The influence of sleep deprivation and oscillating motion on sleepiness, motion sickness, and cognitive and motor performance

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Abstract

Our goal was to determine how sleep deprivation, nauseogenic motion, and a combination of motion and sleep deprivation affect cognitive vigilance, visual-spatial perception, motor learning and retention, and balance. We exposed four groups of subjects to different combinations of normal 8 hours sleep or 4 hours sleep for two nights combined with testing under stationary conditions or during 0.28 Hz horizontal linear oscillation. On the two days following controlled sleep, all subjects underwent four test sessions per day that included evaluations of fatigue, motion sickness, vigilance, perceptual discrimination, perceptual learning, motor performance and learning, and balance. Sleep loss and exposure to linear oscillation had additive or multiplicative relationships to sleepiness, motion sickness severity, decreases in vigilance and in perceptual discrimination and learning. Sleep loss also decelerated the rate of adaptation to motion sickness over repeated sessions. Sleep loss degraded the capacity to compensate for novel robotically induced perturbations of reaching movements but did not adversely affect adaptive recovery of accurate reaching. Overall, tasks requiring substantial attention to cognitive and motor demands were degraded more than tasks that were more automatic. Our findings indicate that predicting performance needs to take into account in addition to sleep loss, the attentional demands and novelty of tasks, the motion environment in which individuals will be performing and their prior susceptibility to motion sickness during exposure to provocative motion stimulation.

1. Introduction

Many military and commercial transportation operations involve simultaneous exposure to motion and altered work schedules. For example, new military operational situations involving littoral combat ships and amphibious assault vehicles combine sleep deprivation and exposure to provocative motion simultaneously. Some concern has been expressed about how each of these factors affect human performance (McCauley et al. 2007), but systematic studies of their conjoint effects on performance are scarce (Dowd et al. 1975; Collins 1988). We have investigated the separate and joint effects of provocative motion and sleep deprivation on cognition and motor performance. We have also investigated the effects of motion exposure and sleep deprivation on sleepiness and motion sickness, because there are few systematic studies of the mutual effects of these stimuli on sleep quality and quantity .

Our work extends the literature on the effects of sleep loss. There are many studies of how sleep loss affects psychomotor performance under stationary laboratory conditions and roughly constant motion conditions, i.e. regular railroad or airline flight routes that are relatively routine in nature (Reifman 2004; Reifman and Gander 2004; Roach et al. 2004a; Roach et al. 2004b; Rosa 2004; Van Dongen and Dinges 2005), but the only studies of sleep in provocative motion conditions are observational (Matsangas et al. 2015). Fatigue studies typically focus on cognitive performance and vigilance tasks (Basner et al. 2013; McCauley et al. 2013; Basner et al. 2015) with less attention to motor tasks (Walker et al. 2002), consequently, we have included tests of motor learning and retention, and balance in our experimental protocols. Interruptions of reaching and of posture from high accelerations during motion exposure have been studied (Matsangas et al. 2014b), but cognitive outcomes less so (Matsangas et al. 2014a), and we have investigated cognitive as well as motor performance. In summary, our study extends the individual literatures on sleep loss and motion exposure and unifies

them by utilizing the two factors individually and jointly and by assessing a common set of outcome measures.

Almost all individuals with normal vestibular function are to some extent susceptible to motion sickness (Kellogg et al. 1965; Johnson et al. 1999), although individual susceptibility varies enormously (Money 1970; Miller and Graybiel 1972; Golding 2006). Low grade motion sickness tend not to be recognized as such because with chronic exposure to low levels of vestibular stimulation some individuals experience fatigue, drowsiness, and mood changes for extended periods of time, rather than typical nausea, and this is unrelieved by sleep. This phenomenon is referred to as the "sopite syndrome" (Graybiel and Knepton 1976; Lawson and Mead 1998; Matsangas and McCauley 2014). Some astronauts experience this state for days and even weeks after entry into space flight (Lackner 2014). With higher amplitudes of vestibular stimulation in a nauseogenic frequency range, such as extreme sea states, and longer exposure, the likelihood of the more familiar signs of motion sickness appearing increases, e.g. stomach discomfort, nausea, cold sweating, vomiting (Kennedy et al. 1968; Lawther and Griffin 1986). It has never been experimentally determined whether the severity of chronic low grade or acute severe motion sickness is influenced by fatigue. We hypothesized that psychomotor performance, sleepiness and motion sickness would show additive and multiplicative effects of motion exposure and sleep deprivation, because of the cited overlap of motion sickness and sleepiness in response to motion exposure.

To achieve these goals, we designed an experiment with four groups of subjects exposed to four different combinations of two nights normal 8 hours sleep or 4 hours sleep, combined with testing under stationary conditions or during 0.28 Hz horizontal linear oscillation. All subjects underwent four test sessions per day that included evaluations of fatigue, motion sickness, vigilance, perceptual discrimination, perceptual learning, motor performance and learning, and balance. Studies involving chronic exposure over days to different amounts of sleep per 24 hour period have shown measurable

performance deficits after the first night with sleep reduced from 8 to 4 hours, and the deficits accumulate progressively over the first, second and subsequent 24 hour periods (Van Dongen and Dinges 2005). Thus, 4 hours of sleep per night for two consecutive days is experimentally powerful enough for the present purposes. Our choice of a horizontal linear oscillation motion stimulus was designed to be operationally relevant to a broad range of ship, aircraft, rail, and road vehicles. Vertical oscillation at about 0.2 Hz (O'Hanlon and McCauley 1974; Lawther and Giffin 1987; Griffin 1990) is the most provocative component of ship motion. Horizontal linear oscillation is also a component of ship motion and car motion (Guignard and McCauley 1982; Griffin and Newman 2004), and it evokes less motion sickness than vertical oscillation under laboratory controlled conditions (Golding and Kerguelen 1992; Mills and Griffin 2000; Golding et al. 2001).

