Fiscal Year:	FY 2013	**Task Last Updated:**	FY 08/12/2013
PI Name:	Seidler, Rachael D. Ph.D.		
Project Title:	Bed Rest as a Spaceflight Analog to Study Neurocognitive Changes: Extent, Longevity, and Neural Bases		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Sensorimotor Adaptation Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **BHP**:Behavioral Health & Performance (archival in 2017)		
Human Research Program Risks:	(1) **HSIA**:Risk of Adverse Outcomes Due to Inadequate Human Systems Integration Architecture (2) **Sensorimotor**:Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	rachaelseidler@ufl.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	352-294-1722
Organization Name:	University of Florida		
PI Address 1:	Applied Physiology & Kinesiology		
PI Address 2:	FLG 142, P.O. Box 118205		
PI Web Page:			
City:	Gainesville	**State:**	FL
Zip Code:	32611-8205	**Congressional District:**	3
Comments:	NOTE: PI moved to University of Florida in July 2017; previous affiliation was University of Michigan.		
Project Type:	GROUND	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	08/01/2012	**End Date:**	07/31/2015
No. of Post Docs:	2	**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:	2	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Mulavara, Ajitkumar (Universities Space Research Association) Wood, Scott (NASA Johnson Space Center)		
Grant/Contract No.:	NCC 9-58-SA02802		
Performance Goal No.:			
Performance Goal Text:			

Task Description:

In this project, our objective is to perform structural and functional brain imaging to identify changes in neurocognitive function due to 70 days of head down tilt bed rest. Our central hypotheses are that measures of brain structure, function, and network integrity will change from pre to post bed rest to a greater extent than that observed in matched control subjects, but to a lesser extent than what we will observe in crewmembers under our NASA funded flight study NNX11AR02G. Our Aims are to: Aim 1- Identify changes in brain structure, function, and network integrity as a function of 60 days head down tilt bed rest and characterize their time course: We will acquire brain structural and functional images at two time points pre, two time points during, and three time points post bed rest in 13 individuals and 13 age and gender-matched controls. We hypothesize that bed rest participants will exhibit changes from pre to post the intervention that are significantly greater than those seen in control participants across the same time period. Scans conducted during and following bed rest will characterize the time course of changes and recovery. Aim 2- Specify relationships between structural and functional brain changes and performance and characterize their time course: We will administer a broad ranging battery of sensory, motor, and cognitive assessments at the time points described for Aim 1. We hypothesize that bed rest participants will exhibit pre- to post-intervention decrements in sensorimotor performance as we have shown in our past work, which will correlate with the neural changes identified under Aim 1. Additionally, for some measures and time points, we expect that there will be no performance effects despite alterations in brain structure and function due to compensatory brain processes that will be identifiable with neuroimaging approaches. To date we have five participants enrolled in the bed rest arm of this study; three of these have completed all seven of the test sessions. To summarize, the measures we acquire can be categorized into behavioral assessments and brain imaging assessments. The behavioral tests measured outside of the scanner include: card and cube rotation tests of spatial working memory; digit symbol substitution test of processing speed; rod and frame test of visual bias; pegboard test of bimanual coordination; sensory organization test of vestibular-mediated balance; functional mobility test of obstacle course navigation; vestibular evoked myogenic potential to assess vestibular function. The neuroimaging tests of brain structure and function include: structural MRI to measure regional brain volumes and relative gray matter density; diffusion weighted scans (often referred to as DTI) to measure structural connectivity integrity; resting state functional MRI to measure functional connectivity integrity; functional MRI to measure brain networks engaged during the performance of various tasks. The latter tasks include imaging of the functional vestibular cortex; brain regions engaged during single and dual tasking of cognitive and motor behaviors; brain regions engaged during adaptation of pointing movements to perturbed visual feedback; brain regions engaged for spatial working memory, and for foot tapping.

