Fiscal Year:	FY 2012	**Task Last Updated:**	FY 01/08/2013
PI Name:	Klerman, Elizabeth B. M.D., Ph.D.		
Project Title:	Designing Individual Countermeasures to Reduce Sleep Disruption and Improve Performance and Alertness in Space		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Human Factors and Performance 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 (2) **Sleep**:Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload		
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:**	2007 Crew Health NNJ07ZSA002N
Start Date:	06/01/2008	**End Date:**	09/30/2012
No. of Post Docs:	0	**No. of PhD Degrees:**	2
No. of PhD Candidates:	0	**No. of Master' Degrees:**	1
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 9/30/2012 (from 5/31/2012) per NSBRI (Ed., 1/24/2012)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Barger, Laura (Brigham and Women's Hospital)		
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Performance Goal No.:			
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Task Description:	Optimal levels of objective neurobehavioral performance, subjective alertness, and high-quality restorative sleep are critically important to astronaut and ground-based crew health and to the overall success of space missions. Neurobehavioral performance and alertness are affected by changes in circadian rhythms, homeostatic sleep/wake regulation, sleep inertia, and the interactions of these processes. Problems with sleep, circadian rhythms, and performance have been widely reported among astronauts and supporting ground crew. Therefore, it is imperative that work and sleep/wake schedules, including the timing of countermeasures such as light and naps, are designed to optimize individual performance, alertness, and sleep quality relative to operational requirements. Our approach is to use mathematical models to describe the underlying physiology of internal circadian timing, alertness, performance, and sleep to design effective countermeasures. We have developed and validated three linked mathematical models: one of the human circadian pacemaker that includes the influence of light and of non-photic processes; one of performance and alertness that includes the effects of circadian rhythms, sleep/wake homeostasis, and sleep inertia; and one of the physiology underlying sleep/wake regulation. Together these models estimate and predict the effects of sleep/wake timing, light exposure, circadian phase, and some pharmaceuticals on performance and alertness. Performance and alertness measures are modeled independently to reflect differences in the underlying physiological processes and effects of sleep/wake on each measure. CPSS, the software that implements this model, has been used by NASA employees and NASA consultants to design light countermeasures for both astronaut pre-launch schedules and in-flight schedules. Our specific aims were to: (1) Replace the current assumption that an individual sleeps the entire time when scheduled to sleep with probabilities of sleep and wake during scheduled sleep times; (2) Improve daily assessment of sleep and sleep disruption using actigraphy data; (3) Add statistical features including confidence limits to the predictions; (4) Update the software per astronaut and ground crew requests for specific features and reports. These projects address NASA's objectives to improve the design of individual countermeasures to reduce sleep disruption and improve performance and alertness in space and on Earth. As part of these overall goals, we published a novel scheduling algorithm called Shifter that automatically designs optimal light countermeasures for user-defined work and sleep schedules. Both experimental and field studies have shown that light interventions minimize fatigue while improving performance and sleep. This work required several mathematical and computational advances, including the development of a novel schedule representation and scheduling algorithm. The utility of this scheduling software extends beyond NASA-related schedules to include any operational setting that relies on work scheduled outside the typical 9am to 5pm shift, including night and rotating shift-work, transmeridian travel, and the design of work schedules for medical residents to improve performance and meet new national guidelines for restricted work hours. To individualize model predictions, we are developing a statistical framework based on easily collected trait information (e.g., age, chronotype) that has been shown to correlate with differences in sleep timing, circadian phase, and performance and alertness. Although changes in physiology have been correlated with specialized questionnaire results (e.g., habitual sleep time is highly correlated with circadian phase), our current results suggest that a simple alteration of the model output using demographic information is not accurate. The work of Dr. Phillips (NSBRI post-doctoral fellow) has quantified mechanisms that may underlie individual differences in physiologically-determined sleep timing and self-reported chronotype (e.g., owl or lark). The use of sleep aids during NASA missions is indicative of the difficulty with initiating and maintaining sleep that astronauts experience during space flight. To assess the ability of individuals to conform to scheduled work hours, Dr. Phillips has integrated the circadian and performance model with a model of the physiological mechanisms that control sleep/wake transitions. This combined model dynamically predicts whether an individual is awake or asleep across a simulated protocol and also allows for predictions of sleep efficiency and the likelihood of falling asleep during scheduled wake periods. This physiologically-based model can be readily extended to incorporate pharmaceutical effects. Using this model, we have now successfully incorporated the effects of melatonin and caffeine at different times and dosages. Actigraphy is an inexpensive and less intrusive alternative to polysomnography and/or sleep/wake diaries to determine an individual's sleep/wake schedule. Prior iterations of the mathematical model relied on user input to generate sleep/wake schedules. Based on the work from this project, we can now use actigraphy to determine the actual sleep/wake schedule of an individual and use this information as input to our mathematical models. We recently completed a project in collaboration with two NSBRI investigators, Drs. Lockley and Barger. In this project, pattern recognition algorithms were used to identify the level of performance impairment in an individual based on a single session of neurobehavioral testing (rather than multiple hours of testing) under both controlled in-patient laboratory conditions and real world conditions, including during the NASA Phoenix Mars study. We continue to work with NASA and NSBRI personnel to meet their requests regarding use of the models and software.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The development of (1) mathematical models of circadian rhythms, sleep, alertness and performance, and (2) 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, health care 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 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 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 previous model assumption that an individual sleeps the entire time that is available to them during a scheduled sleep episode has been improved by the recent incorporation of actigraphy as an input to the mathematical model of the actual sleep/wake times experienced by the individual. The use of actigraphy as a tool to record sleep has improved confidence levels on the daily assessment of sleep when compared to the use of sleep logs or diaries and also has reduced the user requirements for maintaining daily logs. The interface between actigraphy and the software enables