2. Materials and Methods

2.1. Subjects

Sixty-two healthy adults, 34 males and 28 females, were enrolled in the study after signing informed consent. Subjects could terminate participation at any time, and three subjects (1 male, 2 females) withdrew during the study, two for personal reasons unrelated to the study and one due to severe motion sickness. Inclusion criteria were: age 18-30 years, normal or corrected to normal vision and body mass index (BMI) less than 30. This was the population of interest to the funding agency, the U.S. Office of Naval Research. Additional exclusion criteria were based on the following self-reported histories obtained in an oral interview: drug or alcohol abuse, sleep disorders, skeletal or muscular problems that impair movement or posture, neuromotor disease or trauma, psychiatric disorder, developmental disorder, severe susceptibility to motion sickness (Golding 2006), night shift work and/or travel that involved crossing time zones during the three weeks prior to the onset of testing. Only right-

handed subjects were enrolled. All subjects gave saliva and urine samples to be screened for the following disallowed substances: narcotics (cocaine, marijuana, opiates, amphetamines, benzodiazepines, and methadone), nicotine, and alcohol. Subjects were required to abstain from caffeine and all caffeinated products starting 3 days before the onset of testing, and for the whole duration of testing. Females were scheduled for tests outside their menstrual periods. Subject screening was conducted via an initial telephone conversation and a follow-up lab visit. Before participating, subjects read and gave their informed consent to an IRB approved description of all screening and experimental procedures.

2.2. Apparatus

To accommodate the multi-day period of residency in the laboratory for two subjects concurrently, two private laboratory rooms were furnished with single beds, night stands, refrigerators, entertainment systems, and other basic amenities. Shared exercise equipment was also available. The total duration of overnight sleep and abstinence from naps were monitored with Actiwatch-2™ and Actiwatch-Spectrum™ devices and associated software (Philips Respironics). The package consists of a small motion sensor worn on a wrist band, a wireless 1Mbit memory data logger to record activity in a 24 hour period, a photopic light sensor, an event marker, Actiware™ V5.59 sleep scoring software, and a USB-comm. dock/charger with cable and power adapter.

We used a horizontal linear oscillator to partially simulate the provocative motion of ships and other vehicles. See Figure 1. The device was a four pole parallel swing, which was driven at its resonant frequency of .28 Hz, at an amplitude of .45 m (.9 m peak-to-peak). This amplitude was chosen by pre-experiment testing on lab personnel to produce significant, but not excessive, motion sickness symptoms in the exposure duration planned for the experiment. The maximum horizontal velocity of the swing was 1.6 m/s, and the maximum horizontal acceleration was 2.8 m/s^2. An accelerometer installed on the swing recorded swing motion data. To limit visual distractions and visual flow cues

during oscillations, the perimeter of the platform had curtains around all four sides and overhead. A slit behind the seat allowed subjects to enter and exit. A video monitor was installed inside the curtain to enable the experimenter to see the subject's face and monitor possible motion sickness.

Figure 1 about here

Bolted to the center of the platform was a body-fitted NASCAR driver's seat with a five-point harness. When the subjects were seated, their head and torso were vertical and they oscillated along a left-right axis. The subjects were cautioned to limit their head movements during the swing period of the session but no physical restraint was provided. A laptop computer and robotic arm manipulandum rested on a horizontal work surface placed in front of the subject seat at a comfortable height. The laptop computer, which was used for administration of tests described below, was a Velocity Micro with a 17 inch 1680 X 1050 screen with NVIDIA GTX 980M graphics. The robotic manipulandum, which was used for assessing motor performance, was a Sensable Technologies PHANToM Desktop model.

A duplicate setup, identical to the one on the swing, including the curtain, laptop computer and manipulandum, was mounted on the laboratory floor. The stationary duplicate setup allowed two subjects to be run concurrently – one swinging and the other stationary. Each subject was run by their own experimenter, who sat close to the subject, and all communications at each setup were done at reduced levels to prevent interference with the other setup.

Posture stability was tested using Kistler Force Platform, Model 9286. This platform is designed to measure forces and torques applied to its surface, and software was used to derive the center of foot pressure from the raw force plate output.

2.3. Procedure

2.3.1. Assignment to sleep and motion conditions. Each subject participated in one condition of a design which included four combinations of two sleep conditions (8 hours of sleep or 4 hours of sleep) and two motion exposure conditions (horizontal linear oscillation, or stationary, during all performance testing). See Table 1. Subjects were scheduled in concurrent pairs of the same gender, with the same sleep schedule but different motion conditions. One of each pair was randomly assigned to the swinging or stationary condition. Alternate pairs of subjects were assigned to the 4 hour or 8 hour sleep schedule.

Table 1 about here

2.3.2. Test sessions. All pairs of subjects spent 52 consecutive hours supervised in the laboratory, beginning at 8 PM and ending two days later at midnight. Figure 2 shows the timeline of their period of residency. Three days prior to checking into the laboratory, subjects started abstaining from caffeine, nicotine, alcohol, narcotics, and all over-the-counter and prescription medications with the exception of oral contraceptives for females. Twenty four hours before checking into the laboratory, they started wearing the Actiwatch and were reminded to sleep 8 hours. When they arrived in the laboratory at 8 PM, they underwent a final screening for eligibility, submitting saliva and urine samples to be tested for disallowed substances and downloading their Actiwatch data to confirm that they had slept the prescribed 8hrs ± 15 min.

Figure 2 about here

At 10 PM, two subjects concurrently underwent a baseline 80 minute test battery (described below) under stationary conditions. At midnight, they then retired to sleep until either 8 AM or 4 AM,

depending on their assigned sleep condition. A staff member of the same gender as the subjects slept in the laboratory, awakened them at the proper time, and checked their Actiwatch data to confirm sleep for 8 hours ± 15 minutes or 4 hours ± 15 minutes as required by group assignment. The laboratory monitor also escorted subjects to breakfast on the Brandeis campus, and assured abstinence from napping and banned substances. Other than that, subjects were encouraged to do all their regular activities possible within the confines of the laboratory, or entertain themselves. All subjects spent 15 minutes per day walking on a level treadmill at their preferred speed, with supervision.

For the next two full days, subjects underwent performance testing in four 80 minute sessions scheduled 4 hours apart, at 10 AM, 2 PM, 6 PM, and 10 PM. In all sessions, two subjects were tested concurrently under their assigned motion conditions. The baseline (stationary) session on the evening of check-in was designated Session 1, Sessions 2-5 were on the first full day, and Session 6-9 were on the second day.

