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INTRODUCTION

The Behavior and Performance Roadmap lists the following under the "task" heading:

> Errors in critical tasks, breakdown in crew communication and dynamics, and the accumulated stress from living and working in an isolated, confined and closed environment could jeopardize crew health and safety as well as mission objectives. Risk factors include: poor psychological adaptation; **sleep and circadian rhythm problems**; human/system interface problems; and behavioral illness (depression, anxiety, trauma, or other neuropsychiatric dysfunction). Deliverables include: unobtrusive monitoring of stress levels, coping strategies, **performance and sleep; crew screening and performance criteria; techniques to ensure sleep quality**; real-time workload analysis and planning; expert decision-making and VR systems; and guidelines for diagnosing and treating in-flight behavioral illness are also a high priority.

NAG9-1036 ("Sleeping Short") was specifically concerned with the items we have bolded in the above description. In particular, it sought to provide questionnaire and diary instruments designed to assess habitual sleep need, and to assess the circadian regularity of human behaviors. It also had the aim of testing a particular pharmacological countermeasure (Modafinil) to reduced sleep amounts. In particular, Year 03 of NAG9-1036 involved a double-blind placebo-controlled trial of Modafinil as a countermeasure to five consecutive nights where sleep was restricted by 60% (i.e. to 40% of habitual durations).

Thus, in terms of the Critical Path Roadmap for the "Human performance failure because of sleep and circadian rhythm disruption" area, NAG9-1036 sought to address three of the six Critical Questions listed, i.e.:

> Which countermeasure or combination of behavioral and phsyiological countermeasures will optimally mitigate specific performance problems associated with sleep loss and circadian disturbances during a Mars mission? (1)
>
> What individual biological and behavioral characteristics will best predict successful adaptation to long-term space flight of sleep and circadian physiology and the neurobehavioral performance functions they regulate? (NR)
>
> What are the best methods for monitoring the status of sleep and circadian functioning and for assessing the effects of sleep loss and circadian dysrhythmia that are also portable and non-intrusive in the spaceflight environment? (2)

The work done under NAG9-1036 can be divided into three parts: 1) the development of questionnaire instruments to assess habitual sleep need and timing, to identify "naturally short sleepers", assessing the personality and circadian characteristics, also the evaluation of the consequences of unmet sleep need (thus identifying short sleepers who were sleeping short unwisely); 2) the continued development and testing of an easily administered diary instrument to assess circadian regularity in human behavior (the 5-item Social Rhythm Metric SRM-5); and 3) A double-blind placebo-controlled trial of Modafinil as a countermeasure to five consecutive nights where sleep was restricted by 60% (i.e. to 40% of habitual durations). These will be denoted Aim 1, Aim 2, and Aim 3 in the subsequent report. To save space in this report we shall present abstracts of the

relevant studies. The reader is referred to the full publication for further details.

Aim 1a (Identifying and characterizing naturally short sleepers)

The full reference for this publication is Monk, T. H., Buysse, D. J., Welsh, D. K., Kennedy, K. S., & Rose, L. R. (2001). A sleep diary and questionnaire study of naturally short sleepers. Journal of Sleep Research, 10, 173-179.Here we present the abstract of that publication.

Whilst most people require more than six hours of sleep to feel well rested, there appears to be a group of people who can function well on between 3h and 6h of sleep. The aims of the present study were: 1) To compare 12 naturally short (3.0h-6.0h) sleepers (9m, 3f, mean age 39.6y, s.d. age 10.1y) recruited by a media publicity campaign with age and gender matched medium length (7h-8.5h) sleepers on various measures; 2) To determine the prevalence of naturally short sleepers in a volunteer sample of 71 University alumni (24m, 47f, age range 20y-59y); and 3) to examine the distribution of the various measures from the alumni study, and the position of the 12 naturally short sleepers identified in #1 on these distributions, determining the extent, if any, to which they were outliers. Measurement instruments included diaries and questionnaires to assess sleep duration and timing, as well as questionnaire assessments of sleep pathology, morningness-eveningness, extroversion, neuroticism, pathological daytime sleepiness, perceived competence, optimism, depressive symptoms, exercise, and work habits. Few measures showed reliable differences between naturally short sleepers and controls except the obvious ones related to sleep duration. There was, however, some evidence for subclinical hypomanic symptoms in naturally short sleepers. The prevalence of naturally short sleepers in a volunteer alumni sample was about 3% after shift work, daytime sleepiness, psychopathology and sleep disorders had been excluded.

