Fiscal Year:	FY 2018	Task Last Updated:	FY 07/06/2018
PI Name:	Dinges, David F. Ph.D.		
Project Title:	NSCOR for Evaluating Risk Factors and Biomarkers for and Social Processes in ICC/ICE Environments	or Adaptation and Resilien	ce to Spaceflight: Emotional Valence
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:	HUMAN RESEARCHBehavior and performance		
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) HFBP:Human Factors & Behavioral Performance (	IRP Rev H)	
Human Research Program Risks:	<ol> <li>(1) BMed:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders</li> <li>(2) Team:Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team</li> </ol>		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	dinges@pennmedicine.upenn.edu	Fax:	FY
PI Organization Type:	UNIVERSITY	Phone:	215-898-9949
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Zip Code:	19104-4209	Congressional District:	2
Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2016-2017 HERO NNJ16ZSA001N-Crew Health (FLAGSHIP, OMNIBUS). Appendix A-Omnibus, Appendix B-Flagship
Start Date:	09/05/2017	End Date:	09/04/2021
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:	4	Monitoring Center:	NASA JSC
Contact Monitor:	Williams, Thomas	<b>Contact Phone:</b>	281-483-8773
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	July 2018 report: 1) Replaced Dr. Tom Williams with Dr. Pete Roma as Co-Investigator/Institutional PI at JSC. 2) Replaced Dr. Tom Williams with Dr. Bradley C. Nindl as NSCOR Co-Director. 3) Replaced Dr. Brandon Vessey as Co-Investigator with Dr. Lauren Landon as Co-Investigator at JSC. 4) Added Dr. Alexandra Whitmire as Co-Investigator. 5) Added Diana Arias to role of Support for initiating Wyle subcontracts at JSC. 6) Replaced Dr. Sarah McGuire with Dr. Mathias Basner as NSCOR ICARUS Site Environmental Lead in Dr. Dinges' Lab at the University of Pennsylvania. 7) Added Dr. Brian Martin to role of Co-Investigator in Dr. Nindl's laboratory at the University of Pittsburgh. 8) Added Meaghan E. Beckner to role of PhD Research Fellow in Dr. Nindl's laboratory at the University of Pittsburgh. 9) Added Nathaniel Hodgson, PhD to role of Post-Doc in Dr. Hensch's laboratory at Harvard Boston Children's Hospital. 10) Added Gervasio Batista, PhD to role of Post-Doc in Dr. Hensch's laboratory at Harvard Boston Children's Hospital.		

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Grant/Contract No.:	80NSSC17K0644	
Performance Goal No.:		
Performance Goal Text:		
Task Description:	NASA's vision for successful long-duration exploration missions (LDEM) depends on optimizing human performance, adaptability, and resiliency to reduce individual and crew behavioral risks. To date, the major emphasis in optimizing astronauts for their tolerance to prolonged spaceflight has involved human health and performance countermeasures as well as technologies and tools to ensure safety during exploration. However, considerable evidence suggests that there are individual differences among astronauts in their vulnerabilities to the various stressors of spaceflight. The goal of the proposed NSCOR (NASA Specialized Center of Research) is to obtain novel information that will help identify individuals who are resilient to the stressors of prolonged human spaceflight, thereby ensuring successful completion of exploration missions and the preservation of astronaut health over the life of the astronaut. This NSCOR project leverages the NIMH (National Institute of Mental Health) Research Domain Criteria (RDoC) heuristic framework to conduct experimental studies to identify biological domains (molecular, circuitry, physiology) and behavioral domains that relate to individual adaptation and resiliency (as well as behavioral vulnerability) in spaceflight-relevant confined and extreme environments (ICC and ICE). The NSCOR focuses specifically on differences among astronauts in their tolerance of and adaptability to simulated conditions of prolonged spaceflight that impact behavioral health and performance. The NSCOR will provide novel information on the extent to which behavioral and biological factors can be identified that predict astronauts who can maintain positive mood, proactive social processes, a high level of performance and personal well-being, while coping with confinement, meaningless work, limited social support, and living in the extreme environmental conditions of space. By utilizing the RDoC framework, three different human confinement analogs and an animal model, the NSCOR will generate data convergi	
Rationale for HRP Directed Research:		
Research Impact/Earth Benefits:	In year 1, the Hensch lab established the physiological and behavioral consequences of early life stress (ELS) in mice. In a paradigm of fragmented maternal care (neglect), striking sex-specific outcomes were observed. Male mice raised under fragmented maternal care displayed externalizing behaviors as adults, including social dominance, increased territoriality, compulsive behaviors and social memory deficits. Instead, females exhibited internalizing symptoms, like heightened anxiety and perseveration on a rule-switching task. Inhibitory sub-circuits within the prefrontal cortex (PFC) were also differentially affected by sex following ELS: males showed enhanced inhibition of callosal projections, while females had reduced inhibition of sub-cortical projections. These findings indicate the early life history of subjects predisposes them to mental states which need to be considered prior to engaging in long-term spaceflight. They further suggest local circuit changes may be targeted differentially to correct later adult psychopathology in males and females raised under early adversity. During the Definition Phase of this NSCOR project (10/5/17-4/5/18), a literature review was conducted to select biological biomarkers. Blood and saliva samples will be analyzed (to the extent funding is available) for these biomarkers, which the scientific literature indicates are associated with stress, emotional, and/or immune responses. During the Definition Phase of this NSCOR project (10/5/17-4/5/18), a literature review was conducted to select and adapt questionnaires. Selected questionnaires will be administered as screening measures (administered pre-mission), characterization measures (administered pre/post-mission), and/or state-based measures (administered in-mission). Selection, refinement, and development of relevant measures was also major goal of the NSCOR year-1 and Definition Phase activities. For the human research components, the BHP (Behavioral Health & Performance) Laboratory's major contributions were in the	