Each experimental session evaluated four categories of responses using seven different assessments. The assessments for each category and the abbreviations we will use henceforth are listed below; the order of assessments within each experimental session is shown in Figure 2; and each assessment is described in section 2.3.3.

- Subjective states
    1. Subjective sleepiness: Stanford Sleepiness Scale (SSS).
    2. Nausea: 1-10 nausea scale (Nausea)
    3. Motion sickness: Graybiel diagnostic criteria (MS Graybiel)
- Cognitive performance
    4. Vigilance: Perceptual vigilance task (PVT)
    5. Perceptual discrimination and learning: Visual texture discrimination task presented in randomized retinal locations (TDT Random) or fixed retinal loci (TDT Fixed)

- Motor performance and learning

    6. Adaptation of reaching movements to robotic perturbations (Motor Learning Task)

- Postural balance:

    7. Quiet standing in a heel-to-toe stance (Posture Test)

2.3.3. Test battery. Description of Assessments

2.3.3.1. Our measure of subjective fatigue or sleepiness used the Stanford Sleepiness Scale (Guilleminault and Dement 1977). It is a seven point scale subjects use to indicate how alert or sleepy they feel, where 1 is "Feeling very alert, wide awake, and energetic" and 7 is "Very sleepy and cannot stay awake much longer". Ratings made with it do not always correlate highly with measures such as sleep latency (Johnson et al. 1991), but it is nonetheless sensitive to sleep loss (Kraemer et al. 2000). Our subjects were prompted by the laptop computer to report their subjective alertness/sleepiness at the beginning middle, and end of each test session.

2.3.3.2. Subjects were prompted by the computer at eight different points in each session to rate their subjective nausea using a 1 to 10 scale, where 1 signifies no nausea and 10 was nausea so severe that vomiting was imminent. Untrained observers can rapidly use such a scale to make self-ratings that are valid and sensitive (Kennedy et al. 1989; Oman et al. 1990; Turner and Griffin 1999). The eight repeated measurements enabled tracking fluctuations in the severity of nausea throughout the session.

2.3.3.3. Motion sickness assessment was also done with the Graybiel diagnostic criteria (Graybiel et al. 1960; Graybiel et al. 1968; Miller and Graybiel 1970), immediately before and after each test session. This method provides a more nuanced description of motion sickness severity and is sensitive to low level motion sickness symptoms because it relies on trained observers and subjects, but it takes longer because seven cardinal signs and symptoms of motion sickness have to be rated -

stomach discomfort, nausea, pallor, sweating, drowsiness, dizziness, and headache. Each symptom is rated on a six point scale (none, minimal, mild, moderate, major, severe), values of 0, 1, 2, 4, 8 and 16 are assigned to ratings none through severe, and the values for all symptoms are added for total score.

2.3.3.4. An automated version of the psychomotor vigilance task (PVT) of Dinges and Powell (1985) was run shortly after the beginning and before the end of each session, 60 minutes apart. We used the reaction time sub-test of the Automated Neuropsychological Assessment Metrics, Version 4, marketed by C-Shop of University of Oklahoma (ANAM4). The test measures the ability to sustain attention over a 10 minute period by having the subject press a space bar as soon as a white asterisk appears on a blue monochromatic laptop screen. The computer registers the reaction time and starts a variable timer (5 to 15 seconds) until onset of the next stimulus. The outcome measure is the log-normal reaction time of all responses, excluding anticipatory responses (reaction times less than 130 ms).

2.3.3.5. The perceptual discrimination task we utilized was modeled after the visual texture discrimination task (TDT) developed by Karni and Sagi (1991) and presented on the laptop computer. The TDT requires subjects to discriminate the horizontal or vertical orientation of three adjacent, co-linear texture elements (diagonal bars) embedded in a 20 x 20 background array of horizontal bars. The task difficulty is adjusted by presenting a (backward) masking display of randomly oriented texture elements (V's) after an inter-stimulus interval. In our implementation, each trial started with presentation of a blank screen with a central fixation cross for 200 ms, followed by a target display for 17 ms, then a blank screen for a variable inter-stimulus interval, and finally the masking display for 17 ms. The target and masking displays subtended about 10° edge to edge. A tilted letter 'T' or 'L' was displayed in the center of the target display where the fixation cross had been, and the 3-element array of diagonal bars whose orientation was to be discriminated was presented in the middle of one quadrant of the background array, at 5° of eccentricity. After presentation of the mask, subjects were

prompted by the computer to indicate whether the fixation letter had been a 'T' or an 'L' and whether the array of diagonal bars had been vertically or horizontally aligned. The percent correct identification of the letter was used as a measure of foveal fixation on the center of the target array (TDT Fixation, in Table 2), where the spatial quadrant of the 3-element target stimulus would map onto the corresponding quadrant of the retina. The inter-stimulus interval of the blank screen between the target and masking arrays was decreased progressively over blocks of trials from a starting value of 400 ms. The smallest interval at which the subject's accuracy was 80% or better was defined as the TDT threshold. Subjects were tested in this paradigm twice during an experimental session: once at the 25th minute with target stimuli appearing in the same quadrant of the target array for every trial, and again 20 minutes later with target stimuli presented in random quadrants from trial to trial, but never in the quadrant of the fixed target. With presentation in one quadrant, subjects learn to discriminate the horizontal/vertical orientation and sleep consolidates the learning (Karni and Sagi 1991; Stickgold et al. 2000; Walker et al. 2003), but with random presentation there is no learning. The fixed quadrant version of the test enabled measurement of perceptual learning, and excluding the fixed quadrant from the later random quadrant version of the test enabled measurement of stable perceptual discrimination. The primary performance measures were the fixation error (proportion of errors in identifying the fixation target as "T" or "L") and the threshold inter-stimulus interval. Both versions of the TDT required intense attention because the stimuli were so brief and the subject had to simultaneously maintain fixation without blinking, identify the foveal letter, and discriminate the peripheral orientation pattern.