We have made great progress during our first year of support. Our stand alone protocol received IRB approval from the University of Michigan and NASA and was then wrapped into the bed rest Flight Analog Project UTMB IRB protocol. We invested an extensive amount of time and effort into assembling, integrating, and troubleshooting our hardware and software with the bed rest facility resources. This included developing and setting up unique hardware and software to enable functional MRI testing at UTMB Galveston, which previously had only acquired structural and clinical MRI scans. We also ran numerous pilot tests to ensure that we could collect our data within the time allotted and to verify that we were getting clean and reliable metrics. We have made one methodological change as a result of our pilot testing. We initially were stimulating the functional vestibular cortex via auditory clicks of a particular sound decibel. This moves fluid in the inner ear, stimulating vestibular receptor hair cells. The clicks, although within the OSHA safety standards, are quite loud and difficult for some subjects to tolerate. Moreover, the brain activity associated with this mode of stimulation was rather variable across test sessions for the initial subjects. As a result, we have extensively piloted and are now implementing vestibular stimulation with a head tapper device. This pneumatically driven device taps the head at a very low force level. The resulting vibration is transmitted via bone conduction to the vestibular system. Thus far, the brain activation patterns associated with this mode of stimulation appear to have better reliability. Over the next year we will acquire data from additional subjects and continue analyses of our behavioral and MRI data, with a particular emphasis on addressing whether / how the two types of metrics change together as a function of bed rest. Moreover, we will soon be launching our longitudinal control study.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

While the corpus of research on adaptive plasticity associated with behavioral training has greatly expanded over the past two decades, research on maladaptive plasticity occurring with immobilization is scant. A greater understanding of brain structural and functional changes, and the concomitant behavioral effects, resulting from limb disuse and unloading has implications for rehabilitation of those immobilized by injury, disease, or even simple inactivity. In addition, we have been working with Engineering Acoustics Incorporated to have them modify a device that they manufacture for vestibular testing to render it MRI compatible. There are few methods available for stimulating the vestibular cortex that are amenable to functional imaging. For example, one approach involves caloric stimulation via delivery of cool water to the inner ear. This is messy to work with in the MRI environment and can also be quite painful for subjects. We initially developed a system capable of delivering precisely calibrated sound to the inner ear which also results in vestibular stimulation. This is somewhat painful for participants as well. The route that we decided to go with involves applying a very low force tap to the head. Vibration is transmitted via bone conduction to the vestibular system, resulting in depolarization of the hair cell receptors. The ease of this approach is increasing its clinical popularity, and numerous experimental and modeling studies have been conducted recently to verify how the signal is transmitted in the vestibular system. We are the first group to evaluate this method in the functional MRI environment. We are gearing up to conduct a validation study of this type of stimulation at the University of Michigan as an offshoot of our NSBRI project. Being able to image the functional vestibular cortex in human subjects will be important for better understanding of deficits faced by vestibular patients. Moreover, it can be used as a neural marker of balance training effects. We are excited to further develop this line of work.

To date we have five participants enrolled in the bed rest arm of this study; three of these have completed all seven of the test sessions. To summarize, the measures we acquire can be categorized into behavioral assessments and brain imaging assessments. The behavioral tests measured outside of the scanner include: card and cube rotation tests of spatial working memory; digit symbol substitution test of processing speed; rod and frame test of visual bias; pegboard test of bimanual coordination; sensory organization test of vestibular-mediated balance; functional mobility test of obstacle course navigation; vestibular evoked myogenic potential to assess vestibular function. The neuroimaging tests of brain structure and function include: structural MRI to measure regional brain volumes and relative gray matter density; diffusion weighted scans (often referred to as DTI) to measure structural connectivity integrity; resting state functional MRI to measure functional connectivity integrity; functional MRI to measure brain networks engaged during the performance of various tasks. The latter tasks include imaging of the functional vestibular cortex; brain regions engaged

	during single and dual tasking of cognitive and motor behaviors; brain regions engaged during adaptation of pointing movements to perturbed visual feedback; brain regions engaged for spatial working memory, and for foot tapping.
Task Progress:	We have made great progress during our first year of support. Our stand alone protocol received IRB approval from the University of Michigan and NASA and was then wrapped into the bed rest Flight Analog Project UTMB IRB protocol. We invested an extensive amount of time and effort into assembling, integrating, and troubleshooting our hardware and software with the bed rest facility resources. This included developing and setting up unique hardware and software to enable functional MRI testing at UTMB Galveston, which previously had only acquired structural and clinical MRI scans. We also ran numerous pilot tests to ensure that we could collect our data within the time allotted and to verify that we were getting clean and reliable metrics. We have streamlined our analytical approaches to include assessments of test retest reliability across the first two pre test time points as well as repeated measures approaches for evaluating the impact of bed rest. Thus far we have observed high intraclass correlations for our pre test metrics across five participants tested, and robust changes in behavioral and brain functional metrics with bed rest (n = 3 completed). Our analyses of brain structure have not yielded any effects of bed rest; however, data from only two participants have been analyzed thus far, and we also had some challenges with acquiring MRI data using consistent parameters. This issue has been resolved for testing moving forward.
Bibliography Type:	Description: (Last Updated: 01/24/2024)