**Task Progress:** 

In year 1, the Hensch lab established the physiological and behavioral consequences of early life stress (ELS) in mice. In a paradigm of fragmented maternal care (neglect), striking sex-specific outcomes were observed. Male mice raised under fragmented maternal care displayed externalizing behaviors as adults, including social dominance, increased territoriality, compulsive behaviors, and social memory deficits. Instead, females exhibited internalizing symptoms, like heightened anxiety and perseveration on a rule-switching task. Inhibitory sub-circuits within the prefrontal cortex (PFC) were also differentially affected by sex following ELS: males showed enhanced inhibition of callosal projections, while females had reduced inhibition of sub-cortical projections. These findings indicate the early life history of subjects predisposes them to mental states which need to be considered prior to engaging in long-term spaceflight. They further suggest local circuit changes may be targeted differentially to correct later adult psychopathology in males and females raised under early adversity. The following biomarkers, which have all been associated with stress, emotional, or immune responses in prior research,

will be determined in venous blood samples (8 ml serum) collected at baseline and on a regular basis throughout the 3 ICC/E environments: Brain-derived neurotrophic factor (BDNF), vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF-1) (Lin, Suhr et al. 2014), Neuropeptide Y (NPY), Ghrelin and oxytocin, tumor necrosis factor (TNF) (Beste, Baune et al. 2010; Hodes, Pfau et al. 2014; van Zuiden, Kavelaars et al. 2015), interleukin-1 (IL-1), interleukin-6 (IL-6) (Valkanova, Ebmeier et al. 2013), interleukin-10 (IL-10), and vitamin D. Blood samples will be taken by venipuncture in the morning after overnight fasting between 7 and 8 am to avoid circadian rhythm confounds. The Vacutainer® Safety-Lok TM Blood Collection Set and SST TM Tubes with Silica Clot Activator (Beckton, Dickinson & Company) from clinical suppliers certified as medical products (Sarstedt system) will be used to perform the blood draw. Immediately after collection serum samples will be centrifuged for 10 min at 1000 g, and then aliquoted in 8 cryovials of 250 µl each and then stored at -80°C. Serum parameters will be analyzed by ELISA (enzyme-linked immunoarbsorbat assay) kits (R&D Systems GmbH, Wiesbaden, Germany / IBL International GmbH, Hamburg, Germany). Cortisol will be determined from morning collections of saliva specimens, which will be collected by chewing on a salivette for approximately 3 minutes until it is soaked (Salivette; Sarsted, Rommelsdorf, Germany). Samples are immediately centrifuged at 1500 g for 15 min, and will then be stored at -80°C until shipping to Germany. Samples are analyzed for free cortisol by ELISA in accordance with the manufacturer's instructions (IBL International GmbH, Hamburg, Germany). On the same days as blood draws, we will gather 24 h ECG data (e.g., with the eMotion FAROS sensor (Mega Electronics Ltd., Kuopio, Finland) to derive heart rate and heart rate variability measures as a peripheral index of emotion regulatory processes that are affected by prefrontal mechanisms.

