Fiscal Year:	FY 2015	**Task Last Updated:**	FY 04/03/2015
PI Name:	Lee, Michael L Ph.D.		
Project Title:	Assessing the Impact of Chronic Sleep Restriction on Sleep and Performance-Associated Regional Brain Activation Using Near-Infrared Spectroscopy		
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		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	mllee@partners.org	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	617-525-8558
Organization Name:	Brigham and Women's Hospital		
PI Address 1:	Brigham and Women's Hospital		
PI Address 2:	Division of Sleep and Circadian Disorders		
PI Web Page:			
City:	Boston	**State:**	MA
Zip Code:	02115	**Congressional District:**	8
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2012 NSBRI-RFA-12-02 Postdoctoral Fellowships
Start Date:	11/01/2012	**End Date:**	10/31/2014
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Klerman, Elizabeth Ph.D. (MENTOR/ Brigham and Women's Hospital) Strangman, Gary (Massachusetts General Hospital)		
Grant/Contract No.:	NCC 9-58-PF03002		
Performance Goal No.:			
Performance Goal Text:			

POSTDOCTORAL FELLOWSHIP

Task Description:

NASA astronauts and ground crew need to maintain high levels of cognitive performance to ensure successful completion of space missions and safety of astronauts. Astronauts and ground crew are exposed to sleep loss arising from the shifting and extended work schedules often associated with their missions. Therefore, astronauts and ground crew are at risk for fatigue-related accidents. Accurate diagnosis of fatigue is a major challenge. Subjective sleepiness is reported significantly less often than observed objective performance decrements, indicating that self-diagnosis is inaccurate. Sleep deprivation reduces activation in the prefrontal cortex (PFC), a brain region important for cognitive performance. A recently-developed technology, through National Space Biomedical Research Institute (NSBRI) support to Dr. Gary Strangman (co-mentor on this project), quantifies hemodynamic changes in oxygenated and deoxygenated blood within specific brain regions using Near-Infrared Spectroscopy (NIRS). Standard methodology for assessing hemodynamic changes requires large, expensive functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) techniques that are impractical for use in space or most work environments. In contrast, ambulatory NIRS monitoring is relatively portable, inexpensive, simple to apply and can record over 24 hours of data in a single session.

We used NIRS technology to examine PFC activity in experimental volunteers participating in inpatient chronic sleep restriction (CSR) and acute sleep deprivation (ASD) protocols. NIRS monitoring during these protocols allowed us to address the specific aims of the project: 1) To test the hypothesis that hemodynamic responses in the PFC to the psychomotor vigilance task (PVT) will exhibit a circadian rhythm. 2) To test the hypothesis that hemodynamic responses in the PFC to the PVT will be reduced during CSR and ASD. 3) To test the hypothesis that hemodynamic fluctuations in the PFC are associated with PVT performance deficits.

In the past two years, we have successfully collected NIRS recordings from over 1000 cognitive performance testing sessions at multiple circadian phases in 9 participants on the CSR protocol and over 150 testing sessions in 13 participants on the ASD protocol. PFC hemodynamic responses throughout each PVT session were quantified using both block averaging and deconvolution techniques. Metrics of the hemodynamic response, including peak amplitude and area under the curve (AUC) were included in mixed-model analyses with circadian phase, length of time awake, and CSR or non-CSR condition as discrete variables. We identified a significant effect of length of time awake and circadian phase on hemodynamic response using the block-averaged method, addressing Specific Aim 1. We did not find a significant effect of CSR on hemodynamic response, addressing Specific Aim 2. Analyses of the effect of ASD on hemodynamic response are pending. To address Specific Aim 3, we assessed the relationship between PFC hemodynamic response and PVT performance using the deconvolution method, since it allows use of all data for each PVT session. We found that PVT sessions with HbO_2 peak amplitude or AUC less than baseline median were significantly more likely to contain PVT lapses. When peak amplitude was below baseline median compared to above baseline, the relative risk of PVT lapse was 2.0.

