Fiscal Year:	FY 2015	**Task Last Updated:**	FY 01/21/2015
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		
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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:**	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:**	
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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 addresses 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 histological and genetic effects was integrated into our protocol, adding these measures. The use of biotelemetry allows continuous measurement of intracranial pressure from freely moving animals. Additionally, regular intraocular pressure measurements are made by tonometry. MRI images visualizing visual system morphology will also be 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. Changes in retinal/visual function will be regularly assessed electrophysiologically by measuring visual evoked potentials and electroretinograms. This program utilizes both male and female subjects in order to examine possible gender differences in these responses. We are also examining the possible contributory factors of aging and elevated atmospheric carbon dioxide (hypercapnia) on 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 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 that can facilitate the development of countermeasures to alleviate any visual system decrements arising from exposure to the microgravity spaceflight environment. We have successfully completed a 90-day HLS study and a 90-day HLS with 28 days of recovery study in young males as well as all the shorter-term HLS studies (7, 14, and 28 days) on both young males and young females. Fundus imaging, fluorescein angiography, and OCT were completed from HLS and age-matched control animals at baseline and at the end of HLS. Additionally, complete ophthalmic exams and measurement of intraocular pressure using tonometry were performed. The integration of the Zanello proposal into this program added histological and genetic examination of the eye to this study; these tissues were harvested from control and HLS animals. 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 HLS for a longer period of time than is utilized in most studies. At the completion of each HLS study, tissues not utilized in our analyses were harvested and preserved by the Biospecimen Sharing Program at Ames Research Center; they will be available for other researchers, thus increasing the science yielded by this program.
Bibliography Type:	Description: (Last Updated: 12/07/2018)