2.3.3.6. Our motor skill and learning task required subjects to grasp with their right hand the stylus of the PHANToM programmable robot and move it from a proximal visual target to one 20 cm straight ahead on the work surface. Subjects could see the robot arm and their own arm at all times. The manipulandum was programmed to generate a force orthogonal and proportional to reaching

velocity, 4 N/Ms^{-1}. No force was applied when the hand was at rest, and a rightward force was applied when the hand was reaching forward. When this type of force field is initially turned on, it shifts reaching movement endpoints to the right and arcs the reaches into bowed paths with a convexity to the right, but subjects learn to move accurately and straight again after multiple repetitions (Shadmehr and Mussa-Ivaldi 1994; Kurtzer et al. 2004), but there is no sleep-dependent consolidation of learning (Caithness et al. 2004). Subjects made 16 reaches with the robotic force turned off to establish baseline performance and 32 consecutive reaches with the force applied through the robot. The initial endpoint and curvature errors when the perturbing force was present were used as measures of motor disruption, and the final curvature errors compared to initial ones as measures of learning.

2.3.3.7. To examine the effects of sleep loss and exposure to linear oscillation on the stability of posture, we measured body sway as the subjects attempted to maintain stable upright stance after each 80 minute test session. Subjects who had been stationary were able to be tested immediately after the end of the session, but after exposure to linear oscillation subjects were often too motion sick and/or too unsteady to begin the test until they had rested in a chair for 2-3 minutes or more. When ready, subjects mounted the Kistler force plate, assumed a tandem Romberg position with their feet in a straight line, heel to toe, and their arms by their sides. Their eyes were open and the room was normally illuminated. They were asked to direct their gaze to a visual target 4 m away at eye level. When the subjects were in position and ready, they informed the experimenter and the trial began. Four 30 sec trials were run, with 30 sec rest periods between trials. The variable used to evaluate balance performance was the mean sway amplitude of medial-lateral center of pressure, for each trial.

2.3.4. Suspension or discontinuation of tests due to motion sickness. During sessions 2 – 9, if a subject in one of the swinging conditions reported or was observed to have a nausea score of 5 or higher on the 1 – 10 scale, the swing was stopped for at least 5 minutes and tests were paused (except for the PVT which continued if the subject was able to go on) and nausea was assessed repeatedly. If it

subsided to below 5, the swing was re-started and testing resumed. If nausea elevated to 5 again, the swing and tests were paused for at least 10 min and re-started when MS subsided to below 5 again. If nausea elevated to 5 or higher for the third time, or when the total stop time exceeded 20 min, the swing was stopped and the remaining tests of that session were completed stationary. This protocol was instituted to minimize vomiting episodes. Pausing and stopping limited the recorded nausea ratings to 5 for most subjects, although several times nausea cascaded rapidly resulting in vomiting.

3. Results

Sleep deprivation was a between subjects factor with two levels – 8 hours of sleep (8Hr) and 4 hours (4Hr); motion exposure was a between subjects factor with two levels – stationary (Stat) or swinging (Swing); session order was a within subjects factor with eight levels corresponding to the eight 80 minute test sessions that occurred over the two days following controlled sleep nights – designated S2 through S9 in Figures 3-5 (the baseline value taken the night before controlled sleep, designated S1, was not included in statistical analysis). The factorial combinations of these conditions will be abbreviated where necessary by hyphenating the levels of each factor, for example, 8Hr-Stat-S2 refers to the first experimental test session for the subject group with 8 hours of sleep and no motion exposure. In some cases, explained below, we included gender and the day of testing as additional factors. We had no specific predictions on the effect gender would have on any of our dependent variables. It was included because historically this factor has often been included in motion sickness studies.

As noted above, some factors were between subjects (sleep, motion, gender), and day of testing was a within subjects factor, therefore this experiment is a mixed design. We used the SPSS V23 General Linear Model Repeated Measures procedure to do the MANOVAs on each set of dependent variables since it was designed in part to analyze mixed experimental designs. Four separate MANOVAs

were conducted testing the effects of sleep deprivation, motion and session on all variables characterizing subjective state, cognitive performance, motor reaching performance and balance. A summary of all MANOVA results is provided in Table 2.

Table 2 about here

When the MANOVA was significant, the appropriate post hoc ANOVAs were done to determine which dependent variable(s) were responsible for the significant finding. We did predict that the greatest detrimental effects would occur in the group that experienced both sleep deprivation and motion. Therefore, when a MANOVA was not significant, we still did planned comparison ANOVAs comparing that group to the average of the other three. The ANOVAs for individual variables are also shown in Table 2.

3.1. Subjective state variables: sleepiness and motion sickness.

The measures of subjective sleepiness that were analyzed with the initial MANOVA test included the Stanford Sleepiness Scale scores taken at the beginning, middle and end of every 80 minute test session. The motion sickness scores analyzed within the same MANOVA included the Graybiel diagnostic criteria rating taken at the end of each 80 minute session and the maximum of the 1-10 nausea ratings that were taken at 8 points in the session. The MANOVA yielded significant main effects of sleep deprivation (Pillai's Trace, V= .639, $F(5,49)=17.3$, $p<.0005$, $\eta^2=.639$) and motion exposure (V= .666, $F(5,49)=19.5$, $p<.0005$, $\eta^2=.666$). The interaction of these two factors was not significant, but there was a significant interaction of sleep x session (V= .950, $F(14,14)=6.67$, $p<.0005$, $\eta^2=.950$). The patterns were the same for all three measures of subjective sleepiness, but the mid-session measures had the least heterogeneity of variance and the highest signal-to-noise ratios as measured by the ratio of the mean/standard deviation. Therefore follow-up univariate ANOVAs were done only on the mid-session

measures and Greenhouse-Geisser corrections were used because of unequal variances. Parallel patterns were found for the two motion sickness scores, but the 1-10 nausea ratings were used in follow-up analyses because they had the best signal-to-noise ratio. No main effects or interactions appeared in an additional MANOVA run with gender as a factor, so gender was not addressed any further.

3.1.1. Sleepiness. Figure 3 presents the mid-session Stanford Sleepiness Scale score as a function of sleep, motion and session order. Several features are evident in Figure 3 that also emerged as significant in statistical tests. First, sleepiness rose monotonically throughout the first day after subjects got 4 hours sleep, with a greater magnitude of rise for the group tested during swinging motion than for the stationary group. The groups who got 8 hours sleep were less sleepy overall than the 4 hour groups, and they did not show a progressive increase in sleepiness over test sessions, but the subgroup exposed to motion was sleepier than the stationary subgroup.

