

## 3.4

# Assessment Of Sleep Dynamics In A Simulated Space Station Environment

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### SUMMARY

Based on prior experience, it is believed that the unique environmental conditions and work-rest schedules aboard orbital spacecraft (i.e., the International Space Station (ISS)) will result in sleep decrements and fatigue in astronauts. This report details methods for estimating sleep variables and circadian rhythms in a simulated work-rest environment that mimics the schedule of ISS crew activities. Eight healthy subjects in two separate studies stayed for 60 days (Phase IIa) and 91 days (Phase III) in a closed life support test facility at Johnson Space Center. Subjects wore an activity and ambient light monitor (Actillum<sup>TM</sup>), completed sleep logs twice daily, and collected timed saliva and void-by-void urine samples for 48 hours. This protocol was repeated four times during the 60-day chamber study and six times during the 91-day study; results were compared with samples collected before and after each chamber stay. Sleep variables (latency, duration and efficiency) were estimated from the Actillum<sup>TM</sup> data (objective) and from the sleep logs (subjective); acrophases for salivary melatonin and urinary melatonin sulfate were determined from concentration versus time profiles. Objective assessment of sleep efficiency, sleep duration and sleep latency were lower than the corresponding subjective assessments. In addition, the number of awakenings recorded by actigraphy was higher than those from the subjective sleep log scores. There were no significant differences in sleep variables between baseline and chamber stay periods. Changes in sleep variables were independent of chamber stay duration. Self-assessment of sleep quality scores did not reflect any sleep decrements. Wake period light intensity in the chamber was lower (50-100 lux) compared to baseline readings (1000-1500 lux). Salivary melatonin acrophase was delayed during the chamber stay by 2.7 hours and compared well with the urinary melatonin sulfate acrophase, which was delayed 3.0 hours. The chamber light conditions were similar to those of ISS and may be responsible for the melatonin acrophase delays noted during the chamber study. These results indicate that the methods tested here will be sufficiently sensitive to detect sleep decrements and contributing circadian rhythm changes in astronauts aboard ISS. Salivary melatonin levels could serve as a sensitive marker of determining circadian rhythmicity.

## INTRODUCTION

Potential disturbances of circadian rhythmicity in the space flight environment and consequent decrements in performance efficiency and in the well-being of astronauts are major concerns of NASA. In addition to changes in environmental factors, such as the absence of a gravity vector and ultra-shortened light-dark cycles, other factors that contribute to the development of sleep disturbances and fatigue during space flights include the abnormal length of working periods (high work load effect), continuous deviation of the sleep-wake cycle duration from 24 hours ('migrating day') effect, and cyclic noise disturbances.

With respect to sleep during space flight, a continuous reduction of sleep time and an increase in sleep latency were reported from earlier missions (6) and more pronounced sleep disturbances were reported with dual-shift crews (5, 12). Results of a simulation study reflecting the schedule of work-rest periods indicate a distinct increase in awake time as well as a decline of the sleep efficiency index and a desynchrony of circadian rhythms (7, 18). In a more recent study (16) that analyzed crew sleep patterns on Shuttle missions, decreased sleep duration and increased use of sleep medications during dual-shift missions compared to those used on single-shift flights was reported. In an even more recent investigation (14), in-flight use of medications from astronaut debriefings after 79 U.S. Space Shuttle missions was evaluated. From the 219 records obtained, 45% reported usage of medications for sleep disturbances. Furthermore, sleep medications were less efficacious and were therefore administered for longer periods of time (4, 14). In addition to these physiological and sleep disturbances, in order to meet operational demands, crewmembers have been assigned shift-work schedules during certain dual-shift missions.

