Fiscal Year:	FY 2014	**Task Last Updated:**	FY 09/08/2014
PI Name:	Klerman, Elizabeth B. M.D., Ph.D.		
Project Title:	Ultra-Short Light Pulses as Efficient Countermeasures for Circadian Misalignment and Objective Performance and Subjective Alertness Decrements		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Human Factors and Performance Team		
Joint Agency Name:		**TechPort:**	Yes
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:	02115-5804	**Congressional District:**	8
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	08/01/2012	**End Date:**	02/29/2016
No. of Post Docs:	4	**No. of PhD Degrees:**	1
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 2/29/2016 per NSBRI (Ed., 2/1/16) NOTE: End date change to 12/31/2015 per NSBRI (Ed., 10/14/15) NOTE: End date change to 9/30/2015 per NSBRI (Ed., 2/6/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Wang, Wei (Brigham and Women's Hospital) Lockley, Steven (Brigham and Women's Hospital)		
Grant/Contract No.:	NCC 9-58-HFP02802		
Performance Goal No.:			
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Task Description:	Lighting protocols have been recognized by NSBRI (National Space Biomedical Research Institute), NASA, and NIH (National Institutes of Health) as important countermeasures for circadian rhythm and sleep disruptions and their associated effects on performance and alertness for both crews in space and workers on Earth. The current light-based countermeasures involve one or more hours of bright light exposure. We have recently demonstrated significant circadian phase shifting with an ultra-short 2-minute bright light stimulus. The use of such a short duration stimulus as a countermeasure would significantly preserve the ability to work in the International Space Station (ISS) lighting environment and reduce crew resource requirements. We propose to test the relative efficacy of both ultra-short and longer-duration light protocol countermeasures using the newly approved ISS lighting system to induce both adaptive circadian resetting and direct alerting effects. Experiments will be conducted jointly with Dr. S. Lockley and his NSBRI project "The ISS Dynamic Lighting Schedule:An in-flight lighting countermeasure to facilitate circadian adaptation, improve sleep and enhance alertness and performance on the International Space Station." These studies will further our understanding of the physiologic mechanisms that mediate exposure-duration-dependent and wavelength-dependent effects of photic stimuli on circadian phase and performance. Furthermore, results from these experiments will be added to our validated physiologically based mathematical models of light, sleep/wake, and circadian rhythms effects on performance and alertness, including a software application used for determining the optimal timing of light exposure to be employed as a countermeasure for predicted times of poor performance and alertness. The experimental and modeling results will have direct Earth-based applications for workers on early-rising, night, or rotating schedules, as well as for people experiencing jet lag. The proposed work directly addresses one of the NSBRI NASA Research Announcement (NRA) research objectives and two NASA Human Research Program Integrated Research Plan (IRP) Risks. This proposal will also address other NSBRI goals: training of future scientists, collaboration among NSBRI investigators, and a combination of basic science with space-based applications and potential commercial applications.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Light is the major environmental time cue that resets the circadian pacemaker in the Suprachiasmatic Nucleus (SCN) of the mammalian hypothalamus. Light information is captured exclusively by the eyes using specialized intrinsically photosensitive retinal ganglion cells containing the novel blue-light sensitive photopigment melanopsin and transduced directly to the SCN via a dedicated neural pathway, the retinohypothalamic tract. Each day the light-dark cycle resets the internal clock, which in turn synchronizes the physiology, psychology, and behavior controlled by the clock. Failure to receive this light-dark information, as experienced for example by totally blind individuals, causes the circadian pacemaker to revert to its endogenous non-24-hour period and possibly become desynchronized from the 24-hour light-dark cycle. Exposure to irregular light-dark cycles, as experienced for example by psychiatric patients with irregular sleep-wake cycles, can also disrupt circadian rhythms. In addition to its circadian resetting and melatonin suppression effects, light has a direct arousal effect on the brain, improving alertness and performance. This property of light can be useful as a non-pharmacological treatment for fatigue in a number of conditions, and if timed appropriately, these effects can complement the circadian phase resetting effects of light, for example in treating shiftwork and jet-lag disorders, to help maintain alertness at the correct time and subsequently improve sleep. The results of our experiments in which gradual vs. slam-shift changes in schedule along with continuous or intermittent light exposure are tested for their effects on circadian rhythms, sleep, hormones, subjective