Fiscal Year:	FY 2011	**Task Last Updated:**	FY 06/08/2011
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) **Sleep**:Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload (IRP Rev F)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Boston	**State:**	MA
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:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	2	**No. of Master' Degrees:**	1
No. of Master's Candidates:	2	**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	3	**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):			
Grant/Contract No.:	NCC 9-58-HFP01603		
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Task Description:

Objective neurobehavioral performance, subjective alertness, and sleep are critically important to astronaut and ground-based crew health and to ensure the success of space missions. Neurobehavioral performance and alertness are affected by changes in circadian rhythms, homeostatic sleep/wake regulation and sleep inertia, and the interactions of these processes. During space missions, circadian rhythms and sleep are disrupted, both for astronauts and ground-based crew. Problems with sleep, circadian rhythms and performance have been reported in astronauts, and NASA data indicate that sleeping pills are among the most commonly used drugs in space. Therefore, it is imperative that work and sleep/wake schedules, including the timing of countermeasures such as light, are designed to optimize individual performance, alertness, and sleep quality relative to operational requirements. Our approach to designing countermeasures is to develop new scheduling techniques and software that use mathematical models to describe the underlying physiology of internal timing, performance and sleep.
We have developed and validated two linked mathematical models: one of the human circadian pacemaker that includes the influence of light and of non-photic processes, and one of performance and alertness that includes the key processes of circadian rhythms, sleep/wake homeostasis and sleep inertia. Together, these models are able to predict the effects of sleep/wake, sleep inertia and circadian phase on performance and alertness. Each performance or alertness measure has a separate equation, reflecting the underlying physiological processes in the effect of sleep/wake on performance and alertness. CPSS, the software implementing this model, has been used by NASA and consultants when designing light countermeasures for astronaut pre-launch schedules as well as for designing in-flight schedules. To further improve this mathematical model and this method for optimal design of countermeasures, our s modeling work will focus on individual, rather than group, predictions and use novel non-linear mathematical and statistical methods. 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. Our current progress includes:

We developed a novel scheduling algorithm called Shifter that automatically designs optimal light countermeasures for user-defined NASA-related schedules. Light interventions have been demonstrated to minimize fatigue, improve performance, and improve sleep in experimental and field studies. Shifter allows individuals who are not circadian experts to design schedules and light interventions within minutes. Previous design of light interventions, such as for the 24.65-hr Mars Day experimental protocol (NASA and NSBRI supported, Dr. Czeisler, PI), took approximately two weeks. The scheduling framework can be applied to non-NASA-related work schedules including shift-work and transmeridian travel. We are currently applying our methods to the design of schedules for medical residents, so as to provide schedules that predict optimal performance at critical times and meet new national guidelines for restricted physician hours. Abstracts have been accepted on this scheduling work and will be presented at national and international meetings.

We are developing new methods to refine the scheduling algorithm for predicting individual differences in circadian phase and performance. We are individualizing predictions based on easily collected trait information (e.g., age, chronotype), and developing a statistical framework for making individual predictions. Experimental evidence demonstrates changes in physiology are well correlated with age and specialized questionnaire results (e.g., habitual sleep time is highly correlated with circadian phase). The work of Dr. Phillips (NSBRI post-doctoral fellow) has quantified mechanisms underlying individual differences in physiologically-determined sleep timing and self-reported (subjective) chronotype (e.g., "owl" or "lark").

Using synergistic support from a NIH "Grand Opportunities" grant to Dr. Klerman, we are developing and populating a database with studies from the BWH Division of Sleep Medicine. The database has enabled a larger data set for our modeling work and will facilitate the building of individual models using demographic data as described above.

To assess the ability of individuals to conform to scheduled work hours, Dr. Phillips is integrating the circadian and performance model with a model of the physiological mechanisms which control sleep-wake transitions. This combined model dynamically predicts wake/sleep state across a simulated protocol, allowing predictions of sleep efficiency, and likelihood of falling asleep during scheduled wake periods. This model has been validated using BWH datasets; several abstracts have been published on this work. Since the model is physiologically based, it is being extended to incorporate pharmaceutical effects, including simulating the effects of melatonin and caffeine at different times and dosages.