It is well documented that sleep deficits, biological asynchrony with work-rest activities, and sleep-promoting medications will impact alertness and induce fatigue (2). This presents a very high risk for shuttle and ground-operations of the space program and, particularly to crew health and safety. Current strategies for minimizing sleep decrements due to shift-work during flights are based on the theory that exposure to bright light aids shift workers by altering or re-orienting their circadian rhythms (17). To better prepare the subjective night-shift crew and to support launch and landing time activities, crewmembers are entrained to match their work schedules to their sleep-wake activities using artificial light and simultaneous sleep shift schedules. Limited data have been collected from these astronauts before flight, during the light assisted sleep-shifting period in the days just before flight, and immediately after flight (19). In this study salivary melatonin and cortisol rhythms were examined to determine the effectiveness of this entrainment protocol in accomplishing the desired shifting of the endogenous rhythms to match in-flight work-rest activities. Results of this investigation indicated that

targeted shifts were achieved for both cortisol and melatonin rhythms before flight and were restored immediately after return to Earth. However, ambient light levels on the Shuttle were low and may have been insufficient for circadian entrainment.

In order to augment sleep quality, pharmacological agents are often prescribed during flight, in addition to pre-flight entrainment. However, a systematic evaluation of the effectiveness of light treatment on the maintenance of in-flight work-rest demands is missing due to a lack of methods and technologies that are both sufficiently sensitive and flight-suitable. To fill this gap, the present study was conducted to evaluate objective and subjective data collection methods for sleep quality and contributing variables in a ground-based analog environment in human subjects confined to a closed chamber during as part of Phase IIa and Phase III Lunar Mars Life Support Test Project (LMLSTP). Information gained from this study will be useful in the identification and validation of sensitive, non-obtrusive techniques for evaluating sleep and circadian rhythms during space flight.

## METHODS AND MATERIALS

### *Experimental Design*

All procedures involving human subjects for this study were reviewed and approved by the Johnson Space Center Institutional Review Board. The test group consisted of eight subjects, three females and five males, from two separate phases of chamber confinement (Phase IIa and Phase III). Each phase consisted of one pre-chamber, four (Phase IIa) or six (Phase III) in-chamber and one post-chamber data collection session. Each session was 48 hours long during which the following activities were performed by the crewmembers:

An Actillum<sup>TM</sup> was worn on the wrist of the non-dominant arm of each crew member for 48 hours. The activity data recorded by the Actillum<sup>TM</sup> were autoscored for sleep, while the illumination data were analyzed for patterns of light exposure.

An electronic sleep/wake questionnaire was completed upon wake up and before bedtime using the Ames Interactive Reporting Log (AIRLOG). AIRLOG is a tool developed exclusively for research in aviation and ground transportation environments; the instrument was developed by NASA Ames Research Center and includes separate components that relate to the events of the day preceding the sleep period, the quality of sleep period, and the ensuing wake time. These data were analyzed to estimate subjective changes in sleep duration, latency, efficiency and quality during chamber stay.

Saliva samples were collected every two hours while subjects were awake using salivettes (Sarstedt, Inc., Newton, NC). Void-by-void urine samples were also collected during the 48-hour period. All saliva and urine samples were processed and stored at -40°C until analysis. Samples were analyzed using commercial RIA kits to determine levels of melatonin and melatonin sulfate.

### ***Data Analysis***

Illumination data from the Actillum<sup>TM</sup> were analyzed for patterns and intensity of light exposure using vendor provided Action-3 software. Activity data were analyzed using Action-3 software using both the manual and autoscore options in the software to estimate objective sleep variables.

Data from the AIRLOG were analyzed to estimate subjective sleep quality, efficiency and latency. Salivary melatonin concentrations were determined using commercially available direct radioimmunoassay kit (ALPCO). Urine aliquots were assayed to determine 6-hydroxymelatonin sulfate levels by the method of Aldhous and Arendt (1).

Cosinor and cross-correlation methods were used to analyze salivary melatonin and urinary melatonin sulfate measurement data with respect to time (11). Cosinor analysis was based on least-squares fit of the cosine function to a series of observations. This technique allowed characterization of the mesor (the 48-hour time-series mean), acrophase (peak time, referenced to local midnight) and amplitude (half of the peak-to-trough variability). Phase shifts were calculated from the entire 48-hour session by subtracting the baseline acrophase from the in-chamber acrophase.

## **RESULTS**

Objective measurements of sleep variables by Actillum<sup>TM</sup> showed no statistically significant differences between baseline (pre- and post-chamber) and in-chamber periods. These data suggest that crewmembers adjusted with the Space Station analog work-rest activities (Table 3.4-1). Light intensity during waking periods in the chamber was lower compared to baseline readings (Figure 3.4-1). Similar readings of light intensity have been observed on two earlier space flight missions as well (15).