Analysis will encompass the biological basis of social support to assess individual sociability and the neurobehavioral contributions to resiliency and/or adaptability of engaging positively in social interactions, tolerance, and awareness (e.g., affiliation, attachment). Cellular and molecular biomarkers related to social systems (e.g., oxytocin) will reveal changes in the underlying neurobiological systems as a function of social support, before, during, and after being in an ICC/ICE environment. Individual differences in indicators of resilience measured before isolation will predict reported loneliness, higher perceived social support, and healthier social neurobiological systems. Individual differences in emotional regulation will provide the most robust evidence for how the neural circuitry moves up to behavior and social processes in self-report and interactions as well as downward toward cellular/molecular biomarkers (e.g., cortisol, BDNF, oxytocin, etc) with structural changes revealed by the fMRI.

Biomarkers of human performance optimization (Dr. Nindl's Lab) will be tested prospectively within the Neumayer ICE analog. The extensive biomarker panel, analyzed in three separate isolation analogs, will provide insight to the most pertinent biological signatures of resiliency. This information will help guide the down-selection of biomarkers used in the selection of astronauts mostly likely to maintain health and performance in long-duration exploration missions.

During the Definition Phase of this NSCOR project (10/5/17-4/5/18), a literature review was conducted to select and adapt questionnaires. Selected questionnaires will be administered as screening measures (administered pre-mission), characterization measures (administered pre/post-mission), and/or state-based measures (administered in-mission).

The refinement of the biological biomarkers to be measured by blood, saliva, and urine (as funding permits) and refinement of questionnaires to be administered are vital to prepare for the Study Campaigns in each human analog (Neumayer, ICARUS, and HERA). Furthermore, the Meaningfulness of Work Battery that will be implemented in the analogs is crucial for Specific Aim 4.

## References

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Valkanova, V., Ebmeier, K. P., & Allan, C. L. (2013). CRP, IL-6 and depression: a systematic review and meta-analysis of longitudinal studies. Journal of affective disorders, 150(3), 736-744

Bibliography Type:	Description: (Last Updated: 05/08/2025)
Abstracts for Journals and Proceedings	Roma PG, Schneiderman JS, Landon LB, Whitmire AM, Williams TJ. "Overview of NASA Behavioral Health & Performance Standard Measures." Presentation at the annual meeting of the 89th Aerospace Medicine Association Meeting, Dallas, TX, May 6-10, 2018. Aerospace Medicine and Human Performance. 2018 Mar;89(3):218. , Mar-2018

Abstracts for Journals and Proceedings	<ul> <li>Landon LB, Roma PG, Whitmire A. "Team-Level Effects of Sleep and Fatigue: Wake Up, Researchers!" Presentation at the 33rd Annual Conference of the Society for Industrial and Organizational Psychology, Chicago, IL, April 19-21, 2018.</li> <li>33rd Annual Conference of the Society for Industrial and Organizational Psychology, Chicago, IL, April 19-21, 2018.</li> <li>Apr-2018</li> </ul>
Abstracts for Journals and Proceedings	<ul> <li>Roma PG, Schneiderman JS, Landon LB, Whitmire AM. "Overview of NASA Behavioral Health &amp; Performance Standard Measures." Poster presentation at the 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.</li> <li>2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. , Jan-2018</li> </ul>
Abstracts for Journals and Proceedings	<ul> <li>Roma PG, Schneiderman JS, Landon LB, Whitmire AM, Baskin P, Arias DP. "Overview of the NASA Behavioral Health &amp; Performance Laboratory." Poster presentation at the 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.</li> <li>2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.</li> </ul>
Abstracts for Journals and Proceedings	Dinges DF, Basner M, Bilker WB, Gur RC, Hensch T, Nindl BC, Roma P, Stahn AC, and the NSCOR Investigative Group. "NSCOR for Evaluating Risk Factors and Biomarkers for Adaptation and Resilience to Spaceflight: Emotional Valence and Social Processes in ICC/ICE Environments." 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.