We are targeting the use of actigraphy, which is an inexpensive and less intrusive alternative to polysomnography, to determine sleep/wake state and then use the mode to predict circadian phase and performance without other inputs. Several abstracts have been published on this work.

Our NSBRI-funded work is broadly applicable to diverse work environments, ranging from NASA missions to industries such as aviation, transportation, and the military. We are also working with the NSBRI Industry Forum to explore ways to facilitate use of our work in these diverse environments. 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:

The development of (1) mathematical models of circadian rhythms, sleep, alertness and performance, and (2) software based on these models that aid in 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 increased 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 recent FAA reports of air traffic controllers sleeping while scheduled to work at night are related to the work schedule (5 shifts in 4 days) and night-time work. The mathematical models and the available software implementing these models can be used to simulate and quantitatively evaluate different scenarios of sleep/wake schedules and light exposure to predict the resulting circadian phase and amplitude, 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.
The ease of use of the modeling has been improved by the recent incorporation of actigraphy as input of actual sleep/wake time to the mathematical model. The use of actigraphy as a tool to record sleep has improved the confidence levels on the daily assessment of sleep when compared to the use of sleep logs, as well as reduced the user requirements

Research Impact/Earth Benefits:	for maintaining daily logs. The interface between actigraphy and the Circadian Performance Simulation Software (CPSS) 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/countermeasure design program allows users to interactively design schedules and implement mathematically optimal light countermeasures (including intensity, duration and placement) 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 extended duty schedules. The software allows individuals to design countermeasures for their assigned work schedules so that their sleep and wake rhythms will be adjusted for optimal performance at desired times, both with respect to scheduled work events and with 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. The mathematical modeling has been used for basic scientific research. Inclusion of mathematical models in the planning process to optimize measures to be studied in experimental protocols enables more efficient use of research resources and directs new research. If the modeling of existing experimental data is found to be unsatisfactory, then model assumptions may need to be revised; this revision may include identification of a new physiological process not previously described. The mathematical modeling efforts and software have also been used in educational programs and in the popular press to teach students, teachers and health care professionals about circadian rhythms and sleep, work schedules and their effects on alertness and performance.
Task Progress:	Specific Aim 1 (predicting sleep-wake within scheduled sleep). We have integrated the existing circadian/performance model with a physiological model of sleep/wake transitions. This integrated model can predict whether individuals are able to conform to enforced work schedules, including estimated likelihood of insomnia during scheduled sleep periods or difficulty remaining awake during working hours. In the current year, we have been validating this integrated model against human data from a variety of sleep/wake schedule protocols. The model has now been used to relate inter-individual differences in sleep timing (e.g., self-reported chronotype) to differences in underlying physiology and provides a novel method for improving parameter estimates on an individual basis. Specific Aim 2 (actigraphy) We have integrated the output from actigraphy data with the input required to run our Circadian Performance Simulation Software (CPSS), which utilizes our mathematical model of the human circadian pacemaker, performance and alertness, that includes the key processes of circadian rhythms, sleep/wake homeostasis and sleep inertia as well as the effects of light on circadian rhythms. Pre-processing tools have been developed to generate the sleep/wake schedule and light levels from raw or processed actigraphy data. The sleep/wake and lighting schedule thus generated may be used as input to CPSS. In the current year, we have been testing the ability of outpatient actigraphy as input to CPSS to predict inpatient circadian phase for individuals with habitual sleep/wake schedules (sleep at night and wake during the day). Specific Aim 3 (Statistical modeling of individual circadian, sleep, performance and alertness parameters): We have concentrated on statistical modeling of individual circadian parameters of our circadian, performance and alertness models.to obtain a set of parameters for the performance and alertness models unique to each individual. We are using other data collected from the individual, such as age, gender, habitual sleep time, morningness/eveningness preference, etc. to determine correlations between model parameters and individual characteristics. In the current year of this project, we have been working on a new BWH Division of Sleep Medicine Database, supported by both this NSBRI grant and a NIH grant to Dr. Klerman to facilitate the development of individualized models. 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.
Bibliography Type:	Description: (Last Updated: 02/16/2021)
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