Self assessment of sleep variables (sleep latency, number of awakenings, sleep duration and sleep efficiency) by AIRLOG showed no changes between chamber stay and baseline (Table 3.4-1). In addition, sleep quality scores did not reflect any sleep decrements during chamber stays.

A comparison of the sleep variables data from the objective and subjective scores indicate that subjective assessment scores of sleep by the crewmembers were higher than the respective objective measures derived from actigraphy. This observation confirms the general notion among sleep researchers that perception of sleep decrements is always less than actual deficits. Sleep diaries have been used extensively in clinical and research environments to evaluate subjective sleep quality (10). Subjective sleep scores are also useful in linking circadian parameter estimates (e.g. acrophase, mesor) with aspects of sleep quality and personality. It is necessary to assess sleep deficits using both subjective and objective data sets in order to identify any significant changes in sleep hygiene that may adversely affect alertness and performance during space flight. Subjective estimates of sleep latency, duration and efficiency are often inadequate by the very nature of their being subjective, therefore, an objective estima-

tion of these variables, such as actigraphy data, in conjunction with the subjective sleep logs may provide a more comprehensive assessment of sleep hygiene in space. Results from this study indicate that the methods tested here are suitable for in-flight assessment of sleep during long-duration flights. Non-obtrusive wrist-actigraphy appears to be a valuable diagnostic method for the assessment of sleep decrements in astronauts.

It is well known that rectal temperature and urine melatonin sulfate are good indices for determining circadian rhythmicity (3,13). Due to the inconvenience caused by rectal probes during space flight, this is not a preferred means of data collection for astronauts. Although urine sample collection is non-invasive, it places increased demands on spacecraft stowage. Earlier reports indicated that there is good correlation between salivary melatonin and serum melatonin levels suggesting that salivary melatonin rhythm is an accurate predictor of circadian rhythmicity (8). Cosinor analysis of salivary melatonin and urinary melatonin sulfate excretion rates from the present study yielded valuable information on the applicability of salivary data for the assessment of circadian rhythms. When circadian variables derived from both markers are in agreement, acrophase estimates calculated from time profiles of both markers and an accepted measure of circadian shifts, are also in agreement (Figure 3.4-2). Regression analysis of these data indicated that good correlation exists between estimates from the two sets of data (Figure 3.4-3;  $r = 0.79$ ). However, the correlation between delayed salivary melatonin rhythm and sleep duration, although weak ( $r = 0.42$ ) suggests that the desynchronized melatonin rhythm and sleep period may have affected the sleep quality in the chamber crewmembers as depicted by reduced sleep duration (Figure 3.4-4). These results suggest that salivary melatonin rhythms may be successfully employed for estimating circadian rhythms and related sleep decrements in astronauts during space missions. Further analysis of these data is in progress to evaluate the correlation between temperature and salivary melatonin rhythms; results from these analyses may confirm that salivary melatonin can be utilized as a reliable chronotherapeutic marker in place of temperature.

## ACKNOWLEDGMENTS

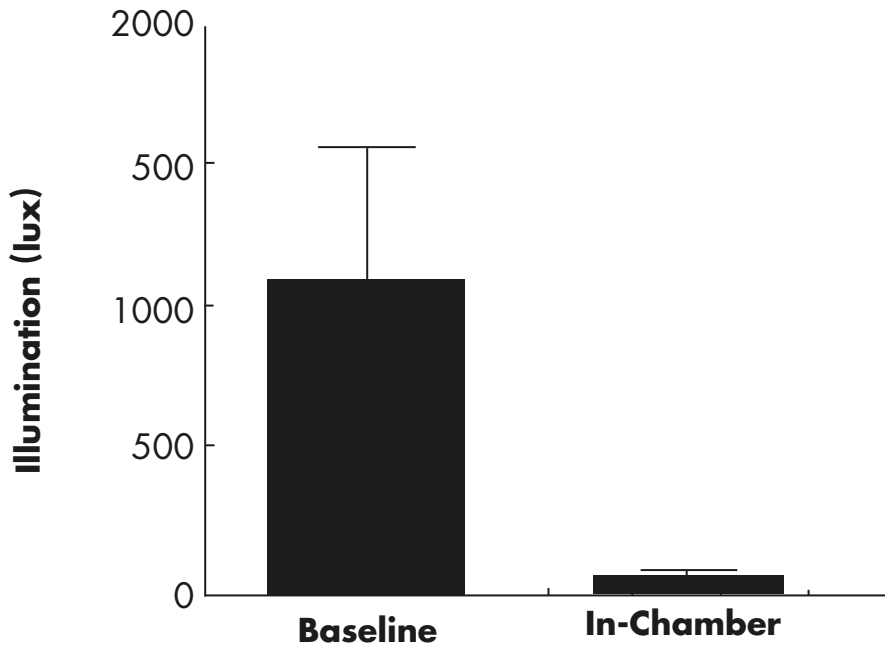
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*Table 3.4-1 Sleep variables in chamber crewmembers\**

