Fiscal Year:	FY 2015	**Task Last Updated:**	FY 07/30/2014
PI Name:	Shea, Steven Ph.D.		
Project Title:	Identification of cardiometabolic vulnerabilities caused by effects of synergistic stressors that are commonly encountered during space missions		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
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:	NOTE: PI currently at Oregon Health & Science University as of June 2016.		
Project Type:	GROUND	**Solicitation / Funding Source:**	2009 Crew Health NNJ09ZSA002N
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No. of Post Docs:	1	**No. of PhD Degrees:**	0
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No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:	NOTE: Extended to 9/30/2015, per PI and NSSC information (Ed., 8/5/14)		
Key Personnel Changes/Previous PI:	July 2013: Since the last annual report, Matthew Butler, PhD has reduced effort and David Barr, PhD has assumed Dr. Butler's project leader duties.		
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Task Description:	The risk of adverse cardiac events has been listed as Priority 1 in the NASA Bioastronautics Roadmap (Risk Areas 5 and 6; 2005; http://bioastroroadmap.nasa.gov). Under extremely physiologically challenging circumstances, i.e. microgravity, astronauts are expected to perform tasks that add additional physical and mental stress to their cardiovascular system such as space walks or robotic operations during EVAs. During space missions astronauts are exposed to unusual light-dark cycles (e.g. Martian day length: 24.65 hrs) that would be expected to cause circadian misalignment resulting in sleep disturbances, sleep loss, and poor quality sleep. In addition, almost all astronauts report chronic sleep curtailment due to mission requirements such as working 'slam shifts' before EVAs and extended shifts during EVAs. The sleeping conditions on the ISS, e.g. cramped crew quarters, noise, and heat, also add to the reported sleep curtailment. Data from laboratory and epidemiological studies have shown that chronic sleep curtailment and circadian misalignment changes endocrine, inflammatory, and cardiovascular function; changes that potentially result in adverse health events, including cardiac arrhythmias, myocardial and peripheral vascular dysfunction, risk of syncope, hypertension, diabetes, and metabolic syndrome. Moreover, adverse cardiac events show a clear day-night pattern, with a peak in the morning. In addition, it is well know than microgravity itself impacts cardiovascular functioning resulting in decreased circulating blood volume, decreased central venous blood pressure, increased stroke volume and increased cardiac output, potentially leading to cardiac rhythm disturbances that have been documented during spaceflight previously. To date we know little to nothing about the synergetic effects of chronic sleep restriction, circadian misalignment, and physical and mental stressors on cardiovascular functioning. The main goals of this NASA project are (1) to characterize the alterations (and potential maladaptations) of cardiovascular function (i.e. hemodynamic, autonomous nervous functioning, cardiac vulnerability) associated with chronic sleep restriction and circadian misalignment potentially occurring during space missions; (2) to characterize the effects of different types of stressors (postural, exercise, and mental stressors; except microgravity) on cardiovascular functioning; and (3) to identify the synergetic effects of chronic sleep restriction, circadian misalignment, and different stressors, potentially identifying vulnerable periods with an increased likelihood of adverse cardiac events during space missions. Our studies of sleep and circadian stressors on cardiovascular performance are relevant to astronauts in space flight as well as the many workers on Earth who experience similar conditions, albeit with gravity, during shift work.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Curtailed sleep and circadian disruptions are common features of modern life, on Earth as well as in space. Night-shift work is common among factory workers, police, fire fighters, and nurses, and such work has been identified as a risk factor for a host of diseases, including cardiovascular disease, stroke, and metabolic disorders. Our work therefore stands to impact health in astronauts, health in workers on earth, and may point to countermeasures and improvements in work-schedule design. The risk of adverse cardiac events has been listed as Priority 1 in the NASA Bioastronautics Roadmap (Risk Areas 5 and 6; 2005; http://bioastroroadmap.nasa.gov). This project specially aims to address gaps CV1 which asks "What are the in-flight alterations in cardiac structure and function?" and Gap CV8 which asks "Can manifestations of sub-clinical or environmentally induced cardiovascular diseases during spaceflight be predicted?" Cardiac arrhythmias have been observed in astronauts and are considered a major risk endangering the success of space missions. In addition to myocardial structural changes, such arrhythmias can be triggered by numerous interacting and summating stressors (e.g., exercise, sleep loss, working during the biological night ['circadian misalignment']) causing changes in cardiovascular risk markers, such as increased blood pressure, cardiac vagal withdrawal, sympathetic activation, and promotion of hemostatic mechanisms. Current research in this focus area examines the clinical expression of cardiac atrophy by using in-flight Holter monitoring and ultrasound assessment of potentially long-term changes in cardiac structure and function with spaceflight (e.g., pre-flight, every 2-4 weeks during flight, and post-flight). Our current study complements these ongoing research activities by elucidating the effects on cardiovascular risk markers of two of the most debilitating aspects of space flight: circadian misalignment and chronic sleep loss. Moreover, to realistically simulate the stresses encountered by astronauts, we are assessing the synergistic effect of behavioral stressors together with the effects of circadian misalignment and prolonged sleep loss. Our project has implications to Risk #27 - Risk of Performance Errors Due to Sleep Loss, Circadian Desynchronization, Fatigue, and Work Overload [Behavioral Health and Performance (BHP) Element of the HRP]. BHP focuses on the effects of sleep loss, fatigue, circadian