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Project Title:	Evaluation of Photic Countermeasures for Circadian Entrainment of Neurobehavioral Performance and Sleep-Wake Regulation Before and During Spaceflight		
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Program/Discipline--Element/Subdiscipline:	NSBRI--Human Factors and Performance Team		
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COI Name (Institution):	Barger, Laura (Brigham and Women's Hospital) Aeschbach, Daniel (Brigham and Women's Hospital)		
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Task Description:

To synchronize astronauts' circadian sleep-wake schedules to variable launch times, timed exposure to bright light and darkness in the crew quarters during the week-long pre-launch quarantine period has been used since 1990. Although successful at circadian entrainment, bright light protocols are complex to administer and astronauts' compliance is compromised because bright light glare compromises computer/television screen visibility, and increased frequency of headaches, irritability and nausea. Moreover, bright light remains unavailable as an in-flight countermeasure, requiring astronauts to rely upon hypnotics or wake-promoting therapeutics to provide symptomatic relief. Recent advances reveal that the human circadian pacemaker is most sensitive to shorter wavelength light for both phase shifting and direct enhancement of alertness and performance. We found that short-wavelength light (~460nm-512nm) in the blue/green range facilitates circadian phase shifting. We therefore propose to test the efficacy of exposure to short wavelength green light at a standard intensity for pre-launch and in-flight phase shifting.

To this end, we propose to test the circadian phase-shifting efficacy of exposure to short wavelength light throughout scheduled wake times on a protocol designed to simulate the schedule of crew members during the pre-launch quarantine period on a mission that requires an 8-hour phase advance of the sleep-wake schedule. Our goal is to demonstrate that exposure to ambient short wavelength fluorescent light will synchronize human circadian rhythms to a shifted sleep/wake schedule within 4-5 days, enhancing alertness and performance during the biological night.

During this proposed 8-day ground-based simulation, participants' sleep-wake schedules will be advanced by 8 hours. This advance shift will be done in 2 different protocol designs: 1) a "slam" shift in which the sleep episode is abruptly advanced by 8 hours and then maintained at this advanced time for 4 days, and 2) a gradual shift in which the sleep episode is advanced by 1.6 hours each day for 5 days until an 8 hour advance is achieved. A total of 44 subjects will be randomized to 1 of 4 protocol conditions which differ by light (ordinary indoor white light (~90 lux) or 90 lux polychromatic green light) and by shift (slam or gradual) resulting in 11 subjects/group. The 4 conditions are 1) white light slam shift, 2) green light slam shift, 3) white light gradual shift, and 4) green light gradual shift.

Our specific aims are to test the hypothesis that:

1. Exposure to ambient polychromatic short wavelength light from fluorescent lamps will be more effective than exposure to an equal illuminance of ambient polychromatic white light from standard fluorescent lamps in shifting the circadian rhythms of test subjects, as measured by dim-light melatonin onset (DLMO), in response to both a gradual 8-hour advance and to an abrupt shift of their sleep-wake schedule.
2. Alertness and neurobehavioral performance in dim light on a constant routine during times at which crew members should be awake on the simulated mission will be significantly greater following 4-5 days of exposure to ambient polychromatic green light vs. ambient white light of equal illuminance, due to more effective circadian entrainment.
3. Alertness and neurobehavioral performance will be significantly better on the first night of exposure to ambient polychromatic short wavelength light vs. ambient white light of equal illuminance, prior to the induced circadian phase shifts, due to the immediate alerting effects of exposure to ambient polychromatic short wavelength light.
4. Sleep efficiency and total sleep time will be significantly increased and latency to persistent sleep and wake time after sleep onset will be significantly decreased during the sleep episode following 4-5 days of exposure to ambient polychromatic green light vs. ambient white light of equal illuminance, due to more effective circadian entrainment.

We predict that, in contrast to white light, simple exposure to polychromatic green light throughout the day will rapidly (within five days) entrain the circadian melatonin rhythm to the shifted sleep-wake schedule, without the need for bright light exposure-rendering obsolete the crew quarters' bright light facility and enabling implementation of this new technology to ensure circadian synchronization both during the pre-flight quarantine period and while aboard NASA flight vehicles.

To date, 22 subjects have completed the 8-day protocol. Four subjects completed the white light slam shift condition in order for us to determine the best level of illuminance to be used for both the white and polychromatic green light. Melatonin samples, alertness and performance testing data, and sleep recording data were collected in these studies and are currently being analyzed to address our specific aims. Based on the melatonin results from the first 4 subjects, we proceeded to use a 90 lux level of illuminance, which is equivalent to that of ordinary indoor room light. We began randomizing enrolled subjects after completing the initial 4 subjects, with a further 18 subjects completing the protocol: 10 subjects have completed the gradual shift protocol, in either polychromatic white (n=5) or shorter-wavelength light (n=5), and 8 subjects have completed the slam shift protocol, in either polychromatic white light (n=3) or shorter-wavelength light (n=5).

As per the supplemental grant (HPF00003), we implemented novel infra-red technologies into this protocol. Eye movement data has been collected (n=15) during periods of extended wake, which will allow us to examine causes of neurobehavioral deficits during periods of extended wake.

We have completed the second year on target for enrollment (11 subjects/year), and anticipate remaining on target by the end of year 3.

Rationale for HRP Directed Research:**Research Impact/Earth Benefits:**

We will be implementing and testing a new polychromatic fluorescent lamp with a peak spectral sensitivity of ~500nm. This is near the peak sensitivity of the human circadian system, and thus should be the most efficacious polychromatic lamp for shifting the timing of the human biological clock. In addition to benefits for NASA flight personnel, this technology will also have application to shiftworkers, to jet travelers, and to any personnel who need to shift the timing of their biological rhythms.

Task Progress:	In the last year, we continued with our research study. We remained consistent with our target enrollment, studying a total of 22 subjects in the laboratory randomly assigned to one of each of the four conditions: 10 subjects completed the gradual shift protocol, in either polychromatic white (n=5) or shorter-wavelength light (n=5), and 12 subjects completed the slam shift protocol, in either polychromatic white light (n=7) or shorter-wavelength light (n=5). Melatonin samples, alertness and performance testing data, and sleep recording data were collected in these studies and are being analyzed to address our specific aims. As per a supplemental grant (HPF00003), we implemented novel infra-red technologies into this protocol, and collected data on eye movements in n=15 subjects during periods of extended wake.
Bibliography Type:	Description: (Last Updated: 02/11/2021)
Abstracts for Journals and Proceedings	Anderson C, Chang AM, Ronda JM, Czeisler CA. "Real-time drowsiness as determined by infra-red reflectance oculography is commensurate with gold standard laboratory measures: a validation study." 24th Annual Meeting of the Associated Professional Sleep Societies, LLC, San Antonio, Texas, June 5-9, 2010. 24th Annual Meeting of the Associated Professional Sleep Societies, LLC, Abstract Book, June 2010. , Jun-2010