

Fiscal Year:	FY 2009	Task Last Updated:	FY 06/05/2009
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		
PI Email:	ebklerman@hms.harvard.edu	Fax:	FY 617-732-4015
PI Organization Type:	UNIVERSITY	Phone:	617-732-8145
Organization Name:	Brigham and Women's Hospital/Harvard Medical Center		
PI Address 1:	Department of Medicine		
PI Address 2:	Division of Sleep Medicine		
PI Web Page:			
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:	05/31/2012
No. of Post Docs:	1	No. of PhD Degrees:	1
No. of PhD Candidates:	3	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:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NCC 9-58-HFP01603		
Performance Goal No.:			
Performance Goal Text:	<p>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 those in space and for those on Earth. Astronaut problems with sleep, circadian rhythms and performance have been reported. NASA data indicate that sleeping pills are among the most commonly used drugs in space. Therefore, it is imperative that schedules and countermeasures are designed to optimize individual performance, alertness, and quality sleep relative to operational requirements.</p> <p>We have developed and validated a mathematical model of the human circadian pacemaker, performance and alertness</p>		

Task Description:

that includes the key processes of circadian rhythms, sleep/wake homeostasis and sleep inertia. The software implementing this model has been used by NASA and consultants when designing light countermeasures for astronaut pre-launch schedules.

For our current NSBRI project, we have developed a mathematical method for optimal design of countermeasures and schedules after a change in timing of sleep, light or critical tasks. Our specific aims are to: (1) Replace the current assumption that an individual sleeps when scheduled to sleep, with probabilities of sleep and wake during those 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. The basic mathematical work will focus on individual, rather than group, predictions and use novel non-linear mathematical and statistical measures. 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.

Rationale for HRP Directed Research:

The development (1) of mathematical models of circadian rhythms, sleep, alertness and performance and (2) of 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 extended duty schedules (pilots, train and truck drivers, shift workers, health care workers, public safety officers, etc.). Attempting to sleep at adverse circadian phases is difficult and sleep efficiency is poor. Attempting to work at adverse circadian phases and/or after long durations of time awake results in poor worker performance and productivity, increased accidents and decreased safety for workers and for others affected by the workers. For example, the accidents at the Chernobyl and Three Mile Island nuclear reactors and the Exxon Valdez grounding all were partially caused by workers working at adverse circadian phases (~ 4 am). The mathematical modeling and the available Circadian Performance Simulation Software (CPSS) 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. CPSS has been requested by members of academia, government and industry (transportation (especially airline personnel), safety, medical, military). Its use could help produce improved schedules for working for people in space and on earth. The software also now includes optimal countermeasure design, so that countermeasures can be planned for times of predicted poor performance and alertness. The schedule/countermeasure design program that allows a user to interactively design a schedule and to automatically design a mathematically optimal countermeasure regime (intensity, duration and placement). This will be valuable to those who schedule people who work at night, on rotating schedules, on non-24-hr schedules or extended duty schedules. Individuals can design countermeasures for their assigned work schedules so that their sleep and wake rhythms will be adjusted for optimal performance at desired times. In addition, if the countermeasure design includes shifting the circadian rhythms to be appropriately aligned with environmental time, then performance, alertness and sleep will all improve. Improving sleep duration and quality can also decrease the risk of accidents and errors, as well as cardiovascular, metabolic, immune and psychological pathologies.

Research Impact/Earth Benefits:

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 data is unsatisfactory, then the model assumptions need to be revised. This revision may include identification of a new physiological process not previously described. As an example, an additional component (non-linear response to ocular light stimuli) was added to the circadian rhythms component of our mathematical model to describe data collected in our clinical research facilities, even before the anatomic and physiologic basis of this component of the mathematical model was found. Later experiments validated this mathematical finding. The mathematical model had demonstrated that previously unknown additional physiological processes were involved.

