Fiscal Year:	FY 2015	**Task Last Updated:**	FY 10/14/2014
PI Name:	Dinges, David F. Ph.D.		
Project Title:	Markers of Susceptibility to Neurobehavioral Decrements in Space Flight		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Neurobehavioral and Psychosocial Factors Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **BHP**:Behavioral Health & Performance (archival in 2017)		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	19104-4209	**Congressional District:**	2
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	10/01/2012	**End Date:**	06/30/2016
No. of Post Docs:	1	**No. of PhD Degrees:**	1
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:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 6/30/2016 per NSBRI (Ed., 3/1/16) NOTE: End date change to 3/31/2016 per NSBRI (Ed., 9/30/15) NOTE: End date changed back to 9/30/2015 per NSBRI submission October 2013 (Ed., 10/16/13) NOTE: Original end date was 9/30/2015; Changed to 9/30/13 per NSBRI 6/2/2012 (Ed., 6/4/12)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Goel, Namni (University of Pennsylvania) Mollicone, Daniel (Pulsar Informatics, Inc.) Rao, Hengyi (University of Pennsylvania) Basner, Mathias (University of Pennsylvania) Mignot, Emmanuel (Stanford University School of Medicine)		
Grant/Contract No.:	NCC 9-58-NBPF02801		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	This project is responsive to the NSBRI Neurobehavioral and Psychosocial Factors Team goal to validate objective markers of susceptibility to stress, fatigue, and neurobehavioral decrements associated with long-duration space flight, and to the NASA HRP Behavioral Health and Performance gap to find individual characteristics that predict successful adaptation and performance in an isolated, confined, and extreme environments, especially for long duration missions. Sleep loss is common in space flight but there are currently no valid objective markers of the large inter-individual differences in susceptibility to its neurobehavioral effects. To fill this gap, the project will validate promising novel markers of susceptibility to fatigue-related neurobehavioral decrements. The project consists of two discrete specific Aims. Specific Aim 1 will identify core dimensions of neurobehavioral responses to both chronic partial and acute sleep loss. This will be achieved by conducting a factor analysis of a historical database of cognitive, subjective, and physiological responses to acute and chronic sleep loss in healthy adults (N=640). The historical data will be separated into two groups, one group of N=175 subjects studied during total sleep deprivation (TSD) and a second group of N=465 subjects studied during chronic partial sleep deprivation (PSD). The primary outcomes to determine the core dimensions of responses to sleep loss for both groups include performance on the Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task, Digit Span, Tower of London, and subjective ratings of mood, sleepiness, and tiredness through the Profile of Mood States, Visual Analog Scales of Fatigue and Tiredness, and Karolinska Sleepiness Scale. These dimensions will then serve as targets for prospectively assessing the predictive power (separately and in combination) of each of five objective markers that include physiological (brain activity, heart rate variability, salivary amylase), behavioral (time on task performance), and genetic (common polymorphisms) measures for susceptibility to neurobehavioral responses to sleep loss. Specifically, the five biomarkers are: (1) Resting arterial spin labeling (ASL fMRI) cerebral blood flow without sleep deprivation; (2) Resting psychomotor vigilance test (PVT) time on task (TOT) without sleep deprivation; (3) Heart rate variability (HRV) during PVT TOT; (4) Salivary a-amylase activity (sAA) during sleep deprivation; (5) Variations in genes regulating sleep, circadian, and cognitive functions. The prospective validation is currently being accomplished by the addition of the predictor markers to three separate studies on sleep deprivation that are currently underway. Across the three studies being leveraged, there will be a total of N=120 healthy adults (diverse in age, gender, ethnicity) on which predictive validation will be performed. Data collection on the five biomarkers continued during the second year of funding. During the second year of funding, data on predictor marker 1 (see above) have been collected on a total of N=18 unique subjects who completed a TSD protocol and N=25 unique subjects who completed a PSD protocol. Projected data collection on biomarker 1 during the second year funding period is expected to be a total of N=22 unique TSD subjects and N=29 PSD subjects. Data on predictor markers, 2, 3, 4, and 5 (see above) have been collected on a total of N=23 unique subjects who completed a TSD protocol and N=31 unique subjects who completed a PSD protocol. Projected data collection on biomarkers 2, 3, 4, and 5 during the second year funding period is expected to be a total of N=27 unique TSD subjects and N=35 PSD subjects. Total data collection on predictor marker 1, which includes years 1 and 2, have yielded collected data on a total of N=42 unique TSD subjects and N=49 unique PSD subjects. Total data collected to date on predictor markers 2, 3, and 5 have yielded collected data on a total of N=49 unique TSD subjects and N=57 unique PSD subjects. Total data collection on predictor marker 4 have yielded data on a total of N=45 unique TSD subjects and N=57 unique PSD subjects. During the third year of funding, the