Fiscal Year:	FY 2016	Task Last Updated:	FY 05/18/2016
PI Name:	Seidler, Rachael D. Ph.D.		
Project Title:	Bed Rest as a Spaceflight Analog to Study Net	rocognitive Changes: Extent, Lor	ngevity, and Neural Bases
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline Element/Subdiscipline:	NSBRISensorimotor Adaptation Team		
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) BHP:Behavioral Health & Performance (ar	chival in 2017)	
Human Research Program Risks:	(1) <b>HSIA</b> :Risk of Adverse Outcomes Due to Ir (2) <b>Sensorimotor</b> :Risk of Altered Sensorimotor		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	32611-8205	<b>Congressional District:</b>	3
Comments:	NOTE: PI moved to University of Florida in Ju	ıly 2017; previous affiliation was	University of Michigan.
Project Type:	GROUND	Solicitation / Funding Source:	2011 Crew Health NNJ11ZSA002NA
Start Date:	08/01/2012	End Date:	12/31/2015
No. of Post Docs:	2	No. of PhD Degrees:	0
No. of PhD Candidates:	1	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:	NSBRI
Contact Monitor:		<b>Contact Phone:</b>	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 12/31/2015 per NS	BRI (Ed., 7/7/15)	
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Mulavara, Ajitkumar (Universities Space Res Wood, Scott (Azusa Pacific University)	search Association )	
Grant/Contract No.:	NCC 9-58-SA02802		
Performance Goal No.:			
Performance Goal Text:			

	In this project, our objective was 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 were that measures of brain structure, function, and network integrity would 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 were to:	
Task Description:	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 acquired brain structural and functional images at two time points pre-, two time points during, and three time points post- bed rest in 18 individuals and 16 controls who were tested at four time points but otherwise went around their daily lives. We hypothesized that bed rest participants would exhibit changes from pre- to post- the intervention that were significantly greater than those seen in control participants across the same time period. Scans conducted during and following bed rest characterized 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 administered a broad ranging battery of sensory, motor, and cognitive assessments at the time points described for Aim 1. We hypothesized that bed rest participants would exhibit pre- to post-intervention decrements in sensorimotor performance as we have shown in our past work, which we expected would correlate with the neural changes identified under Aim 1. Additionally, for some measures and time points, we expected that there might be no performance effects despite alterations in brain structure and function due to compensatory brain processes, which would be identifiable with neuroimaging approaches. The measures we acquired can be categorized into behavioral assessments and brain imaging assessments. The behavioral tests measured outside of the scanner included: 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 and vestibular evoked myogenic potential to assess vestibular function.	
	The neuroimaging tests of brain structure and function included: 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, and functional MRI to measure brain networks engaged during the performance of various tasks. The latter tasks included: 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, and brain regions engaged for spatial working memory and foot tapping.	
	We have nearly completed data analyses and manuscript preparation. We have one paper published, one under second review, and several more that are nearly ready to submit. We found robust changes with bed rest in balance and functional mobility, replicating other studies that have previously reported sensorimotor declines. We also observed changes in brain gray matter volume, functional connectivity, and task based activation that were specific to the time period of the bed rest intervention, many of which were associated with the magnitude of behavioral change. Some metrics exhibited complete recovery by our last time point 12 days post bed rest, while others were trending towards recovery but had not yet returned to baseline levels.	
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. We also have been transferring our new methods for imaging the functional vestibular cortex to the University of Michigan. We will leverage the experience that we attained through development and validation of these methods to conduct some (separately funded) studies related to aging, balance, and vestibular function.	
Task Progress:	We are completing our analyses of bed rest induced changes in brain activity during sensorimotor adaptation, spatial working memory, foot movement, and vestibular stimulation tasks. These analyses are nearly complete and we are drafting manuscripts. Publication in revision: Kopplemans V, Bloomberg JJ, De Dios YE, Wood SJ, Reuter-Lorenz PA, Kofman IS, Riascos R, Mulavara AP, & Seidler R., "Brain plasticity and sensorimotor deterioration as a function of 70 days head down tilt bed rest." [Ed. note August 2017now published August 2017 in PLoS One; see Bibliography section]	
