) has been an established technique modeling microgravity for over 40 years. Recent observations showed that astronauts on long-duration spaceflight missions develop visual defects. This program examined whether these could be duplicated in the rat HLS (hindlimb suspension) model. Also of interest were any effects on intracranial pressure and their possible connection to the observed visual changes. Overall, the project proved successful; within limits, the rat continues to be a useful translational animal model for spaceflight research. The use of the rat allows continuous recording of physiological measurements using indwelling technology leading to the collection of large amounts of data from freely behaving subjects. In summary, the rats evidenced • some, but not all, of the visual changes seen in long-duration astronauts. • a small, but sustained increase in intracranial pressure (ICP) that appears to be time of day dependent in that differences between HLS and baseline ICP were greater during the animals' rest period, leading to a decrease in the circadian rhythm amplitude of ICP. • alterations in circadian timing. The reduction in the amplitude of the rhythm of ICP is consistent with results from the rhythms of Tb and EEG. Changes were also seen in the circadian mean and phasing of these rhythms. This type of circadian dysfunction is known to occur during spaceflight, and can lead to overall physiological and behavioral deficits. There was a gender and also an age factor in the responses. Comparison of the responses between Young male and Young female rats showed that the effects were much smaller in female rats. Comparison between Old and Young male rats revealed larger effects in the older animals. These observations are of interest because the increase in ICP during the rest period may also have led to a decreased turnover of CSF (cerebrospinal fluid) and/or other CNS (central nervous sytem) fluid exchanges. Such decreases over extended periods of time may have resulted in CNS inflammatory responses. DECEMBER 2018 ANNUAL REPORT: During this period of performance, the research team has concluded the collection of data from all cohorts. These included young males, young females (to examine possible gender differences), older males (to examine possible age effects) and, finally, older males exposed to a hypercapnic environment similar to that present on International Space Station (ISS). Older males were chosen for hypercapnic exposure as this group presented the most significant response to HLS. Analysis of the data from this group will allow us to determine if there is a role of increased CO_2 exposure in the etiology of these visual changes. Intracranial pressure, body temperature, and EEG were recorded via biotelemetry. Biotelemetry data have been collected from the young male, young female, older male, and older male hypercapnic cohorts. Data analysis is underway. Additional measurements of visual system function including complete ophthalmic clinical exams and measurement of intraocular pressure by tonometry have been performed. The retinal imaging performed during this program included both fundus imaging with fluorescein angiography and optical coherence tomography (OCT). The tissue histology studies that will complement these data are underway.
Bibliography Type:	Description: (Last Updated: 12/07/2018)
Abstracts for Journals and Proceedings	Fuller CA, Robinson EL, McElroy AL, Gompf H, Hoban-Higgins TM. "Head-down tilt as a model for intracranial pressure changes during spaceflight." Presented at the Neuroscience 2018, San Diego, CA, November 3-7, 2018. Neuroscience 2018, San Diego, CA, November 3-7, 2018. Abstract 318.08. , Nov-2018

Abstracts for Journals and Proceedings	Fuller CA, Robinson EL, Hoban-Higgins TM, Fuller PM. "Sleep and circadian homeostasis during long duration cephalic fluid shifts." Presented at Neuroscience 2018, San Diego, CA, November 3-7, 2018. Neuroscience 2018, San Diego, CA, November 3-7, 2018. Abstract 779.15. , Nov-2018
Abstracts for Journals and Proceedings	Fuller CA, Hoban-Higgins TM, Gompf H, Robinson EL. "Head-down tilt as a model for intracranial and intraocular pressures, and retinal changes during spaceflight." Presented at 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. , Jan-2018