faster and possibly more accurate predictions of circadian phase and performance parameters. The Shifter software now includes optimal countermeasure design, so that countermeasures can be planned for times of predicted poor performance and alertness. The schedule and countermeasure design program allows users to interactively design schedules and implement mathematically optimized light countermeasures (including intensity, duration and timing within the wake episode) to minimize worker fatigue. This scheduling software will be valuable to those who work at night, on rotating schedules, on non-24-hr schedules, or on extended duty schedules. The software allows individuals to design countermeasures for their assigned work schedules so that their sleep/ wake rhythms will be adjusted to ensure optimal performance at desired times, with respect to both scheduled work events and their circadian phase. Improving sleep duration and quality can also decrease the risk of accidents and errors, as well as decrease the long-term risks of cardiovascular, metabolic, immune, and psychological pathologies. We continue to work with NASA and NSBRI personnel to meet their requests regarding use of the models and software. We continue to work with Dr. Dorit Donoviel, Associate NSBRI Research Director, and Marti Fleming, NSBRI commercialization consultant, to promote commercialization of the work. 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:

Specific Aim 1 (predicting sleep/wake amounts within a scheduled sleep episode): We have integrated the existing circadian/performance model with a physiologically-based model of sleep/wake transitions. This integrated model can predict whether individuals are able to conform to enforced work schedules and includes estimates for the likelihood of insomnia during scheduled sleep periods or the likelihood that the individual will experience difficulty remaining awake during working hours. We have validated this integrated model against human data for caffeine and melatonin and we have related inter-individual differences in sleep timing (e.g., self-reported chronotype) to differences in the underlying physiology.
Specific Aim 2 (actigraphy): We have integrated the output from actigraphy software with the input required to run our Circadian Performance Simulation Software (CPSS). CPSS implements our mathematical model of the human circadian pacemaker, performance, and alertness, which includes the key processes of circadian rhythms, sleep/wake homeostasis, and sleep inertia on performance and alertness, as well as the effects of light on circadian rhythms. Pre-processing tools were developed to generate the sleep/wake schedule and light levels from either raw or processed actigraphy data. We have tested the ability to use outpatient actigraphy as input to CPSS to predict circadian phase for individuals under circadian entrained and phase-shift conditions.

Specific Aim 3 (Statistical modeling of individual circadian, sleep, performance, and alertness parameters): We have concentrated on statistical modeling of individual parameters of our circadian, performance, and alertness models. By fitting the model to individual data, rather than group averages, we obtain a set of parameters for the performance and alertness models that are unique to each individual. We can then use other data collected from the individual, such as age, sex, habitual sleep time, morningness/eveningness preference, to determine correlations between model parameters and individual characteristics.

Specific Aim 4 (Work with NASA and NSBRI personnel to revise features of our current software to meet their specifications for administratively scheduling sleep, wake, and countermeasure design to minimize fatigue and performance issues): We have had discussions with NASA and NSBRI personnel to revise features of our current software to meet their specifications for administratively scheduling sleep, wake, and countermeasure design to minimize fatigue and performance issues, as well as incorporating the models into other modeling work performed by NASA. Dr. Barger used the software for NASA supported studies of sleep in ISS and Shuttle crew. We also developed a novel scheduling algorithm that automatically designs optimal light countermeasures for user-defined schedules The scheduling framework is applicable to other work schedules including shift-work and transmeridian travel.

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