Aim 1b (Development of a questionnaire instrument to assess sleep duration and timing)

Preamble: The initial proposal called for a development of a Sleep Length Index (SLI). However, rather than limiting ourselves to *sleep length* only, we felt it better to develop an instrument yielding measures of both *timing* and *duration* of the habitual sleep episodes. This resulted in the development of the Sleep Timing Questionnaire (STQ). A manuscript introducing this instrument has just been accepted for publication in the journal Sleep (Monk, Buysse, Kennedy, Potts, DeGrazia, and Miewald, in press). The abstract is reproduced here.

Study objectives: To develop a single-administration instrument yielding equivalent measures of sleep to those obtained from a formal (2-week) sleep diary.
Design & setting: A single-administration Sleep Timing Questionnaire (STQ) is

described (and reproduced in the Appendix). Test-retest reliability was examined in 40 subjects who were given the STQ on two occasions separated by less than one year. Convergent validity was measured both by comparing STQ derived measures with objective measures derived from wrist actigraphy (n=23), and by comparing STQ derived measures with other subjective measures derived from a detailed 2-week sleep diary in two non-overlapping samples (n=101, 93). Correlations of STQ measures with age and morningness-eveningness (chronotype) were also examined. **Subjects:** The analyses used sample sizes of 40, 23, 101 and 93 (both genders, overall age range 20y - 89y). Most subjects were healthy volunteers; some Study 4 subjects were patients (enrolled in research protocols). **Results:** Test-retest reliability for the STQ was demonstrated for estimates of bedtime ($r=0.705$, $p<0.001$) and waketime ($r=0.826$, $p<0.001$). Convergent validity using wrist actigraphy was demonstrated by correlations of 0.592 ($p<0.005$) for bedtime, and of 0.769 ($p<0.001$) for waketime. Diary studies indicated STQ bedtime and waketime data to be highly correlated (at about 0.8) with those obtained from a formal 2-week sleep diary. The STQ also provided data on estimated Sleep Latency (SL) and Wake After Sleep Onset (WASO) which correlated reliably (at about 0.7) with average nightly ratings of these variables from a 2-week sleep diary. Mean estimated values of SL and WASO from the two instruments were within one minute of each other. STQ-derived bedtimes and waketimes correlated with both age and chronotype in the expected direction (*older subjects earlier, morning types earlier*). **Conclusion:** The STQ may be a reliable, valid measure of sleep timing that could provide a time-efficient alternative to traditional sleep diaries.

Aim 1c (Consequences of sleeping short unwisely)

This work was supported by NAG9-1036, but utilized data that had been collected previously. The reader is referred to Monk, T. H., Buysse, D. J., Rose, L. R., Hall, J. A., & Kupfer, D. J. (2000). The sleep of healthy people - A diary study. Chronobiology International, 17, 49-60. Here we include the abstract of that paper:

> In order to provide baseline data for various research studies at the University of Pittsburgh over a ten year period, 266 healthy subjects (144m, 122f, age 20-50y) meeting certain criteria each completed a 14-night sleep diary. For each night, the diary allowed the subjective measurement of bedtime, wake time, Time In Bed (TIB), sleep efficiency, number of minutes of Wake After Sleep Onset (WASO), alertness upon awakening, and percentage of mornings needing an alarm (or a person functioning as one). Weeknight versus weekend night differences in TIB (TIBdiff), weekday alertness, and reliance on alarms were examined as possible indicators of sleep debt. Additionally, general descriptive data were tabulated. On average, bedtimes were at 23:48 and wake times at 07:23, yielding a mean TIB of 7 hours 35 mins.. As expected, bedtimes and wake times were later on weekend nights than on weeknights. Bedtimes were 26 mins. later, wake times 53 mins. later, yielding a mean weekend TIB increase of 27 mins.. Overall, subjects perceived their sleep latency to be 10.5 mins., reported an average of one wakening during the night (with an average of 6.4 mins. of WASO), had a diary

sleep efficiency of 96.3 %, and awoke with an alertness rating of 69.5%. These variables differed little between weeknight and weekend nights. Subjects used an alarm (or a person functioning as an alarm) on 60.9 % nights overall, 68.3 % on weeknights, 42.5 % on weekends. When TIBdiff was used as an estimate of sleep debt (comparing subjects with TIBdiff>75 mins. with those with a TIBdiff <30 mins.), the group with more "catch up sleep" on weekends had shorter weeknight TIB durations (by about 24 mins.) and relied more on an alarm for weekday waking (by about 22%), indicating the possible utility of these variables as sleep debt indices.

Aim 2 (Continuing and testing a brief diary device to evaluate daily lifestyle regularity)

Please note that some of the early part of this work was not supported by NAG9-1036. Moreover, although later analyses and writing were supported by NAG9-1036, in the following report, Studies 1 and 2 comprise a re-analysis of previously collected data (supported by other grants). However, all Study 3 data were collected with the support of NAG9-1036. In the interests of space, only the abstract will be reported here. The reader is referred to Monk, T. H., Frank, E., Potts, J. M., & Kupfer, D. J. (2002). A simple way to measure daily lifestyle regularity. Journal of Sleep Research, 11, 183-190.

