Fiscal Year:	FY 2005	**Task Last Updated:**	FY 01/04/2007
PI Name:	Klerman, Elizabeth B. M.D., Ph.D.		
Project Title:	Mathematical Modeling of Circadian/Performance Countermeasures		
Division Name:	Human Research		
Program/Discipline:	NSBRI Teams		
Program/Discipline--Element/Subdiscipline:	NSBRI Teams--Human Performance Factors, Sleep, and Chronobiology 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 (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		
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:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
Start Date:	06/01/2004	**End Date:**	05/31/2008
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:	3	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
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Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NCC 9-58-HPF00405		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Objective neurobehavioral performance, subjective alertness and mood, and sleep are critically important to astronaut health and the success of space missions. Neurobehavioral performance, alertness and mood are affected by circadian rhythms, homeostatic sleep regulation, sleep inertia, and interactions of these processes. Countermeasures to ensure optimal neurobehavioral performance, subjective alertness, and quality sleep therefore are required for space missions, during which circadian rhythms and sleep are disrupted. We have developed and validated a mathematical model of the human circadian pacemaker and neurobehavioral performance and alertness that includes these three key processes. A previous version of this model, with a focus on light-dark scheduling, has been used by NASA to design astronaut pre-launch schedules. We propose to extend this model to be useful in testing emerging countermeasures for neurobehavioral problems due to space missions. Since the potential countermeasures, singly or in combination, are different for each crewmember on each mission, it would be difficult, time consuming and expensive to conduct all the experimental protocols required to mimic all combinations of possible situations and proposed countermeasures received by any given crewmember. A mathematical model, on the other hand, is a powerful tool for the design of countermeasures because there are no limits to the number of patterns of astronaut light exposure or sleep/wake schedules and countermeasures that can be efficiently assessed. Our model is available for use via a user-friendly software program for users to test countermeasures. We propose to extend the current model so that it will include: (1) melatonin markers of circadian amplitude and phase; (2) chronic sleep restriction and its effects on neurobehavioral performance; and (3) the effects of specific wavelengths of light on the circadian pacemaker. Then we will amend our current software to include schedule assessment and countermeasure design components. We will cooperate with other members of the selected NSBRI Human Performance Factors team: simulating their protocols, modeling the data and adjusting and re-validating the model as required. The mathematical modeling of circadian rhythms, sleep, subjective alertness and mood, and neurobehavioral performance is a vital and effective component of design and testing of potential countermeasures for optimal astronaut health and mission success. Our Specific Aims are: Specific Aim 1: Develop and refine the current circadian, neurobehavioral performance and subjective alertness (CNPA) model with melatonin as a marker rhythm to accurately predict phase and amplitude of the circadian pacemaker (Countermeasure Readiness Level (CRL) 4) Specific Aim 2: Refine and validate the current CNPA model by using data from chronic sleep restriction protocols (CRL 4) Specific Aim 3: Refine the current CNPA model to incorporate wavelength of light information (CRL 3) Specific Aim 4: Develop Schedule Assessment and Countermeasure Design Software using the amended CPNA model from Specific Aims 1, 2 and 3 to evaluate schedules and design and test appropriate countermeasures (CRL 5) .
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This work advances science and applications in other areas besides our specific aims. This research focuses on the further development of mathematical models and software that aid in schedule design to improve performance and thereby public safety for people who work at night, on rotating schedules, on non-24 h schedules or extended duty schedules. (pilots, train and truck drivers, shift workers, health care workers, public safety officers, etc.). The mathematical modeling and the available CPSS software can be used to simulate different scenarios of sleep/wake schedules and light exposure and predict the resulting circadian phase and amplitude, subjective alertness and neurobehavioral performance. Attempting to sleep at adverse circadian phases is difficult and the sleep efficiency is poor. Attempting to work at adverse circadian phases and/or after long durations of time awake causes poor worker performance and productivity, increased accidents and decreased safety for workers and for others affected by the workers. For example, the accidents at Chernobyl and Three Mile Island nuclear reactors and the Exxon Valdez grounding all were partially caused by workers attempting to perform at adverse circadian phases (~ 4 am). CPSS has been requested by members of academia, government and industry. Its use could help produce improved schedules for working. The development of optimal and interactive scheduling tools will also be applicable to earth-based industry and government.
Task Progress:	Specific Aims 1, 3, 4 plus the requested work on inter-individual differences are currently in progress. For Specific Aim 1, we have begun to test a physiologic-based mathematical model of plasma melatonin levels on existing datasets. For Specific Aim 3, a new component has been added to the current model that incorporates wavelength of light information. This new model is capable of predicting the effect of wavelength on the phase-shifting response of the human circadian pacemaker using wavelength and lux as light inputs. For Specific Aim 4, we have developed a methodology for using mathematical models of the effect of light on the circadian pacemaker to automatically generate optimal circadian adjustment schedules that can be applied to our existing user-friendly Circadian Performance Simulation Software (CPSS). For the inter-individual work, which was not in our original proposal, we have begun work to include inter-individual differences in our model. We have begun to look at different methods to incorporate these differences. We are currently working with Dr. Laura Barger, who has worked on both NSBRI and NASA projects, to develop methods to evaluate actigraphy data collected in space and on the ground. Pre-flight prediction of the circadian load of the sleep-wake shift, as determined by our models, is provided prior to launch. Actigraphy data will provide information about the individual sleep/wake and light exposure of each individual; this information can be used to target the model simulations for each individuals.
Bibliography Type:	Description: (Last Updated: 06/25/2025)
Articles in Peer-reviewed Journals	Indic P, Forger DB, St Hilaire MA, Dean DA 2nd, Brown EN, Kronauer RE, Klerman EB, Jewett ME. "Comparison of amplitude recovery dynamics of two limit cycle oscillator models of the human circadian pacemaker." Chronobiol Int. 2005;22(4):613-29. PMID: 16147894 , Sep-2005