historical database of Specific Aim 1 will be complete and statistical analyses to determine the core dimensions of responses to acute and partial sleep deprivation will be executed. Data collection on the five biomarkers of Specific Aim 2 will continue to be collected resulting in a projected total of N=34 unique TSD subjects and N=34 unique PSD subjects during the third year of funding. Additionally, data from N=24 unique subjects were collected in both TSD and PSD conditions. The identification of biomarkers addresses multiple NASA BHP risk and gaps by identifying indicators of vulnerabilities and resiliencies to sleep loss (Sleep Gap 4), defining characteristics of individuals resilient to the neurobehavioral decrements from sleep loss (BMed5), and by identifying psychological measures that can be used to select individuals for long duration space flight (Team Gap 4). Finding valid markers of susceptibility to neurobehavioral deficits from total and chronic partial sleep loss will make it possible to optimize crew resources and fatigue management during long-duration space flight, and it will have substantial benefits for fatigue management in many Earth-based, safety-sensitive operations. The project deliverable will be a technique (technology) for discriminating those who are more resistant versus those more susceptible to the adverse effects of fatigue on neurobehavioral functions. The functions to be predicted include separate and common variance among outcomes in the domains of behavioral and physiological alertness, cognitive performance, subjective fatigue/sleepiness, and homeostatic sleep response.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The research builds on an extensive body of work we have conducted to help manage the cognitive and neurobehavioral performance of astronauts in space while being exposed to chronic partial or total sleep deprivation. The acquisition of critical knowledge of objective markers of the large inter-individual differences in susceptibility to the neurobehavioral decrements from sleep-related fatigue help predict successful adaptation and performance in isolated, confined, and extreme environments. The identification of predictive biomarkers will have utility in a broad range of Earth-based applications in which sleep restriction, stress, and neurobehavioral stability have major adverse impacts on human performance (e.g., transportation modes, power plants, military operations).
	This project is comprised of two different experiments: (1) the identification of core dimensions of neurobehavioral responses to sleep loss (Specific Aim 1) using a historical database of cognitive, subjective, and physiological responses to acute and chronic sleep loss in healthy adults (N=640); and (2) using the core dimensions of neurobehavioral responses to sleep loss to prospectively assess the validity of biomarkers of susceptibility to the neurobehavioral deficits from sleep loss. We are currently creating the historical database to achieve Specific Aim 1 by locating and formatting historical data from N=640 healthy adults. The historical database includes data from experiments manipulating sleep duration in healthy adults through both total sleep deprivation (TSD) and chronic partial sleep deprivation (PSD) protocols conducted over the past 25 years. Of the proposed total N=640 subjects, a subset of N=175 unique subjects participated in one of ten TSD experiments and a subset of N=465 unique subjects participated in one of nine PSD experiments. Data on ten primary outcomes collected across the 19 studies are being included in the statistical determination of the core dimensions of responses to sleep loss. In addition to the progress constructing the historical

Task Progress:	database, data collection on predictor biomarkers (Specific Aim 2) has begun. During the second year of funding, assessments of predictor markers were collected in three currently funded scientific experimental protocols, which expose participants to total and/or chronic partial sleep deprivation. The five predictor markers are: (1) Resting arterial spin labeling (ASL fMRI) cerebral blood flow without sleep deprivation; (2) Resting psychomotor vigilance test (PVT) time on task (TOT) without sleep deprivation; (3) Heart rate variability (HRV) during PVT TOT; (4) Salivary a-amylase activity (sAA) during sleep deprivation; (5) Variations in genes regulating sleep, circadian, and cognitive functions. Collected data includes neuroimaging of non sleep deprived subjects at baseline, Psychomotor Vigilance Task (PVT) performance, electrocardiograms during the 20-minute PVT, saliva samples during PSD, and blood draws during both TSD and PSD. During year 2, data on predictor marker 1 have been collected on a total of N=18 unique TSD subjects and N=25 unique PSD subjects. Projected data collection on biomarker 1 for year 2 is expected to total of N=22 unique TSD and N=29 PSD subjects. Data on predictor markers, 2, 3, 4, and 5 have been collected on a total of N=23 unique TSD subjects and N=31 unique PSD subjects. Projected data collection on biomarkers 2, 3, 4, and 5 during year 2 is expected to total of N=27 unique TSD and N=35 PSD subjects. Data collection on the five biomarkers of Specific Aim 2 will continue in year 3 with a projected total of N=34 unique TSD subjects and N=34 unique PSD subjects. Additionally, data from N=24 unique subjects were collected in both TSD and PSD conditions.
Bibliography Type:	Description: (Last Updated: 05/08/2025)
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