Fiscal Year:	FY 2023	**Task Last Updated:**	FY 10/02/2022
PI Name:	Wood, Scott J. Ph.D.		
Project Title:	Sensorimotor Predictors of Postlanding Functional Task Performance		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **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		
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Comments:	NOTE: PI returned to NASA JSC in January 2017. PI was at Azusa Pacific University from August 2013 – January 2017; prior to August 2013, PI was at NASA JSC.		
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	10/01/2019	**End Date:**	09/30/2023
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:	NOTE: End date changed to 9/30/2023 per PI (Ed., 7/7/21)		
Key Personnel Changes/Previous PI:	Drs. Bloomberg, Reschke and Feiveson have retired. Dr. Bloomberg and Reschke have continued as unpaid collaborators.		
COI Name (Institution):	Bloomberg, Jacob Ph.D. (NASA Johnson Space Center--Emeritus) Clark, Torin Ph.D. (University of Colorado Boulder, Aerospace Engineering Sciences) Koppelmans, Vincent Ph.D. (University of Utah) Oddsson, Lars Ph.D. (University of Minnesota) Peters, Brian Ph.D. (KBR/NASA Johnson Space Center) Reschke, Millard Ph.D. (NASA Johnson Space Center) Seidler, Rachael Ph.D. (University of Florida) Theriot, Corey Ph.D. (University of Texas Medical Branch)		
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Spaceflight drives adaptive changes in healthy individuals appropriate for sensorimotor function in a microgravity environment. These changes are maladaptive for return to earth's gravity. The inter-individual variability of sensorimotor decrements is striking, although poorly understood. The goal of this study is to identify a set of behavioral, neuroimaging and genetic measures that can be used to predict early post-flight performance on a set of sensorimotor tasks. Astronauts are being recruited who previously participated in sensorimotor field tests and/or posturography soon after long-duration spaceflight. Behavioral tests include assessments of sensory dependency and adaptability. Visual dependency involves treadmill walking while viewing a moving virtual visual scene. Vestibular sensitivity is measured while seated with eyes closed during lateral translations. Proprioception dependency is measured during one-legged stance with eyes closed on a horizontal air-bearing surface. Ground assessment of adaptability is performed (1) during treadmill walking with a virtual linear hallway and a moving walking surface, and (2) during multiple trials of navigating an obstacle course while wearing reversing prisms. The neuroimaging tests will characterize individual differences in regional brain volumes (using Structural MRI) and white matter microstructure (using Diffusion Tensor Imaging) to serve as potential predictors of adaptive capacity. The genetic tests will utilize saliva samples to examine variations in four genes chosen because of their ability to differentiate sensorimotor adaptation ability in a normative population, including Catechol-O-methyltransferase (COMT), Dopamine Receptor D2 (DRD2), Brain-derived neurotrophic factor (BDNF) and the a2-adrenergic receptor. A subjective survey was introduced to obtain ordinal measures of how sensorimotor adaptation impacted tasks both early inflight and postflight, and the general timeframe that movements were restricted. This study will utilize data (n=6 astronauts) from a previous Predictors study (PI Mulavara, grant NCC 9-58-SA03801). Deliverables: Statistical models will use combinations of behavioral metrics, brain structure metrics and genomic polymorphisms to understand individual decrements in post-flight functional task outcomes. We expect that understanding the relationships between these sensorimotor biomarkers and post-flight functional task performance will improve both our understanding of the individual variability and our strategy to optimize sensorimotor countermeasures. Study Participants: This study will target recruitment of up to 30 astronauts who previously flew on ISS, including 6 obtained via the original Predictors study. Risk Characterization, Quantification, Evidence: This project was directed toward the risk titled “Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks.” This study is addressing gaps SM-101 (risk characterization of postural control and locomotion) and SM-104 (evaluate weightlessness-induced changes in sensorimotor/vestibular function with changes in other brain functions). This study will help quantify inter-individual variability of sensorimotor decrements. Countermeasure, Prototype Hardware or Software: The information derived from this study may be applied towards optimizing countermeasures based on preflight tests of sensorimotor biomarkers.
Rationale for HRP Directed Research:	The proposed works qualifies for directed research under the "Highly Constrained Research" category in the Human Research Program (HRP) Unique Processes, Criteria, and Guidelines. This project will utilize the findings from two previous studies (SM Predictors-Ground, SM Predictors-Retrospective) that were funded by the NASA Human Research Program (HRP) through a National Space Biomedical Research Institute (NSBRI) cooperative agreement. These studies have validated, in a non-astronaut ground population, a unique set of measures that were predictive of adaptation in response to exposure to novel sensorimotor environments. Predictors were evaluated in three categories, including: 1) behavioral tests to assess sensory bias and adaptability; 2) imaging to determine individual brain morphological and functional features; and 3) genotype markers for genetic polymorphisms that play a role in the neural pathways underlying sensorimotor adaptation. These two studies were conducted to help characterize the sensorimotor risk profile and design sensorimotor adaptability training countermeasures that may be customized for each crewmember’s individual characteristics. In addition to collecting data from ground subjects, the SM Predictors-Retrospective study gathered data from six crewmembers, and from three subjects who participated in a bed rest campaign in the past. While these data supported the validity of the tested measures, the small number of subjects in this part of the study limited the interpretation of the collected data, and logistical challenges (namely, the end of the NSBRI cooperative agreement) precluded recruiting additional astronaut subjects until now. Meeting HRP’s goal of addressing gap SM 24 requires collection of data from additional crewmembers who fit the recruitment criteria for this study (crewmembers for whom functional task performance data sets exists after previous spaceflight missions). This proposed effort will thus build-upon the findings from the previous studies, with the full data set (from both the prior study and the proposed one) used to build predictive models of postflight functional task performance capabilities. Since this study directly builds upon the two prior studies and data needs to be collected seamlessly, it requires the specific expertise that has been developed within the NASA Johnson Space Center Neurosciences Laboratory. Therefore, the work reflects "focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal."
Research Impact/Earth Benefits:	The goal of this study is to identify a set of behavioral, neuroimaging and genetic measures that can be used to better understand the inter-subject variability in early post-flight performance on a set of sensorimotor tasks. We expect that understanding the relationships between biomarkers and post-flight functional task performance will improve our strategy to optimize sensorimotor countermeasures. These same biomarkers may also be useful for understanding individual variability in balance function in the general population, and predicting sensory compensation associated with aging and/or the onset of vestibular disease.
	A total of 21 of 30 long-duration astronauts have participated in this study to date, including 6 from this past year after testing resumed post-COVID. The 21 participants include 17M, 4F and 12 veterans, and 9 first time flyers with a mean age of 51.7 years (range 42.1-68.6). Their International Space Station (ISS) missions were 182 ± 32 days, mean ± std, in duration. The majority of the subjects returned on Soyuz; however, the inclusion of crewmembers returning on SpaceX, including three added this past year, is being pursued to complete our recruitment goals. The behavioral and genetic measures have been obtained 2.2 ± 1.8 years, mean ± std, following their last missions. Post-flight Outcome Measures: Computerized dynamic posturography was performed in 20 of 21 participants. Field testing (recovery from fall and tandem walk) was performed in 20 of 21 subjects, although not consistently at the same time points. For this preliminary analysis, we are using the time points that occur following return to Johnson Space Center (JSC), given these are available for all participants and more closely match when the posturography measures have been made. All of these measures continue to demonstrate high intersubject variability that is characteristic of