To assess the visual impressions, we did a univariate ANOVA on mid-session sleepiness, and it showed significant main effects of sleep deprivation ($F(1)=85.6$, $p<.0005$, $\eta^2=.618$) and of motion ($F(1)=20.1$, $p=.0005$, $\eta^2=.275$). There was not a significant interaction of sleep x motion, but there was a significant interaction of sleep x session ($F(6.45)=4.24$, $p<.0005$, $\eta^2=.074$). The average sleepiness level across the eight post-sleep sessions was greater for the 4Hr than the 8Hr groups and was greater for the Swing than the Stat groups. The failure to detect an interaction between sleep and motion implies that the increase in sleepiness due to sleep loss was not affected by motion exposure. In other words, the effects of sleep and motion exposure on sleepiness were additive, as illustrated by the parallel lines for the two motion conditions averaged across sessions, in Figure 4A.

The sleep x session interaction confirms the impression from Figure 3 that sleepiness increased over sessions for the 4Hr groups but not for the 8Hr groups. Polynomial contrasts run on the sessions factor revealed a significant quadratic trend for the 4Hr-Swing group, confirming the visual impression

from Figure 3 of rising sleepiness on day 1 followed by a plateau on day 2. There was also a significant quadratic trend for the 8Hr-Stat group, with a slight decline in sleepiness over the course of two days.

Figures 3-5 about here

3.1.2. Nausea. Figure 5 plots the maximum 1-10 nausea rating score by session for each study group. The groups tested while stationary reported virtually no nausea, identical to their baseline (stationary) sessions. The groups tested during horizontal linear oscillation reported nausea severity between 30% to 40% of the maximum on the 1-10 nausea scale (10 signifies that vomiting is imminent) in their first motion session. The 4Hr-Swing group showed more severe symptoms than the 8Hr-Swing group, though both groups showed declining nausea severity ratings over the eight sessions (adaptation), with both groups showing the same rate of decline.

A univariate ANOVA on the maximum nausea ratings per session showed significant main effects of sleep deprivation ($F(1)=4.12$, $p<.047$, $\eta^2=.072$) and of motion ($F(1)=31.1$, $p<.0005$, $\eta^2=.546$). The average nausea across the eight post-sleep sessions was greater for the Swing than the Stat groups and was greater for the 4Hr than the 8Hr groups. We found no significant interaction of sleep x motion, which would at first analysis rule out the *a priori* hypothesis that motion sickness susceptibility during linear oscillation is exacerbated by sleep loss. However, there was a trend toward a significant interaction ($F(1)=3.10$, $p=.084$, $\eta^2=.055$), which is illustrated in Figure 4B. In the Discussion, we address the liklihood that our policy of pausing sessions in order to limit the severity of motion sickness could have artificially reduced our power to detect such an interaction.

The approximately linear decrease in nausea as a function of repeated swinging test sessions that is evident in Figure 5 was confirmed by polynomial contrasts that revealed significant linear trends (declines) across sessions for both the 8Hr-Swing and 4Hr-Swing groups. The rates of decline did not

differ across sleep groups. Since motion sickness adaptation is a type of learning and several types of learning have been shown to consolidate during sleep (Brashers-Krug et al. 1996; Willingham et al. 2002; Stickgold and Walker 2007), we conducted an ANOVA comparing the 4Hr-Swing and 8Hr-Swing groups across sessions 5 and 6, which span the second night of differential sleep. We found no significant effect of session.

3.2. Cognitive performance: vigilance and perceptual discrimination.

Six measures of cognitive performance were analyzed with a MANOVA that included sleep deprivation, motion exposure, and sessions as factors. The six dependent variables were the reaction times for the two PVT tests administered at approximately the 5^{th} and 65^{th} minutes of each 80 minute session and the perception thresholds (inter-stimulus intervals) and fixation accuracies for the two TDT tests with stimuli presented in fixed and random retinal quadrants, at approximately the 25^{th} and 45^{th} minutes, respectively. There were no significant main effects for sleep, motion, or their interaction, but there was a significant effect of sleep x sessions (Pillai's Trace, V=.225, $F(48, 2352)=1.91$, $p<.0005$, $\eta^2=.037$) that reflected a consistent, approximately linear trend for performance decrements across sessions – increased reaction times in the PVT tests and increased detection thresholds and decreased fixation accuracy in the TDT tests – and suggested that the extent of progressive decrement depended on the amount of night time sleep loss. We tested this hypothesis for each variable with follow-up univariate ANOVAs configured to test only the sleep x session interaction. The sleep x session interaction was only significant for the discrimination threshold in the TDT test in which stimuli were presented in random retinal quadrants ($F(4.36)=2.52$, $p= .037$, $\eta^2=.049$). However, the ANOVAs included planned comparisons contrasting the performance of the 4Hr-Swing group to the three other groups combined, and these contrasts were significant for all six variables ($p= .05$ or better). This lends support to the hypothesis that sleep loss and motion together produce greater performance decrements than either factor alone, and that their effects are additive. Figure 6 presents the thresholds for the TDT test

with random retinal quadrant stimulation for the four sleep x motion conditions on day 1 (S2-S5) and day 2 (S6-S9).

Figure 6 about here

Given the subject-to-subject variability evident in the error bars of Figure 6, we used Spearman correlations to test for associations of cognitive performance with subjective sleepiness and nausea ratings across all sessions (Table 3). There were significant positive correlations between the Stanford Sleepiness Scale scores (mid-session) and all six cognitive variables (p= .014 at least), although the percent variance accounted for was low, 9.1% or less. There were also significant positive correlations between the 1-10 nausea scores and five of six cognitive variables (p= .019 at least), with 3.6% or less variance accounted for (the correlation was not significant for the threshold of the TDT test with repeated stimulation of one retinal quadrant).