The findings from this study demonstrate the potential use of NIRS technology to objectively monitor PFC decrements associated with reduced performance. NIRS monitoring of PFC may lead to the improved identification and prediction of decreased performance and times of sleepiness in shift-working populations, including astronauts, ground crew, firefighters, pilots, health care providers, truck drivers, and military personnel and therefore reduce fatigue-related accidents.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Our current funded project is important not only to the space program, but to the general population. Astronauts and ground crew face challenges during a space mission that disrupt sleep and circadian alignment that can lead to increased risk of fatigue-related accidents. Sleep loss and circadian misalignment are prevalent amongst the 15% of the US labor force that participates in shift work, including rotating, evening, and/or night shifts. Ground-based professions that require shift work schedules include health care professionals (e.g., physicians, nurses, pharmacists), air traffic controllers, pilots, and commercial drivers, all of whom frequently perform tasks that require high levels of attention and cognitive function under conditions of sleepiness. Fatigue impairs attention and increases risk of accidents that can result in injury, death, or significant monetary loss. Therefore, fatigue-induced cognitive impairment poses a serious risk to the success of space missions and ground-based operations. Understanding and diagnosing such impairment would be of great benefit in many critical operations on Earth. The prefrontal cortex (PFC) brain region is easily accessible to NIRS imaging. This study investigated the impact of chronic sleep restriction (CSR) on the PFC using NIRS imaging. We found PFC activation is dependent upon circadian phase and length of time awake. We also found an inverse relationship between PFC activation and PVT performance. The findings from this study may help improve the identification of vulnerable times of decreased performance in populations susceptible to fatigue-related accidents. This study was the first to monitor activity in the PFC with NIRS during cognitive performance testing while an individual experiences CSR. Results from this study demonstrate the potentially low-cost, effective use of NIRS to detect performance impairment, objectively monitor fatigue, and may lead to reduction in fatigue-related accidents with important applications for the successful completion of NASA space missions and the health and safety of the general population.

Task Progress:

During the 2 years of NSBRI First Award support, Dr. Lee made substantial progress in addressing the specific aims. Data was collected using Near-Infrared Spectroscopy (NIRS) on a 32-day National Institutes of Health (NIH) chronic sleep restriction (CSR) study and 8-day NSBRI acute sleep deprivation (ASD) study. We collected NIRS recordings from over 1000 cognitive performance testing sessions (from 9 participants) during the 32-day CSR study and over 150 testing sessions from 13 participants during an 8-day ASD protocol. We modified analysis software developed by Dr. Strangman for use in our experimental conditions. Assessment of the hemodynamic response to individual psychomotor vigilance task (PVT) trial presentation reveals after ~2.5 seconds, an increase in oxygenated hemoglobin, followed by return to baseline, while deoxygenated hemoglobin shows an inverse response. This pattern of hemodynamic response has been described in the visual cortex in previous studies using visual stimuli and demonstrates the operational success of the data collection.

For Specific Aim 1, NIRS data relative to melatonin phase (a circadian marker) were used to quantify the circadian rhythmicity in the hemodynamic response in the prefrontal cortex (PFC) in response to PVT presentation. We found a significant effect of circadian phase and length of time awake on PFC activation.

For Specific Aim 2, comparisons of hemodynamic responses to PVT from the beginning of the CSR protocol compared