	<b>Objective Measurements</b>		<b>Subjective Measurements</b>	
	<b>Baseline</b>	<b>Chamber</b>	<b>Baseline</b>	<b>Chamber</b>
Duration(h)	6.62 ± 0.31	6.00 ± 0.24	6.78 ± 0.27	6.21 ± 0.21
% Efficiency	88.50 ± 1.44	88.10 ± 1.73	96.40 ± 1.16	95.66 ± 1.03
Latency (h)	0.27 ± 0.06	0.20 ± 0.05	0.20 ± 0.05	0.24 ± 0.05
WASO**	0.90 ± 0.12	0.86 ± 0.15	N/A	N/A
Quality	N/A	N/A	1.31 ± 0.11	1.08 ± 0.21
Number of Awakenings	4.65 ± 1.43	4.22 ± 0.59	7.11 ± 0.31	7.33 ± 0.30

\*Values are Mean ± SEM of 8 subjects

\*\*Wake after sleep onset



*Figure 3.4-1 Light Exposure During Wake Period*

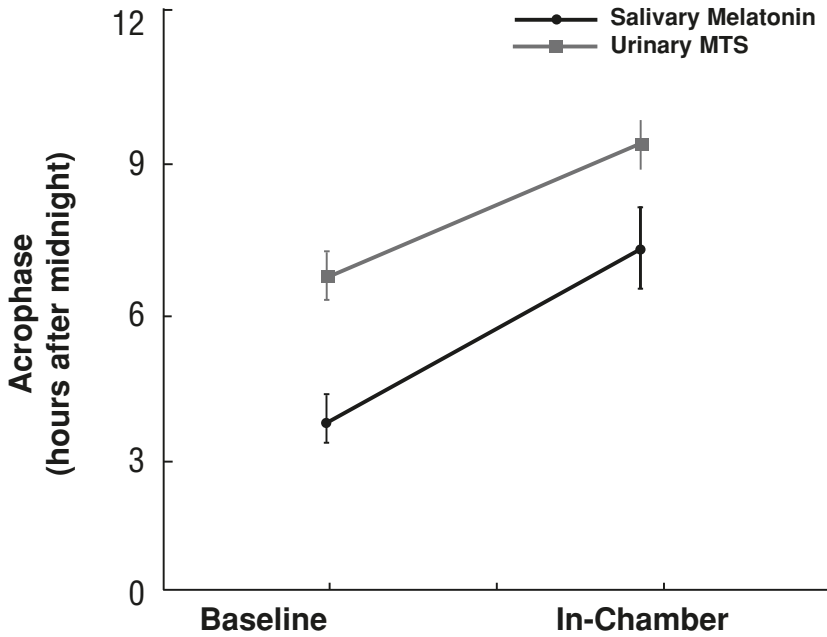


Figure 3.4-2 Comparative Estimates of Circadian Rhythm Changes

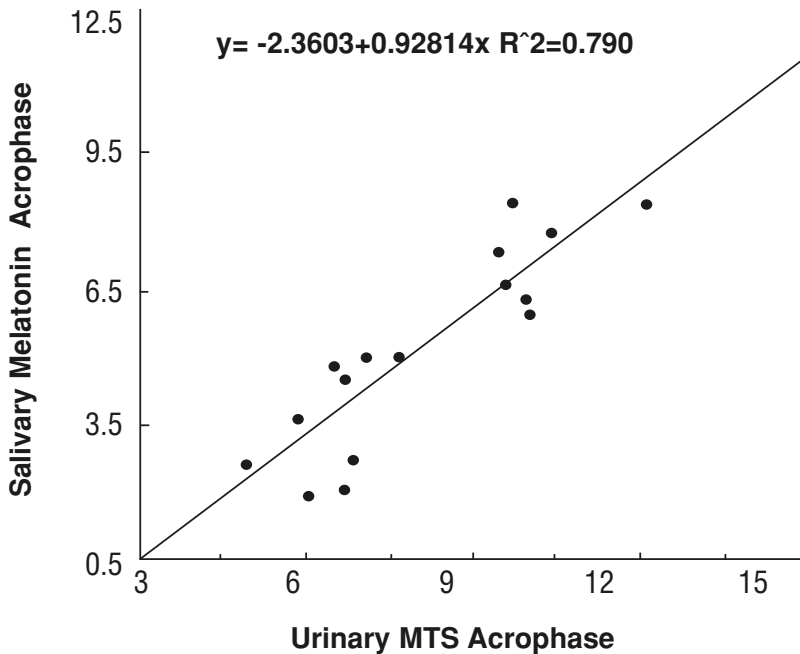
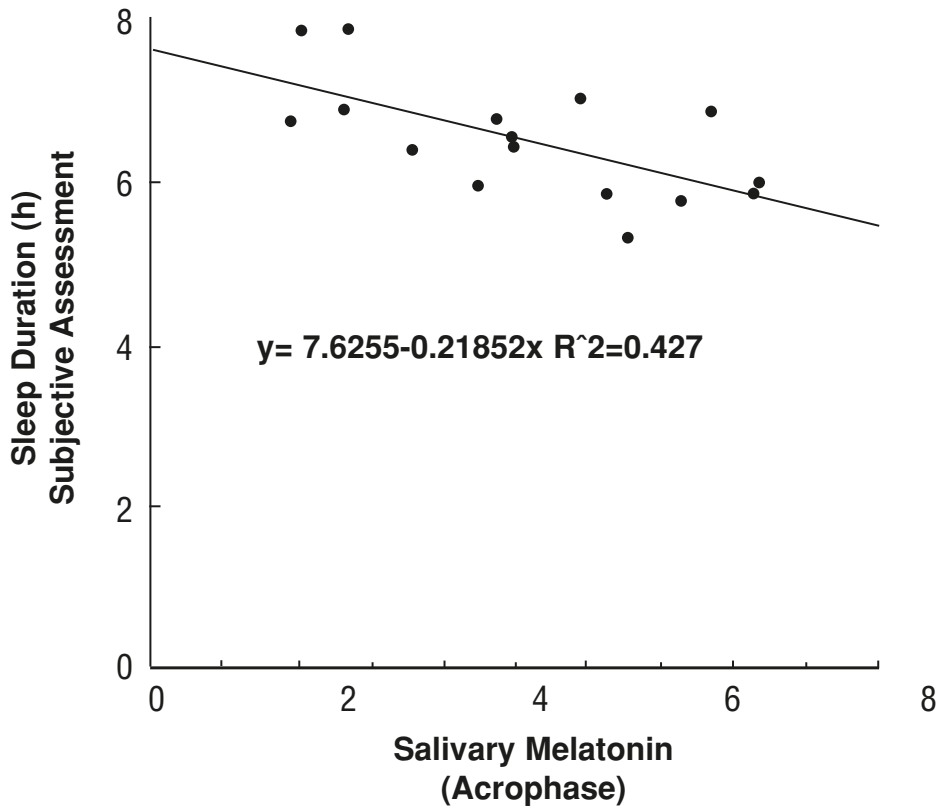


Figure 3.4-3 Correlation between Urinary MTS and Salivary Melatonin Acrophases



*Figure 3.4-4 Correlation of Rhythm Markers (Salivary Melatonin Acrophase) with Sleep Duration*

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