Bibliography Type:	Description: (Last Updated: 01/24/2024)	
Articles in Peer-reviewed Journals	Koppelmans V, Mulavara AP, Yuan P, Cassady KE, Cooke KA, Wood SJ, Reuter-Lorenz PA, De Dios YE, Stepanyan V, Szecsy DL, Gadd NE, Kofman I, Scott JM, Downs ME, Bloomberg JJ, Ploutz-Snyder L, Seidler RD. "Exercise as potential countermeasure for the effects of 70 days of bed rest on cognitive and sensorimotor performance." Front Syst Neurosci. 2015 Sep 3;9:121. eCollection 2015. <u>http://dx.doi.org/10.3389/fnsys.2015.00121</u> ; PubMed <u>PMID: 26388746</u> ; PubMed Central <u>PMCID: PMC4558429</u> , Sep-2015	
Articles in Peer-reviewed Journals	Yuan P, Koppelmans V, Reuter-Lorenz P, De Dios Y, Gadd N, Riascos R, Kofman I, Bloomberg J, Mulavara A, Seidler RD. "Change of cortical foot activation following 70 days of head down bed rest." J Neurophysiol. 2018 Jun 1;119(6):2145-52. Epub 2018 Feb 28. <u>https://doi.org/10.1152/jn.00693.2017</u> ; PubMed <u>PMID: 29488843</u> ; PubMed Central <u>PMCID: PMC6032127</u> , Jun-2018	
Articles in Peer-reviewed Journals	Koppelmans V, Bloomberg JJ, De Dios YE, Wood SJ, Reuter-Lorenz PA, Kofman IS, Riascos R, Mulavara AP, Seidler RD. "Brain plasticity and sensorimotor deterioration as a function of 70 days head down tilt bed rest." PLoS One. 2017 Aug 2;12(8):e0182236. eCollection 2017. <u>https://doi.org/10.1371/journal.pone.0182236</u> ; PubMed <u>PMID: 28767698</u> ; PubMed Central <u>PMCID: PMC5540603</u> , Aug-2017	

Articles in Peer-reviewed Journals	Koppelmans V, Scott JM, Downs ME, Cassady KE, Yuan P, Pasternak O, Wood SJ, De Dios YE, Gadd NE, Kofman I, Riascos R, Reuter-Lorenz PA, Bloomberg JJ, Mulavara AP, Ploutz-Snyder LL, Seidler RD. "Exercise effects on bed rest-induced brain changes." PLoS One. 2018 Oct 11;13(10):e0205515. <u>https://doi.org/10.1371/journal.pone.0205515</u> ; PubMed PMID: 30308004; PubMed Central PMCID: PMC6181401, Oct-2018
Articles in Peer-reviewed Journals	Hupfeld KE, Lee JK, Gadd NE, Kofman IS, De Dios YE, Bloomberg JJ, Mulavara AP, Seidler RD. "Neural correlates of vestibular processing during a spaceflight analog with elevated carbon dioxide (CO2): A pilot study." Front Syst Neurosci. 2020 Jan 10;13:80. <u>https://doi.org/10.3389/fnsys.2019.00080</u> ; PubMed <u>PMID: 31998084</u> ; PubMed Central <u>PMCID: PMC6965349</u> , Jan-2020
Articles in Peer-reviewed Journals	Lee JK, De Dios Y, Kofman I, Mulavara AP, Bloomberg JJ, Seidler RD. "Head down tilt bed rest plus elevated CO2 as a spaceflight analog: Effects on cognitive and sensorimotor performance." Front Hum Neurosci. 2019 Oct 17;13:355. https://doi.org/10.3389/fnhum.2019.00355; PubMed PMID: 31680909; PubMed Central PMCID: PMC6811492, Oct-2019
Articles in Peer-reviewed Journals	Noohi F, Kinnaird C, De Dios Y, Kofman I, Wood SJ, Bloomberg JJ, Mulavara AP, Sienko KH, Polk TA, Seidler RD. "Deactivation of somatosensory and visual cortices during vestibular stimulation is associated with older age and poorer balance." PLoS One. 2019 Sep 13;14(9):e0221954. <u>https://doi.org/10.1371/journal.pone.0221954</u> ; PubMed <u>PMID:</u> <u>31513630</u> ; PubMed Central <u>PMCID: PMC6742389</u> , Sep-2019
Articles in Peer-reviewed Journals	Koppelmans V, Hirsiger S, Mérillat S, Jäncke L, Seidler RD. "Cerebellar gray and white matter volume and their relation with age and manual motor performance in healthy older adults." Hum Brain Mapp. 2015 Jun;36(6):2352-63. Epub 2015 Feb 19. <u>http://dx.doi.org/10.1002/hbm.22775</u> ; PubMed <u>PMID: 25704867</u> , Jun-2015
Articles in Peer-reviewed Journals	Noohi F, Kinnaird C, De Dios Y, Kofman IS, Wood S, Bloomberg J, Mulavara A, Seidler R. "Functional brain activation in response to a clinical vestibular test correlates with balance." Frontiers in Systems Neuroscience.2017 Mar 10;11:11. eCollection 2017. <u>https://doi.org/10.3389/fnsys.2017.00011</u> ; PubMed <u>PMID: 28344549</u> ; PubMed Central <u>PMCID: PMC5344901</u> , Mar-2017
Articles in Peer-reviewed Journals	Salazar AP, Hupfeld KE, Lee JK, Beltran NE, Kofman IS, De Dios YE, Mulder E, Bloomberg JJ, Mulavara AP, Seidler RD. "Neural working memory changes during a spaceflight analog with elevated carbon dioxide: A pilot study. " Front Syst Neurosci. 2020 Jul 28;14:48. <u>https://doi.org/10.3389/fnsys.2020.00048</u> ; <u>PMID: 32848641</u> ; <u>PMCID: PMC7399639</u> , Jul-2020
Articles in Peer-reviewed Journals	Noohi F, Kinnaird C, De Dios Y, Kofman IS, Wood SJ, Bloomberg J, Mulavara A, Sienko KH, Polk TA, Seidler RD. "Age differences in vestibular brain connectivity are associated with balance performance." Front Aging Neurosci. 2020 Nov 16;12:566331. <u>https://doi.org/10.3389/fnagi.2020.566331</u> ; <u>PMID: 33312123</u> ; <u>PMCID: PMC7703342</u> , Nov-2020
Articles in Peer-reviewed Journals	Lee JK, Koppelmans V, Pasternak O, Beltran NE, Kofman IS, De Dios YE, Mulder ER, Mulavara AP, Bloomberg JJ, Seidler RD. "Effects of spaceflight stressors on brain volume, microstructure, and intracranial fluid distribution." Cereb Cortex Commun. 2021 Mar 30;2(2):tgab022. <u>https://doi.org/10.1093/texcom/tgab022</u> ; <u>PMID: 34296167</u> ; <u>PMCID: PMC8152913</u> , Mar-2021