Fiscal Year:	FY 2017	**Task Last Updated:**	FY 09/06/2017
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:**	12/31/2017
No. of Post Docs:	0	**No. of PhD Degrees:**	3
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:	Allcorn, Aaron	**Contact Phone:**	281.244.8402
Contact Email:	aaron.j.allcorn@nasa.gov		
Flight Program:			
Flight Assignment:	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 (University of California, Davis) Murphy, Christopher (University of California, Davis) Robinson, Edward (University of California, Davis) Gompf, Heinrich (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. Changes in retinal/visual function will be regularly assessed electrophysiologically by measuring visual evoked potentials and electroretinograms. 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:	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 are examining 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. A proposal examining additional histological and genetic effects was integrated into our protocol, adding these measures. Animals are chronically instrumented with biotelemetry to continuously measure intracranial pressure. Additionally, regular intraocular pressure measurements are made by tonometry during long-term exposure to cephalic fluid shifts induced by suspension. MRI images visualizing the visual system morphology have also been collected from HLS and control animals at regular intervals. Retinal morphology and ultrastructure are being examined at specified intervals both during HLS and post-HLS recovery by both ophthalmic examinations and tissue histology evaluation. This program utilizes both male and female subjects in order to examine possible gender differences in these responses. We are examining 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 are examining 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 the development of a translational mammalian model; the data generated using this model would be used to facilitate the development of countermeasures to alleviate any visual system decrements arising from exposure to the microgravity spaceflight environment. During this period of performance, the research team has expanded the study of cohorts of young males, young females (to examine possible gender differences) and older males (to examine possible age effects). The older male cohort currently presents the most significant response to HLS and will be studied in a hypercapnic environment (similar to that experienced on the International Space Station--ISS). This will allow us to determine if there is a role of increased CO2 exposure in the etiology of these visual changes. We are utilizing biotelemetry to record intracranial pressure. We have reviewed and tested three biotelemetry systems, all of which claim to allow continuous recording of biological presssure. We have extensively revised the data acquisition software, which has been necessary to both improve the ease and accuracy of data collection, as well as to tailor the system to meet the needs of this research program. Biotelemetry data have been collected from both male cohorts and we are currently expanding this to the female cohort. Additional measurements of visual system function include complete ophthalmic clinical exams, measurement of intraocular pressure by tonometry, and, ultimately, tissue histology. The retinal imaging performed during this program include both fundus imaging with fluorescein angiography and OCT. This program is aimed at determining if long-term cephalic fluid shift can cause the effects seen on visual system structure and function during and after long-duration spaceflight. As such, animals are exposed to HDT (head down tilt) for a longer period of time than is utilized in most studies. We are working with the Biospecimen Sharing Program at Ames Research Center to ensure that tissues not utilized in our analyses are available for other researchers, thus increasing the science yielded by this program.
Bibliography Type:	Description: (Last Updated: 12/07/2018)
Abstracts for Journals and Proceedings	Gompf H, Hoban-Higgins TM, Robinson EL, Theriot CA, Murphy CJ, Zanello SB, Fuller CA. "Head-down tilt as a model for intracranial and intraocular pressures, and retinal changes during spaceflight." Presented at the 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. , Jan-2017

Abstracts for Journals and Proceedings	Fuller CA, Gompf H, Robinson EL, Hoban-Higgin TM. "Head-down Tilt as a Model for Intracranial Hypertension during Spaceflight." Presented at Experimental Biology 2016, San Diego, CA, April 2-6, 2016. FASEB Journal. 2016 Apr;30(1 Suppl):762.9. See also http://www.fasebj.org/content/30/1_Supplement.toc for searching. , Apr-2016