Table 3 about here

3.3. Motor reaching performance

We looked at the effect of sleep loss, horizontal oscillation, and their interactions across sessions 2 through 9 in the task where the robot manipulandum laterally deviated the path and endpoint of reaching movements and the subject had to learn to move straight and accurately again. The dependent variables were the initial and final reaching curvatures and endpoint errors. A MANOVA yielded significant main effects of sleep (Pillai's Trace, V=.236, F(3,44)=4.54, p= .007 η^2=.236) and gender (V=.274, F(3,44)=5.54, p<.003, η^2=.274) but no other main effects or interactions. Univariate tests showed that the sleep effect was significant only for the initial movement curvature (F(1)=4.52, p= .039, η^2=.089). The initial curvature induced by the robotic perturbation was larger in the sleep deprived

groups. As was done for the cognitive variables, we compared the four reaching variables for 4Hr-Swing group against the averages of each variable in the other three groups, in planned comparisons testing for additivity of sleep and motion effects, but none of these was significant.

For Gender, we have the unusual situation where there is a significant multivariate test, but no corresponding significance in the univariate tests (see Table 2). If one looks at the means, the males do a little better on initial curvature, and the females on final curvature. The males also had a slight edge on reaching error, but none of these differences are statistically significant. However, the MANOVA found a significant unspecified linear combination of these three dependent measures that separates the genders. To look at this linear combination in more detail, a follow up Discriminate Function Analysis was done. The largest coefficients were on final curvature, with initial curvature being second, and reaching error a distant third. Looking at the pattern of these three variables across sessions, the discriminate function was able to correctly classify the gender of the subject an average of 79.6% of the time. There was no significant difference between men and women in the final state of adaptation, but there was a difference in how they got there. This was the only significant gender effect found in this study.

3.4. Posture performance

The force plate data was first preprocessed through a 5 Hz cutoff low-pass Butterworth filter. For the heel-to-toe balancing test that was conducted after each session, we looked at the mean amplitude of medial-lateral sway in the first trial, the last (fourth) trial, and the difference between them, over sessions 2 through 9. The MANOVA showed no main effects or interactions of sleep loss, linear oscillation, session, or gender.

4. Discussion

Our results showing that subjective sleepiness increased over two days after 4 hours of sleep are consistent with prior work on the effects of sleep deprivation (Van Dongen and Dinges 2005). Moreover, our results extend prior work by showing that sleepiness is further increased by the introduction of horizontal linear oscillation and that the effects of sleep deprivation and of exposure to motion on sleepiness are approximately linearly additive. That is, the addition of horizontal oscillation increased subjective sleepiness alike in subjects who had slept 4 hours or 8 hours. In the future, models for predicting sleepiness (Fletcher and Dawson 1997; Balkin et al. 2004; Hursh et al. 2004) will have to take effects of motion into account.

In our study, neither sleep loss nor linear oscillation alone degraded performance on the PVT and TDT tasks, however there was direct and indirect evidence of a multiplicative effect of sleep loss and motion on these measures. The direct evidence comes from the significance of the planned comparisons in which performance of the sleep deprived group while swinging was worse than for all other groups combined, for all PVT and TDT measures. This indicates that sleep loss and motion together produce greater performance decrements than either factor alone. It is likely that the effect of each factor individually was below threshold for a measureable effect but their additive combination was sufficient in this context. Indirect evidence for an additive effect of sleep loss and motion comes from the significant correlations of nausea and sleepiness to PVT and TDT performance. These findings suggest contributions of sleep loss and motion exposure jointly but not individually to cognitive deficits at the stimulus levels used in this study. It is not surprising that fixation accuracy was one of the variables degraded by sleep loss plus motion exposure, because maintaining fixation on the head fixed computer screen required suppression of vestibulo-ocular reflexes elicited by the horizontal oscillation and such suppression is known to be degraded by alcohol and other intoxicants (Baloh et al. 1979;

Schmal et al. 2003). Since fixation is critical for PVT reaction time and TDT threshold it could be the underlying contributor to these cognitive deficits.

Our results showed that sleep loss alone made nausea worse in the groups exposed to horizontal oscillation. In addition, there was a marginally statistically significant interaction of sleep loss and motion exposure in which nausea was worse in the sleep deprived than the rested group. There is statistical support for the post-hoc hypothesis that an artificial ceiling on nausea ratings that operated preferentially on the sleep deprived subjects cloaked a sleep x motion interaction. Our experimental protocol required pausing testing when the nausea rating reached a score of 5 or higher (half way to vomiting) to protect subjects from extremely adverse experiences, and we ended sessions permanently when the ratings remained at 5 or higher for more than 20 minutes. More than half of the subjects in the swinging conditions had to stop, and without stops the mean nausea ratings would have been higher for both swing groups. Figure 7 shows that a larger number of stops occurred in the 4Hr than the 8Hr group, and an ANOVA with sleep group and sessions as factors confirmed a main effect of sleep ($p<.004$) on stops. In addition, the first swinging session had the highest number of stops. Figure 4B illustrates the observed sleep x motion interaction. Without stops the mean nausea ratings would have been higher for the swinging subjects and differentially higher in the sleep deprived subjects, and the interaction might have been significant. Thus, our results support at least additive effects of sleep and motion on nausea and probably multiplicative effects. The presence of a sleep x motion interaction would not be surprising in view of the fact that sleepiness is a principal and sometimes lone sign of motion sickness (Graybiel et al. 1968; Graybiel and Knepton 1976; Lawson and Mead 1998; Matsangas and McCauley 2014). Future physiological and anatomical studies of the effects of sleep loss or motion exposure or both could benefit from taking into account manipulating both factors and measuring both motion sickness and sleepiness.

Figure 7 about here

The nausea ratings given by subjects during swinging motion declined and the sleepiness ratings increased over the course of two days of testing for both sleep groups, though the rested group showed less nausea and sleepiness on average across sessions. The decline in nausea across days and sessions represents adaptation to repeated motion exposure, while the increase in sleepiness reflects the accumulated sleep debt. In addition, the extent of cognitive performance deficits increased over swinging sessions for the sleep deprived but not the rested group. Overall, our findings indicate that models for predicting workload and performance limits should account for *individual motion exposure history* in addition to sleep loss, motion exposure, and individual susceptibility to motion sickness. No differential effects were found on TDT measures of stable performance (random quadrant test) versus TDT learning (fixed quadrant test).