alertness, and objective performance will be applicable to conditions such as jet lag, and shift-work or night-work. Millions of workers in the safety, security, transportation, healthcare, and industrial sectors are affected by these conditions yearly, with effects on health and safety. The development of (i) mathematical models of circadian rhythms, sleep, alertness, and performance, and (ii) software based on these models to facilitate schedule design, can improve performance and alertness and thereby effectiveness and public safety for people who work at night, on rotating schedules, on non-24-hr schedules, or on extended duty schedules (e.g., pilots, train and truck drivers, shift workers, healthcare workers, public safety officers). Attempting to sleep at adverse circadian phases is difficult, resulting in poor sleep efficiency. Similarly, attempting to work at adverse circadian phases, and/or after a long time awake, results in poor worker performance and productivity and leads to an increase in errors. For example, the accidents at the Chernobyl and Three Mile Island nuclear reactors and the Exxon Valdez grounding were all partially attributed to employees working at adverse circadian phases and the Federal Aviation Administration (FAA) reports of air traffic controllers sleeping while scheduled to work at night are related to their work schedule. The mathematical models and the available software that implements these models can be used to simulate and quantitatively evaluate different work and light exposure schedules to predict the expected circadian phase, subjective alertness, and performance in an individual. Our software has been requested by members of NASA, academia, government, and industry, including airline, safety, medical, and military applications. Its use could help produce improved work schedules for both astronauts and ground-crew. It is currently being used to evaluate potential work schedules for medical residents to improve performance while complying with new national work hour standards. The mathematical modeling efforts and software have also been used in educational programs and in the popular press to teach students and teachers about circadian rhythms and sleep and their effects on alertness and performance.
Task Progress:	1) Experimental: We began our recruitment efforts in Jan 2013 and to date we have screened 81 potential participants, 32 participants have been excluded based on study inclusion/exclusion criteria, 18 participants have completed the study, and an additional 10 participants are completing the screening portion of the study. One participant was disempanelled from the study. We expect to complete studies in an additional 18 participants by the end of July 2015. Participants are randomized to either the gradual or slam shift arms of the study on the day of admission. The dynamic lighting is generated using the Solid State Lighting Module for Research (SSLM-R), a functional ISS lighting analog that mimics both the geometry of the light sources aboard ISS and the light source and spectra that will eventually be deployed. Primary outcome measures of the study include: a) Circadian phase shifts: Shift in endogenous circadian phase (Dim Light Melatonin Onset; DLMO) between initial and final phase assessment. b) Cognitive performance: Subjective sleepiness measured using the Karolinska Sleepiness Scale. Objective measures of alertness include the visual and auditory psychomotor vigilance tests (PVT) and EEG correlates of alertness. c) Sleep structure and architecture: Polysomnographic assessment of sleep structure and architecture including latency and efficiency. Additionally, prefrontal cortex hemodynamic responses to PVT stimuli and sleep are monitored using Near Infrared Spectroscopy (NIRS). We have monitored via NIRS from 6 participants. We expect to monitor an additional 18 participants by the end of July 2015. 2) Modeling: The mathematical model is continuing to be updated with information from the experimental work and data from the Division of Sleep and Circadian Disorders database. The mathematical model was also used to inform the design of Experiment 1, including to optimize the timing of the lighting to maximize circadian phase shifts. We have also continued development of the linked circadian, sleep, and performance model to include the use of multiple

	countermeasures (e.g., sleep, light, pharmaceuticals) in tandem. These additions will greatly improve the utility of the models in real-world conditions, including long duration spaceflights, where chronic sleep restriction is common. The significance of the modeling will be better understanding and prediction of the effects of light on human circadian rhythms, sleep, hormones, performance, and alertness. In addition, we have developed a new, physiologically based model of the effects of chronic sleep restriction. This new model has been designed so that it can be easily integrated within our existing linked model. Progress also addresses other goals within NSBRI: training of future scientists, collaboration between and among NSBRI teams, combination of basic science, space based applications and other, potentially commercial, applications.
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