The modeling work on the differential effects of different wavelength of light on circadian rhythms and alertness can be used for designing artificial (indoor) lighting systems that can maximize circadian or alerting response.

The mathematical modeling efforts and CPSS 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.

For our first year, we have concentrated on Specific Aim 2, with preliminary work on the other Specific Aims. Specific Aim 2 (Improve the assessment of sleep and sleep disruption through the development of an improved actigraphy-to-sleep/wake classification algorithm): We developed a new sleep-wake classification algorithm that has been tested on actigraphy data collected under various conditions. A new algorithm exploits the assumption that there exists an implicit bimodal distribution in the actigraphy time series and that the extraction of this can clearly segregate sleep and wake cycles. A statistical bimodal distribution is not possible to obtain directly from the time series due to the presence of both inflated zeros and over-dispersion that result in a zero-inflated negative binomial distribution. Therefore we have developed a new method by which bimodal distribution obtained can be indirectly related to sleep-wake epochs of the activity count data.

Specificity, sensitivity, accuracy and predictive value of sleep and wake are determined by comparing epoch by epoch of actigraph data with that of polysomnographic data to test the algorithm. Both high specificity and sensitivity are obtained by the application of present algorithm; in contrast, most of the published algorithms have either high sensitivity or specificity, but not both. This algorithm also has high sensitivity and specificity using the data collected from two different instruments (Actiwatch and Motionlogger): therefore this algorithm works well irrespective of the instrument or the way data is collected.

Task Progress:

As future work, actigraphy data collected under habitual conditions, under conditions of quiet extended wake (which is difficult to distinguish from sleep), under conditions of forced desynchrony of sleep/wake cycle and circadian rhythms (to explore the effect of circadian phase) and under conditions of extended sleep (which induces insomnia or quiet wake during scheduled sleep, which is also difficult to differentiate from sleep) will be determined to further test the performance of the algorithm and will be compared with other threshold algorithms. Two manuscripts of this work are in preparation.

Specific Aim 3 (Statistical modeling of individual circadian, sleep, performance and alertness parameters): We have

	<p>begun the first step in this work by concentrating on statistical modeling of individual circadian parameters.</p> <p>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.</p>
Bibliography Type:	Description: (Last Updated: 02/16/2021)
Abstracts for Journals and Proceedings	<p>Dead DA, Wyatt JK, Dijk D, Czeisler CA, Klerman EB. "Quantifying practice effects within groups and individuals: examples from a month long forced desynchrony protocol." Sleep 2008, 22nd Annual Meeting, Balitmore, MD, June 7-12, 2008. Sleep. 2008;31(Suppl): A54. , Jun-2008</p>
Abstracts for Journals and Proceedings	<p>St Hilaire MA, Klerman EB. "Robustness of parameters in a circadian and neurobehavioral performance and alertness model suggest trait-like characteristics of the homeostatic process." Sleep 2008, 22nd Annual Meeting, Balitmore, MD, June 7-12, 2008. Sleep 2008:31(Suppl):A117. , Jun-2008</p>
Abstracts for Journals and Proceedings	<p>St Hilaire MA, Klerman EB. "Pattern recognition algorithms to classify performance on the psychomotor vigilance task." 2009 International Conference on Fatigue Management in Transportation Operations: A Framework for Progress, Boston, MA, March 24-26, 2009. 2009 International Conference on Fatigue Management in Transportation Operations: A Framework for Progress, Abstract Book, March 2009. , Mar-2009</p>
Abstracts for Journals and Proceedings	<p>Torgovitsky R, Wang W, De Gruttola V, Klerman EB. "Subject-specific evaluation of performance based on forced desynchrony data." 2009 International Conference on Fatigue Management in Transportation Operations: A Framework for Progress, Boston, MA, March 24-26, 2009. 2009 International Conference on Fatigue Management in Transportation Operations: A Framework for Progress, Abstract Book, March 2009. , Mar-2009</p>