Fiscal Year:	FY 2014	**Task Last Updated:**	FY 02/15/2014
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:**	01/31/2016
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
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Flight Program:			
Flight Assignment:			
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)		
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:	2013 ANNUAL PROGRESS REPORT. NASA Grant NNX13AD94G 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. A proposal examining additional histological and genetic effects was integrated into our protocol, adding these measures. 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. During this initial period of performance, the research team has been hired and trained, major equipment purchased, and facilities set-up. We have put into place the core techniques and capabilities that will be necessary for the successful execution and completion of this program. This has included establishing a flow for the employment of the tail suspension model using the pigmented Long-Evans rat. While our initial subjects will be young males, we will also study cohorts of young females (to examine possible gender differences) and older males (to examine possible age effects). The cohort that presents the most significant response to HLS will be studied in a hypercapnic environment (similar to that experienced on the 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. This has required working with the vendor to develop a custom redesign of the transmitters. The successful redesign is currently being evaluated and confirmed. We have taken this opportunity to refine our surgical implant technique. Additionally, 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. The biotelemetry system will also be used to record evoked visual potentials. Having in situ leads will ensure the accuracy and reproducibility of measurements taken over the entire study (up to 180 days). Additional measurements of visual system function will include complete ophthalmic clinical exams, measurement of intraocular pressure by tonometry, and, ultimately, tissue histology. The retinal imaging that will be performed during this program includes both fundus imaging with fluorescein angiography and OCT. The manufacturers of the equipment used to provide these images have both provided training sessions for team personnel. Additional practice sessions have been continued to ensure successful capture of images and a second training session has been scheduled with the OCT manufacturer. 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 will be exposed to HDT 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 will be available for other researchers, thus increasing the science yielded by this program.
Bibliography Type:	Description: (Last Updated: 10/09/2024)