postflight sensorimotor responses. The posture Sensory Organization Tests (SOT) use a continuous equilibrium score ranging between 0-100, with higher numbers representing better performance. A difference score (post-flight - pre-flight performance) was calculated, with more negative values representing greater deficits in performance relative to each individual's preflight baseline. The range of SOT-5 (head erect) post-pre differences was 7 to -29 (median = -3.8), while the range of SOT-5M (head moving) was 6 to -83 (median = -19.4). Thus, the SOT-5M ratio scores are more sensitive given the timeframe of these measures (>R+24hrs) and are preferred to understand the variability in performance during vestibular contributions to standing balance. The recovery from fall (RFF) used time to stability in sec, with lower numbers representing better performance. Therefore, difference scores were calculated using preflight - postflight, so more negative values would also represent greater deficits in performance relative to each individual's preflight baseline. The range in differences at R+0c was 1.7 to -9.1 (median = -3.0). For reference, the median difference score for recovery from fall at R+0a was -9.4 (range -0.6 to -15.6). The tandem walk was performed with eyes open (TW-EO), and eyes closed (TW-EC) and scored as a percent of correct steps ranging from 0 to 100. Note that for eyes open, all crewmembers scored a perfect 100 on this task preflight. Since higher numbers represent better performance, these difference scores were calculated using post-flight - pre-flight performance, so more negative values would continue to represent greater deficits in performance across all outcome measures. For eyes closed, the range in differences at R+0c was -11.1 to -97.0 (median = -44.8). For reference, the median difference score for tandem walk eyes closed at R+0a was -77.2 (range -34.8 to -97.0). For eyes open, the range in differences at R+0c was 0 to -100.0 (median = -10). For reference, the median difference score for tandem walk eyes open at R+0a was -59.6 (range -12.5 to -100.0). Not surprisingly, tasks with eyes open tend to exhibit fewer decrements by R+0c since visual compensation is one means of dealing with the postflight vestibular disruption. The relatively poor correlation between these postflight measures may reflect differences in how crewmembers utilize visual compensation. For example, the Spearman's rho correlation between difference scores for SOT-5M and RFF was 0.105 (p = 0.67) and between TW-EC and TW-EO was 0.384 (p = 0.10).