misalignment and work overload on performance. Current countermeasures under investigation include recommendations concerning sleep hygiene, work-rest schedules, and optimal lighting requirements for the space vehicle, as well as safe and efficacious methods for implementing lighting as a countermeasure. Specifically, we share interest with the following identified gaps: •Sleep 4 - How can individual astronauts' vulnerabilities to sleep loss and circadian rhythms best be determined?; •Sleep 5 - How can light be used to optimally minimize circadian problems in space; •Sleep 8 - How are physical and cognitive workloads managed optimally in space relative to fatigue and recovery? Knowledge about impaired cardiovascular function and periods of vulnerability for adverse cardiac events would contribute substantially to the above mentioned gaps and would enable knowledge integration between the Cardiovascular Alterations Team and the Human Factors and Performance Team. Astronauts experience circadian misalignment, sleep loss, and different mental and physical stressors during missions; it is possible that these conditions contribute to sub-optimal cardiovascular function and that these effects will be exacerbated by stressors such as exercise during EVAs and postural stresses on return to Earth. Nevertheless, to date, we have little-to-no knowledge about how the relevant hemodynamic, autonomic, hemostatic, vascular, and endothelial biomarkers that comprise our dependent variables, react to simultaneous challenging circumstances of circadian misalignment, sleep loss and physical or mental exertion/stress. Once the effects of circadian misalignment, sleep loss, and different stressors are determined and vulnerable periods are identified, we hope to develop measures to alleviate or limit the risks by both ensuring proper circadian entrainment and sleep, and by ensuring activities that particularly challenge the cardiovascular system are avoided at specific vulnerable states of circadian misalignment and sleep loss. This could inform a new gap related to 'inter-individual vulnerabilities' to challenging work environments, including countermeasures and improvements of already existing challenging work environments (space flight and shift work), and better screening tools for future employees experiencing these work environments. Finally, our previous work with healthy volunteers on Earth has shown that circadian disruption adversely affects metabolism and cardiovascular reactivity to stressors; two results with broad impact for society on Earth. The current project extends this work to consider the impact of short sleep, common across modern society, on how the circadian

	clock controls times of metabolic and cardiovascular vulnerability.
Task Progress:	We are studying healthy subjects throughout a within-subject design, with each subject undergoing two 11-day circadian misalignment protocols, achieved by advancing sleep periods by 4 hours every day (i.e., recurring 20 h 'days'). One protocol provides adequate sleep (8.33 h of sleep opportunity per 20 h 'day'; equivalent to 10 h of sleep opportunity per 24 h day) while the other protocol provides only 5 h of sleep opportunity per 20 h 'day' (equivalent to 6 h of sleep opportunity per 24 h day), thereby mimicking the average reported sleep duration of astronauts. In both protocols, subjects perform a stress battery each experimental 'day' while their responses to mental, exercise (bicycle), and postural (tilt-table) stresses are assessed. For each stressor we record baseline, stress-related, and recovery data. Cardiovascular function is assessed by markers of hemodynamic, hemostatic, autonomic, and vascular endothelial function. Using this approach, with subjects in conditions free of time cues, the effects of the stressors are being assessed at all phases of the internal biological clock. In addition to these variables obtained daily, all subjects participate in an intensive clinically relevant cardiovascular test battery before and after the sleep and circadian treatments. These include echocardiography to measure heart function and structure, brachial artery ultrasound to examine blood vessel function and stiffness, a maximum exercise test, and a longer postural stress to assess blood pressure regulation, including susceptibility to syncope. Recruiting Report : To date we have received calls from 2148 people, of whom 125 were deemed eligible, available to participate, and were sufficiently interested to give their consent to start the screening procedures. Of these 125 subjects, 98 were found to be ineligible based on tests and/or examinations results and in a few cases because of a subject's inability or unwillingness to liberate the many weeks of free time required for successful participation in the study. The remaining 27 subjects all gave informed consent for participation in the intensive research phase of the study. Prior to entry in the lab, 8 subjects either withdrew or were excluded from the study. Some of the reasons for withdrawal were non compliance to required sleep wake cycle, low fitness levels determined from maximal exercise test, loss of interest or changes in personal circumstances impacting ability to commit the time required for the in-laboratory stays in the hospital. We intended to study 16 subjects in the laboratory. We initiated in-patient studies in the remaining 19 participants, 14 have completed the protocol successfully, with only partial data sets from the remaining 5 participants who did not fully complete both of the 11-day in-lab studies. Data Analysis and Results. This project covers one experiment with two randomized, single blind conditions. Thus, we cannot yet report un-blinded results until all group analyses have been performed. We are beginning data analysis of individuals and preparing for group analysis. We anticipate all group analyses, including un-blinding, will be completed by early 2015.
Bibliography Type:	Description: (Last Updated: 08/14/2018)
Abstracts for Journals and Proceedings	Barr DA, Butler MP, Rueger M, Myers S, Ollmann A, Smales C, Tzingantcheva AD, Crucian BE, Mehta SK, Pierson DL, Quiriarte H, Scheer FAJL, Shea SA. "BLINDED PRELIMINARY DATA: Identification of cardiometabolic vulnerabilities caused by effects of synergistic stressors commonly encountered during space missions." 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. , Feb-2014