Fiscal Year:	FY 2016	**Task Last Updated:**	FY 12/04/2015
PI Name:	Koppelmans, Vincent Ph.D.		
Project Title:	Exercise Effects on Central Nervous System Function and Structure in Bed Rest		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Sensorimotor Adaptation Team		
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Zip Code:	48109-2208	**Congressional District:**	12
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POSTDOCTORAL FELLOWSHIP
Original aims/objectives

The goal of the study is to determine whether exercise may serve as a preventive measure and/or countermeasure to the adverse effects of microgravity on the central nervous system using a microgravity analog design. This overarching goal can be subdivided into four sub-aims: 1) to investigate exercise as a preventive and/or countermeasure to mitigate the effects of microgravity on motor behavior and cognition; 2) to investigate exercise as a preventive and/or countermeasure to mitigate the effects of microgravity on central nervous system (CNS) plasticity and function objectified with structural and functional neuroimaging techniques; 3) to investigate the potentially mediating role of exercise on the relationship between changes in behavior and CNS plasticity and function; and 4) to identify if physical

Task Description:	health markers on the single subject level can predict behavioral adaptability to a microgravity environment. Key findings Six degrees head down tilt bed rest adversely affected functional mobility of both bed rest exercise subjects and bed rest control subjects in relation to their pre bed rest performance, as well as in comparison with a normative control group. Performance of both bed rest groups recovered post bed rest, with the exercise subjects recovering faster. Bed rest did not affect cognitive performance. Furthermore, our T1 MRI (magnetic resonance imaging) data showed that head down bed rest resulted in decreases in gray matter volume in the frontal regions of the brain and increases in posterior parietal regions. Analyses uncorrected for multiple comparisons showed significant differential effects of bed rest on exercise subjects relative to bed rest control subjects in the bilateral primary motor cortex and cerebellar regions. Relative to pre bed rest, exercise subjects had smaller increases in gray matter in these brain regions that were visible after 50 days in bed rest. Impact of key findings on hypotheses, technology requirements, objectives, and specific aims of the original proposal Our findings support our hypothesis that exercise would mitigate bed rest-induced changes in sensorimotor behavior and that may be related to differential changes in brain structure. Also in line with our hypothesis we found associations between brain structural and sensorimotor behavior changes. Although we had hypothesized cognitive deterioration as a result of bed rest, no such effects were observed. Thus, further objectives of our study will focus more on relationships between sensorimotor outcome measures, our remaining MRI measures, and physical fitness measures. Proposed research plan for the coming year In the next year we will further investigate the effects of exercise in bed rest on microstructural aspects of the brain on the basis of our diffusion weighted imaging data. We are currently establishing a collaboration that allows us to use an advanced technique that can distinguish between different causes for changes in microstructural integrity. Furthermore, we aim to investigate effects of exercise in bed rest on resting state functional connectivity on the basis of fMRI data. Finally, we plan to explore the association between measures of physical fitness (e.g., resting state metabolism and VO2 max) and cognitive, sensorimotor performance, and brain structural and functional outcome measures over the course of bed rest.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our results are relevant for Earth because results of our microgravity bed rest analog intervention may also be applicable to subjects in regular long-duration bed rest or long-duration unloading. It is not uncommon that elderly inhabitants of nursing homes and immobile patients spend long parts of the day in bed and do not participate in regular exercise. In our study long-duration bed rest resulted in wide-spread changes in brain gray matter volume that was related to balance performance. Our uncorrected results showed effects of exercise in the supine position on bed rest induced gray matter changes. Furthermore, exercise resulted in faster recovery of bed rest induced balance problems. The effects of head down tilt bed rest on sensorimotor performance and brain structure might also occur in disabled elderly and immobile patients, for example, post surgery. Our results suggest that exercise could also be an effective countermeasure for the potential sensorimotor deterioration that could take place in long-duration bed rest here on Earth.
Task Progress:	For this project, I am analyzing data that was collected in the framework of previously conducted bed rest studies. To date, we have analyzed cognitive and sensorimotor performance data as well as T1-weighted imaging data and diffusion tensor imaging data. We have developed longitudinal processing pipelines for our MRI data and analysis models to optimally detect potential mediating effects of exercise on the effects of head down bed rest on cognitive functioning, sensorimotor performance, and various brain structural outcome measures. We recently tested a novel algorithm on our diffusion tensor imaging data that allows us to distinguish between different mechanisms of microstructural brain changes that could result from head down bed rest or exercise in bed rest. The pilot analysis with this algorithm was successful and we are now ready to apply it to our full dataset. To further explain any effects of bed rest and exercise we are now also leveraging data from a normative control study. For this study a group of NASA ground personnel completed the same neurocognitive and sensorimotor measures and MRI protocol as our bed rest subjects. These assessments were repeated three times over a time course that matches up with the time course of our bed rest measurements. This allows us to compare the effects of bed rest and exercise in supine position during bed rest to the time course of these outcome measures in normative healthy control subjects.
Bibliography Type:	Description: (Last Updated: 05/16/2019)
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." Frontiers in Systems Neuroscience. 2015 Sep 3;9:121. eCollection 2015. http://dx.doi.org/10.3389/fnsys.2015.00121 ; PubMed PMID: 26388746; PubMed Central PMCID: PMC4558429 , Sep-2015