	to responses at the end of the CSR protocol and between CSR and control participants were used to quantify the impact of CSR on brain activation in the PFC. We did not find a significant effect of CSR on PFC activation. For Specific Aim 3, the PFC response and PVT lapses were analyzed between baseline and non-baseline days to identify a relationship between PFC activation and PVT performance. When PFC activation was lower than baseline, we found a significantly higher relative risk of PVT lapses in the same session.
Bibliography Type:	Description: (Last Updated: 08/25/2020)
Abstracts for Journals and Proceedings	Lee ML, Howard ME, Horrey WJ, Liang Y, Anderson C, Shreeve M, O'Brien C, Czeisler CA. "Drowsiness, impaired driving performance and critical driving events among shift workers driving an actual motor vehicle after night shift work." SLEEP 2013—27th Associated Professional Sleep Societies LLC (APSS) Annual Meeting, Baltimore, MD, June 1-5, 2013. Sleep. 2013;36(Abstract Suppl):A63. Abstract 0167. http://www.journalsleep.org/Resources/Documents/2013AbstractSupplement.pdf , Jun-2013
Abstracts for Journals and Proceedings	Lee ML, Strangman GE, Hull JT, Kamath T, Rahman SA, Lockley SW, Lockhandwala J, Zhang Q, Czeisler C, Klerman EB. "Assessing the Impact of Chronic Sleep Restriction and Acute Sleep Deprivation on Performance-Associated Regional Brain Activation using Near Infrared Spectroscopy." SRBR 2014. 14th Biennial Meeting, Society for Research on Biological Rhythms (SRBR), Big Sky, Montana, June 14-18, 2014. Program and Abstracts. SRBR 2014. 14th Biennial Meeting, Society for Research on Biological Rhythms (SRBR), Big Sky, Montana, June 14-18, 2014. Abstract P10, p. 122. http://srbr.org/wp-content/uploads/2015/02/SRBR2014ShortProgramv4.pdf ; accessed 4/8/15. , Jun-2014
Abstracts for Journals and Proceedings	Lee ML, Strangman GE, Hull JT, Kamath T, Wang W, Rahman SA, Lockley SW, Ivkovic V, Zhang Q, Klerman EB. "Assessing the Impact of Chronic Sleep Restriction on Sleep and Performance-Associated Regional Brain Activation Using Near Infrared Spectroscopy." 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. http://www.hou.usra.edu/meetings/hrp2014/pdf/3284.pdf ; accessed 5/21/15. , Feb-2014
Abstracts for Journals and Proceedings	Lee ML, Strangman GE, Hull JT, Rahman SA, Lockley SW, Ivkovic V, Zhang Q, Klerman EB. "Assessing the Impact of Chronic Sleep Restriction and Acute Sleep Deprivation on Performance-Associated Regional Brain Activation Using Near Infrared Spectroscopy." SLEEP 2014, 28th Annual Meeting of the Associated Professional Sleep Societies, Minneapolis MN, May 31-June 4, 2014. Sleep. 2014;37(Abstract Suppl):A82-A33. Abstract 0228. http://www.journalsleep.org/Resources/Documents/2014AbstractSupplement.pdf ; accessed 5/21/15. , Jun-2014
Abstracts for Journals and Proceedings	Lee ML, Zhang Q, Strangman GE, Klerman EB. "Assessing the Impact of Chronic Sleep Restriction on Sleep and Performance-Associated Regional Brain Activation Using Near Infrared Spectroscopy." 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. , Feb-2013
Articles in Peer-reviewed Journals	Lee ML, Howard ME, Horrey WJ, Liang Y, Anderson C, Shreeve M, O'Brien C, Czeisler CA. "High risk of near-crash driving events following night-shift work." Proc Natl Acad Sci U S A. 2016 Jan 5;113(1):176-81. https://doi.org/10.1073/pnas.1510383112 ; PMID: 26699470; PMCID: PMC4711869 [note reported previously in May 2015 as "Submitted"] , Jan-2016
Articles in Peer-reviewed Journals	Liang Y, Horrey WJ, Howard ME, Lee ML, Anderson C, Shreeve MS, O'Brien CS, Czeisler CA. "Prediction of drowsiness events in night shift workers during morning driving. " Accid Anal Prev. 2019 May;126:105-14. Epub 2017 Nov 7. https://doi.org/10.1016/j.aap.2017.11.004 ; PMID: 29126462 , May-2019
Awards	Lee M. (Michael Lee) "Runner-Up: Dr. David Watson Postdoctoral Fellow Poster Contest, February 2014." Feb-2014
Awards	Lee M. (Michael Lee) "SRS Abstract Meritorious Award. Sleep Research Society, June 2013." Jun-2013
Books/Book Chapters	de la Iglesia HO, Lee ML. "A time to wake, a time to sleep." in "Mechanisms of Circadian Systems in Animals and Their Clinical Relevance." Ed. R. Aguilar-Roblero, M. Díaz-Muñoz, M.L. Fanjul-Moles. New York, NY: Springer Publishing, 2015. p. 197-217. http://dx.doi.org/10.1007/978-3-319-08945-4_11 , Jan-2015
Significant Media Coverage	Lee ML, Howard M, Horrey W, Liang Y, Anderson C, Shreeve M. O'Brien C, Czeisler C. "Asleep at the Wheel ... and You Don't Even Know It! News coverage of this research on The Rachael Ray Show." News coverage of this research on The Rachael Ray Show. Aired May 15, 2013. http://www.rachaelrayshow.com/lifestyle/health/7879_Asleep_at_the_Wheel_and_You_Dont_Even_Know_It/ ; accessed 5/21/15., May-2013