This past year we added a Qualtrics survey to capture subjective ratings of both inflight and postflight adaptation to supplement the objective ratings. For both early inflight and postflight periods, crewmembers were asked to rate how severely adaptation impacted their ability to perform functional tasks, from 0 being no impact to 4, representing severe impacts, including not attempting tasks and/or deliberate restriction of motion. Based on the limited sample of responses received to date (n = 10 of 21), crewmembers tended to rate postflight adaptation impacting their task performance (median = 3, range 2 - 4) more than inflight (median = 2, range 0 - 3). A different question asked how long they restricted movements, from 0 = no impact or restriction of movements to 4 representing more than 3 days. Again, crewmembers indicated they needed to restrict movements over a longer period postflight (median = 3, range 0 - 4) than inflight (median = 2, range 0 – 3). The survey also included open questions to capture what recommendations they had for enhancing adaptation based on their own experience, e.g., closing eyes during parachute opening, initially restricting then incrementally increasing movements, prophylactic medication, and allowing for sleep.

Task Progress:

Sensory Dependency Measures: Sensitivity to visual motion was measured during treadmill walking while viewing a moving (virtual hallway) visual scene. The dependent variable was lateral torso translation during scene oscillation (amplitude at 0.3 Hz scene motion). Higher visual dependency appears related to lower recovery on tandem walk eyes closed (rho = -0.45, p = 0.04, n = 20). Vestibular sensitivity involves a perceptual direction-recognition task while seated with eyes closed during lateral translations. The dependent variables (threshold and bias) were derived from psychometric curve fit. Preliminary analysis suggests higher vestibular sensitivity was marginally correlated with higher recovery on SOT-5M (rho = -0.5, p=0.07). The ability to balance using proprioception is assessed by monitoring medial-lateral COP during a one-legged stance on a horizontal air-bearing surface (eyes open & eyes closed). Measures include both range and root mean square (RMS) center of pressure (COP), although medial-lateral and anterior-posterior directions from the force plate.

Sensory Adaptability Measures: The Adaptive Functional Mobility Test (AFMT) measured the time to complete navigating an obstacle course while wearing up/down reversing prisms (5 trials). While the performance continued to improve on average throughout the 5 trials, the variability in performance was greatest during the first trial (range 65 – 422 sec to complete the course). Slower AFMT times were significantly correlated with lower recovery on tandem walk eyes closed (rho = -0.5, p=0.025, n=20). Not surprisingly, the AFMT trial 1 times are highly correlated with our visual dependency measure described above (rho = 0.56, p = 0.008, n=21). Adaptability is also being assessed with the Treadmill Sensory Discordance Test. Changes in both stride frequency and reaction time to an auditory cue while walking with a virtual linear hallway on an oscillating treadmill are recorded after 1 and 4 minutes of walking on the oscillating treadmill.