The literature is replete with studies of sleep-dependent learning of motor sequences under normal, stationary conditions (Walker et al. 2002), but sleep deprivation studies have not addressed the motor learning task employed here, namely adaptation of visually aimed reaching movements to novel, velocity dependent perturbations. Our findings showed that sleep loss caused an increase in the initial curvature of movements induced by the robotic perturbation, which measures skill at dealing with novel motor demands. However, there was no sleep effect on the subjects' ability to learn to move accurately again in the face of repeated perturbations. These results are of especial significance for the ability to carry out reaching and aiming tasks in environments that produce unexpected motion-induced perturbations (Matsangas et al. 2014b) under operational conditions in which sleep deprivation is experienced.

Static balance was not affected by either sleep or motion. However, this finding should be considered tentative due to a similar issue to the ceiling effect on motion sickness severity. In the

motion conditions, a substantial fraction of the subjects were experiencing symptoms of motion sickness even after the swinging motion stopped. Postural testing had to be delayed until the motion sickness symptoms abated to the point where subjects were able to assume the heel-to-toe stance, so measureable effects might have decayed prior to testing. Rapid decay of postural aftereffects is seen, for example, in astronauts returning from space flight (Paloski et al. 1992). The four test trials in each session were relatively brief, 30 sec, in duration and it is possible that longer test periods, e.g. 2 min, might have uncovered influences of sleep deprivation or exposure to motion. In addition, balance was tested under stationary conditions. Future studies should include balance and stability measurements collected on the moving vehicle where motion exposure is taking place.

The only significant gender effect found was that males and females adapt differently in the reaching task. Otherwise, gender differences in sleepiness, sickness levels and incidence, cognitive performance, and posture were absent – there were no significant differences between males and females on any of these test measures. We also found no evidence of circadian fluctuations across daily sessions in any of our measures nor any evidence of consolidation of learning (motion sickness adaptation, perceptual learning in the TDT task, and motor learning in the reaching task) across a night of sleep.

The overall pattern of our results suggests a consistent theme, the more attention demanding and cognitive the task, the more likely the task performance will be degraded by sleep deprivation and motion exposure. The quiet stance postural task is the most automatic – it was performed under stationary conditions without any perturbation or distraction – and was unaffected by sleep loss. The motor adaptation reaching experiment also has low cognitive demands. The subject simply has to point to a target. Adaptation to perturbation of the movement is relatively “automatic” and requires little attention demand (Shadmehr et al. 2010; Taylor et al. 2010), and the retention of learning was not degraded by sleep deprivation and motion exposure. The PVT appears to be more attention demanding

than the motor task and showed decrements related to both sleep deprivation and motion exposure. The TDT task seems to be even more attention demanding requiring identification of the fixation target letter while also identifying the horizontal or vertical orientation of the briefly flashed target in the periphery. All measures of the TDT task showed additive performance decrements due to the combination of sleep loss and motion exposure.

This study has dealt with moderate levels of sleep deprivation (4 vs 8 hours of sleep for two nights) and relatively brief exposures (80 min scheduled) to provocative motion over 8 experimental sessions spanning two days. If we had used higher levels of sleep deprivation or longer motion exposure all of our dependent measures most likely would have shown significant individual effects of sleep and motion because the effects of sleep deprivation and motion are cumulative. If we had not stopped the subjects undergoing horizontal linear oscillation when their nausea rating reached 5, more than half of them most likely would have been unable to complete the TDT, motor learning, and balance tasks in the latter part of a session, because it is extremely difficult if not impossible for subjects to perform any meaningful task during extreme malaise or repeated bouts of vomiting and uncontrollable retching, which we observed in several cases even though we took precautions to try to prevent this from happening. This fact is of key significance because the motion exposure our subjects underwent was only during the 80 minute test session periods and they were in a stationary environment the rest of the time. Under operational conditions, motion exposure can be much more prolonged, and sleep deprivation can be for days rather than hours. Consequently, the resulting degradations of performance can confidently be assumed to be much greater. Moreover, a subject who encounters high levels of nausea outside the laboratory is likely to self-limit his or her activity and discontinue ongoing tasks. Withdrawal from performing tasks in operational conditions should be considered a negative impact in itself, in addition to the performance deficits we have demonstrated in completed tasks. Future studies should include more challenging postural control tasks that involve whole body and limb movement

coordination such as turn and reach movements that involve high velocity torso rotation coupled with limb movements and object handling to more closely approximate potential operational situations (Pigeon et al. 2003a; Pigeon et al. 2003b; Pigeon et al. 2013). In addition, such testing of active postural control should be tested *during* exposure to motion because posture control is challenging and very important on board ship (Matsangas et al. 2014b).

The results of this study provide an empirical basis for future research aimed at optimizing human performance in emerging military and industrial operations that involve simultaneous exposure to motion and work schedules that result in sleep loss. Space motion sickness is typically experienced during early days of space flight, and typicall sleep cycles are disrupted as well, suggesting a ?????. Past studies that manipulated just sleep deprivation or motion exposure or measured just fatigue or motion sickness and not a broad range of cognitive, fine motor, and gross motor functions do not capture the range and magnitude of deficits that we have identified and are not adequate for developing predictive models. Additional experimental studies involving extended sleep deprivation combined with multi-axis 6DOF motion platforms would provide the means to simulate more adequately actual operational conditions encountered in different commercial and military domains. Our findings indicate that predicting performance requires accounting for sleep loss, the motion environment in which the individuals will perform, their recent exposure to and retention of adaptation to motion environments, and the attentional demands and novelty of tasks.

