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Project Title:	Exercise Effects on Central Nervous System Function and Structure in Bed Rest		
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Contact Monitor:		**Contact Phone:**	
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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 (CNS) 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 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 health markers on the single

Task Description:	subject level can predict behavioral adaptability to a microgravity environment. Key findings YEAR 2: Long duration bed rest results in water redistribution in areas that are largely overlapping with those areas in which we observed gray matter changes. Gray matter decreases co-occurred with water increases and vice versa. This indicates that in our study the gray matter changes observed on T1 MRI largely reflects water redistribution. No significant differences were observed in changes in focal cerebral water contact or white matter microstructure between the bed rest exercise group and the bed rest control group, neither during bed rest or during the post bed rest recovery period. Bed rest was associated with functional connectivity changes between several sensorimotor and vestibular brain regions. We observed significant group by time interaction effects in changes in functional connectivity during bed rest and during the period post bed rest. During bed rest there was an increase in connectivity between the right premotor cortex and a large cluster in the superior frontal gyrus in bed rest exercise subjects while at the same time bed rest control subjects showed a decrease in functional connectivity between these regions. In addition, post bed rest there was an increase in connectivity between the right posterior parietal cortex and a cluster in the left postcentral gyrus in bed rest exercise subjects while at the same time bed rest control subjects showed a slight decrease in functional connectivity between these regions. These results indicate that aerobic and resistance exercise during bed rest can at least partially mitigate the effects of bed rest on the functional connectivity between sensory and motor brain regions and on recovery post bed rest. Impact of key findings on hypotheses, technology requirements, objectives and specific aims of the original proposal YEAR 1 + YEAR 2: 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 and changes in white matter microstructure as a result of bed rest, no such effects were observed. We further hypothesized that bed rest would affect functional connectivity of sensorimotor and vestibular brain regions, and that exercise could mitigate these effects. This showed to be the case for a selection, but not all of the sensorimotor and vestibular brain regions under investigation. Thus, exercise could partially mitigate some specific effects of bed rest on functional connectivity, but several other bed rest related changes in functional connectivity are not mediated by exercise. If the effects of bed rest on motor behavior, brain plasticity, and brain function are affected by physical fitness changes at baseline or changes in physical fitness over the course of bed rest is topic of ongoing analyses.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	YEAR 1 + YEAR 2 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 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. In addition, we showed that bed rest results in cerebral water redistribution but that it does not affect white matter microstructure. The latter is reassuring for bedridden patients on Earth. Whether fluid redistribution has detrimental effects in the long run warrants further investigation. Our observation of changes in functional connectivity with bed rest suggest that bed rest could result in changes in how certain sensorimotor brain regions communicate. Although some of these effects were partially mitigated by exercise, not all of these effects benefited from the aerobic and resistance exercise program. Thus, in general, although exercise can have beneficial effects on the adverse effects of bed rest on brain structure, function, and motor behavior, it is not enough to counter all effects.
Task Progress:	YEAR 1 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, 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. YEAR 2 In the last year we have further investigated effects of bed rest and exercise during bed rest on white matter microstructure and focal water content. We created a pipeline that allows the direct comparison of bed rest data and data from control subjects by creating individual percent signal change images. To investigate changes in how brain regions are functionally connected during the course of bed rest and how this is affected by exercise we analyzed resting state functional connectivity MRI data. A region of interest approach was used to investigate changes of brain connectivity with 11 sensorimotor and vestibular brain regions during bed rest and during the post bed rest recovery period. In addition, an intrinsic functional connectivity contrast was applied to assess changes in overall brain connectivity with bed rest and exercise. Currently we are working to analyze how physical fitness at baseline and changes in physical

	fitness from pre bed rest to the end of bed rest are associated with changes in motor behavior, cognition, brain structure and function over the course of bed rest. All data have been preprocessed and physical fitness measures have been collected and pruned.
Bibliography Type:	Description: (Last Updated: 05/16/2019)
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