Neuroimaging measures: This past year, we published a manuscript describing preliminary findings assessing the relationships of metrics derived from MRI scans collected from astronauts with motor performance post-flight. Structural and diffusion MRI scans from 14 astronauts were collected before launch and motor measures (balance performance, speed of recovery from fall, and tandem walk step accuracy) collected pre-flight and post-flight were analyzed. Regional measures of gray matter volume (motor cortex, paracentral lobule, and cerebellum), myelin density (motor cortex, paracentral lobule, and corticospinal tract), and white matter microstructure (corticospinal tract) were derived as a-priori predictors. Additional whole-brain analyses of cortical thickness, cerebellar gray matter and cortical myelin were also tested for associations with post-flight and pre-to-post-flight motor performance. The pre-selected regional measures were not significantly associated with motor behavior. However, whole-brain analyses showed that paracentral and precentral gyri thickness significantly predicted recovery from fall post-spaceflight. The thickness of vestibular and sensorimotor regions, including the posterior insula and the superior temporal gyrus, predicted balance performance post-flight and pre-to-post-flight decrements. Greater cortical thickness pre-flight predicted better performance post-flight. Regional thickness of somatosensory, motor, and vestibular brain regions has some predictive value for post-flight motor performance in astronauts, which may be used for the identification of training and countermeasure strategies targeted for maintaining operational task performance.

Genetic measures: Variations in four genes have been analyzed from saliva samples, including Catechol-O-methyltransferase (COMT), Dopamine Receptor D2 (DRD2), Brain-derived neurotrophic factor (BDNF), and the a2-adrenergic receptor. The distribution of the different alleles was within the expected range. There does not appear to be a clear pattern of alleles in any of the four genes that predict post-flight performance. Genetic analysis of the 6 new subjects is on hold for batch processing.

Summary of Preliminary Findings: There is considerable variability among the post-flight performance outcomes for the 21 participants to date. Based on a partial sample using an ordinal scale survey, 80% indicated their ability to perform functional tasks was more impacted postflight relative to inflight with, 50% indicating they needed to restrict movements

	for a longer period postflight relative to inflight. While there is a strong association within tests obtained at different R+0 timepoints, R+24 hr performance on one post-flight test does not necessarily correlate with performance on other post-flight tests. Based on our preliminary findings, there are apparent relationships between individual measures and specific post-flight outcome measures. We anticipate that combining biomarkers will increase predictive power, and this will be explored with future analyses. Our preliminary findings underscore the importance of a comprehensive post-flight test battery, including different types of tasks with varying sensory feedback. We expect that understanding the relationships between these sensorimotor biomarkers and post-flight functional task performance will improve both our understanding of the individual variability and our strategy to optimize sensorimotor countermeasures.
Bibliography Type:	Description: (Last Updated: 04/29/2024)
Abstracts for Journals and Proceedings	Koppelmans V, Bloomberg JJ, Seidler RD, De Dios YE, Wood SJ. "Cortical thickness of primary motor and vestibular brain regions predicts recovery from fall and balance directly after spaceflight." NASA Human Research Program Investigators' Workshop, virtual, February 7-10, 2022. NASA Human Research Program Investigators' Workshop, virtual, February 7-10, 2022. , Feb-2022
Abstracts for Journals and Proceedings	Wood SJ, De Dios YE, Peters BT, Beltran NE, Caldwell EE, Rosenberg MJ, Koppelmans V, Clark TK, Seidler RD, Oddsson L, Theriot CA, Reschke MF, Feiveson AF, Bloomberg JJ. "Sensorimotor predictors: Examining the relationship between measures of post-landing sensorimotor functional task performance. " NASA Human Research Program Investigators' Workshop, virtual, February 7-10, 2022. NASA Human Research Program Investigators' Workshop, virtual, February 7-10, 2022. , Feb-2022
Articles in Peer-reviewed Journals	Koppelmans V, Mulavara AP, Seidler RD, YDe Dios YE, Bloomberg JJ, Wood SJ. "Cortical thickness of primary motor and vestibular brain regions predicts recovery from fall and balance directly after spaceflight." Brain Struct Funct. 2022 Apr 25. https://doi.org/10.1007/s00429-022-02492-z ; PubMed PMID: 35469104 , Apr-2022