A brief diary instrument to quantify daily lifestyle regularity (SRM-5) is developed and compared to a much longer version of the instrument (SRM-17) described and used previously. Three studies are described. In Study 1, SRM-17 scores (2 weeks) were collected from a total of 293 healthy control subjects (both genders) aged between 19 years (y) and 92y. Five items (*1) Get out of bed, 2) First contact with another person, 3) Start work, housework or volunteer activities, 4) Have dinner, and 5) Go to bed*) were then selected from the 17 items and SRM-5 scores calculated as if these 5 items were the only ones collected. Comparisons were made with SRM-17 scores from the same subject-weeks, looking at correlations between the two SRM measures, and the effects of age and gender on lifestyle regularity as measured by the two instruments. In Study 2 this process was repeated in a group of 27 subjects who were in remission from unipolar depression after treatment with psychotherapy and who completed SRM-17 for at least 20 successive weeks. SRM-5 and SRM-17 scores were then correlated *within an individual* using *time* as the random variable, allowing an indication of how successful SRM-5 was in tracking changes in lifestyle regularity (within an individual) over time. In Study 3 a SRM-5 diary instrument was administered to 101 healthy control subjects (both genders, aged 20y - 59y) for two successive weeks to obtain normative measures and to test for correlations with age and morningness. Measures of lifestyle regularity from SRM-5 correlated quite well (about 0.8) with those from SRM-17 both between subjects, and within-subjects over time. As a detector of irregularity as defined by SRM-17, the SRM-5 instrument showed acceptable values of kappa (0.69), sensitivity (74%) and specificity (95%). There were, however, differences in mean level, with SRM-5 scores being about 0.9 units (about one standard deviation - s.d.) above SRM-17 scores from the

same subject-weeks. SRM-5 scores also deviated more from a Gaussian distribution than did SRM-17 ones. In a study with a sample size of 101, the new SRM-5 instrument yielded scores with a mean of 4.11 and a s.d. of 1.13. Correlations between lifestyle regularity and age, and between lifestyle regularity and morningness appeared similar whether 5-item or 17-item SRM measures were used. When a gender difference in lifestyle regularity appeared, it was detected by both SRM-5 and SRM-17 measures.

Aim 3 (a controlled trial of Modafinil as a countermeasure to sleep restriction)

This study was a small-sample (10 subject) double-blind placebo controlled study of Modafinil as a countermeasure to five consecutive nights of partial sleep restriction (to 40% of habitual time in bed). The tenth subject was only completed at the end of September, and data analysis is ongoing, so the final results of this study cannot yet be reported. The study was a within-subjects cross-over design in which subjects experienced both drug and placebo conditions in two week-long sessions, separated from each other by two weeks. Each session involved the subject living in a time isolation apartment with no time cues or knowledge of clock time. The routine was specified by technicians who informed the subject when to get up, go to bed, take meals, etc. All sleeps were polysomnographically recorded, rectal temperature measured continuously, evening salivary samples collected (to detect the timing of the Dim Light Melatonin Onset - DLMO), and a battery of mood, alertness and performance measures (5 times per day)taken on each day of the study. On the final day of the study (before the recovery sleep) a Multiple Sleep Latency Test (MSLT) was given to assess daytime sleepiness under drug and placebo conditions. Bedtime and waketime on the first night (of each week) were at the subject's habitual times. On nights 2 through 6 bedtimes were made later and waketimes earlier (by equal amounts) until time in bed (TIB) was at 40% of baseline levels (a 60% reduction). A placebo pill was taken at breakfast on the first morning (after the full night of sleep) and pill (either placebo or drug depending on condition) at breakfast on the mornings following nights 2 through 6. The first two subjects also took a pill at lunchtime. The dose of Modafinil at each administration was 200mg. In all cases, between 100% and 150% of habitual TIB was made available for sleep on night 7 (the recovery night). With the exception of drug versus placebo, the procedure was identical for the two sessions for a given subject. One subject terminated the study early for family reasons, thus data analysis is proceeding using nine subjects (6f, 3m, age 21-58y).

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Monk, T. H., Buysse, D. J., Welsh, D. K., Kennedy, K. S., & Rose, L. R. (2001). A sleep diary and questionnaire study of naturally short sleepers. Journal of Sleep Research, 10, 173-179.

Monk, T. H., Buysse, D. J., Kennedy, K. S., Potts, J. M., DeGrazia, J. M., & Miewald, J. M. Measuring sleep habits without using a diary: The sleep timing questionnaire (STQ). Sleep (in press).

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