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Table 1. Overall Study Design		
	8 Hours Sleep	4 Hours Sleep
No Motion Exposure	Group: 8Hr-Stat n=14 Female=6, Male=8	Group: 4Hr-Stat n=16 Female=7, Male=9
Linear Oscillation	Group: 8Hr-Swing n=14 Female=6, Male=8	Group: 4Hr-Swing n=15 Female=7, Male=8

Table 2. p-value Summary

		Sleep	Motion	Session	Sleep x Motion	Sleep x Session	Motion x Session	Sleep x Motion x Session	Gender	All Gender Interactions
State Variables MANOVA		**.0005**	**.0005**	**.0005**	.075	**.0005**	**.0005**	.280	.638	> .409
Dependent Variable Comparisons	Sleepiness	**.0005**	**.0005**	**.025**		**.0005**	.161			
	Nausea	**.047**	**.0005**	**.0005**		.599	**.0005**			
Cognitive Performance MANOVA		.172	.382	**.0005**	.708	**.0005**	.778	.658	.779	>.330
Dependent Variable Comparisons	PVT1	**.032***		**.009**		.064				
	PVT2	**.037***		.167		.077				
	TDT Random, Fixation	**.037***		.824		.099				
	TDT Random, Threshold	**.033***		.076		.077				
	TDT Fixed, Fixation	**.028***		**.043**		**.044**				
	TDT Fixed, Threshold	**.002***		**.027**		**.037**				
Motor Performance MANOVA		**.021**	.657	.707	.423	.373	.666	.151	**.003**	> .371
Dependent Variable Comparisons	Initial Curvature	**.048**	.718*						.121	
	Final Curvature	.131	.336*						.096	
	Reaching Error	.272	.392*						.548	
Balance Performance MANOVA		.875	.988	.669	.888	.298	.117	.849	.513	> .345
Dependent Variable Comparisons	ML Sway First Trial	.394*								
	ML Sway Last Trial	.572*								
	ML Sway Last - First	.392*								

Significant results are in bold, non-significant in gray.

If there is no entry in a cell, the significance of the corresponding dependent variable was not considered, because the MANOVA for that effect was not significant.

* Indicates the p-value given here is for the planned comparison between the group receiving sleep deprivation and motion to the average of the other three groups.

Table 3. Spearman Correlations of Sleepiness and Nausea with Cognitive Variables

		rho	Significance*	% Variance	N*
Sleepiness	PVT 1	**.301**	**.0005**	**9.1**	**460**
	PVT 2	**.275**	**.0005**	**7.6**	**460**
	TDT Random, Fixation	**.104**	**.014**	**1.1**	**447**
	TDT Random, Threshold	**.199**	**.0005**	**4.0**	**447**
	TDT Fixed, Fixation	**.153**	**.001**	**2.3**	**447**
	TDT Fixed, Threshold	**.215**	**.0005**	**4.6**	**447**
Nausea	PVT 1	**.097**	**.019**	**1.0**	**464**
	PVT 2	**.171**	**.0005**	**2.9**	**464**
	TDT Random, Fixation	**.190**	**.0005**	**3.6**	**451**
	TDT Random, Threshold	.008	.430	0.8	451
	TDT Fixed, Fixation	**.162**	**.0005**	**2.6**	**451**
	TDT Fixed, Threshold	**.137**	**.002**	**1.9**	**451**

Significant results are in black, non-significant in gray.

* Each correlation was calculated for all subjects, sessions, and test repetitions combined.

Figure Captions

Figure 1. Schematic illustration of the parallel swing used to produce horizontal linear oscillation. For clarity, the drive system and the curtain surrounding the test station are not shown. A duplicate test station was mounted on the floor of the laboratory, allowing for simultaneous testing of an oscillating and a stationary subject.

Figure 2. Schedule of test sessions and sleep periods for the two day experiment and timeline for individual test sessions. Abbreviations are: Stat= stationary, Swing= .28 Hz horizontal oscillation at .45 m amplitude; S1-9= sessions 1 (pre-sleep) to 9; MS Graybiel= Graybiel diagnostic criteria; Nausea (1-10)= subjective nausea rating; TDT= texture discrimination task; PVT= psychomotor vigilance task.

Figure 3. Plots of Stanford Sleepiness Scale scores (mean and standard error) per session for the four experimental groups.

Figure 4. A. Plot of Stanford Sleepiness Scale scores averaged across sessions for the four experimental groups. **B.** Plot of maximum nausea rating scores averaged across sessions for the four experimental groups.

Figure 5. Plots of the maximum nausea rating per session (mean and standard error) for the four experimental groups.

Figure 6. Plots of performance in the TDT test with presentation of stimuli in random quadrants for the four experimental groups. The mean and 95% confidence intervals across each day are shown for the threshold inter-stimulus interval for 80% correct detection of stimulus orientation and for the proportion of errors in identifying the fixation target.

Figure 7. Plots of the number of subjects paused or stopped due to a nausea rating of 5 or higher on a 1-10 scale during exposure to horizontal linear oscillation for the rested and sleep deprived groups.

Figure 1

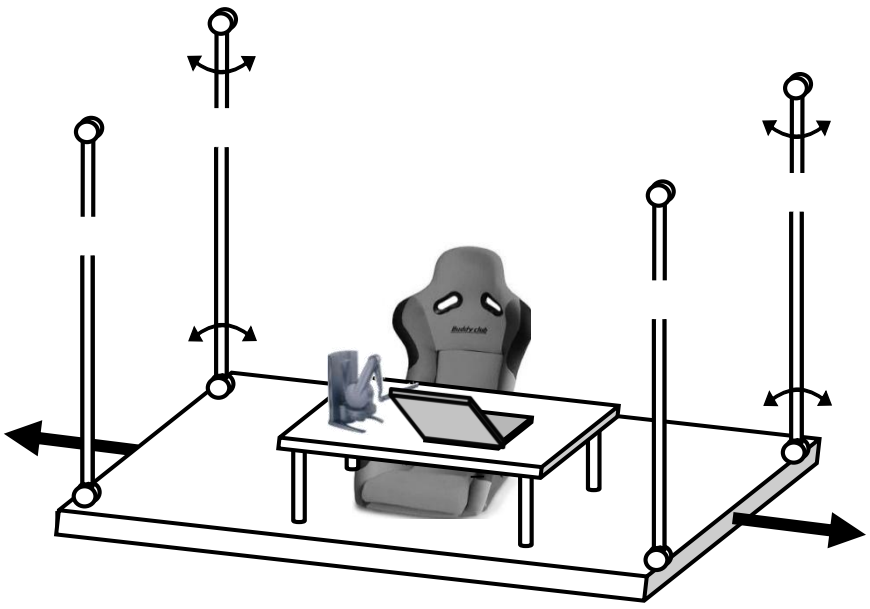


Figure 2

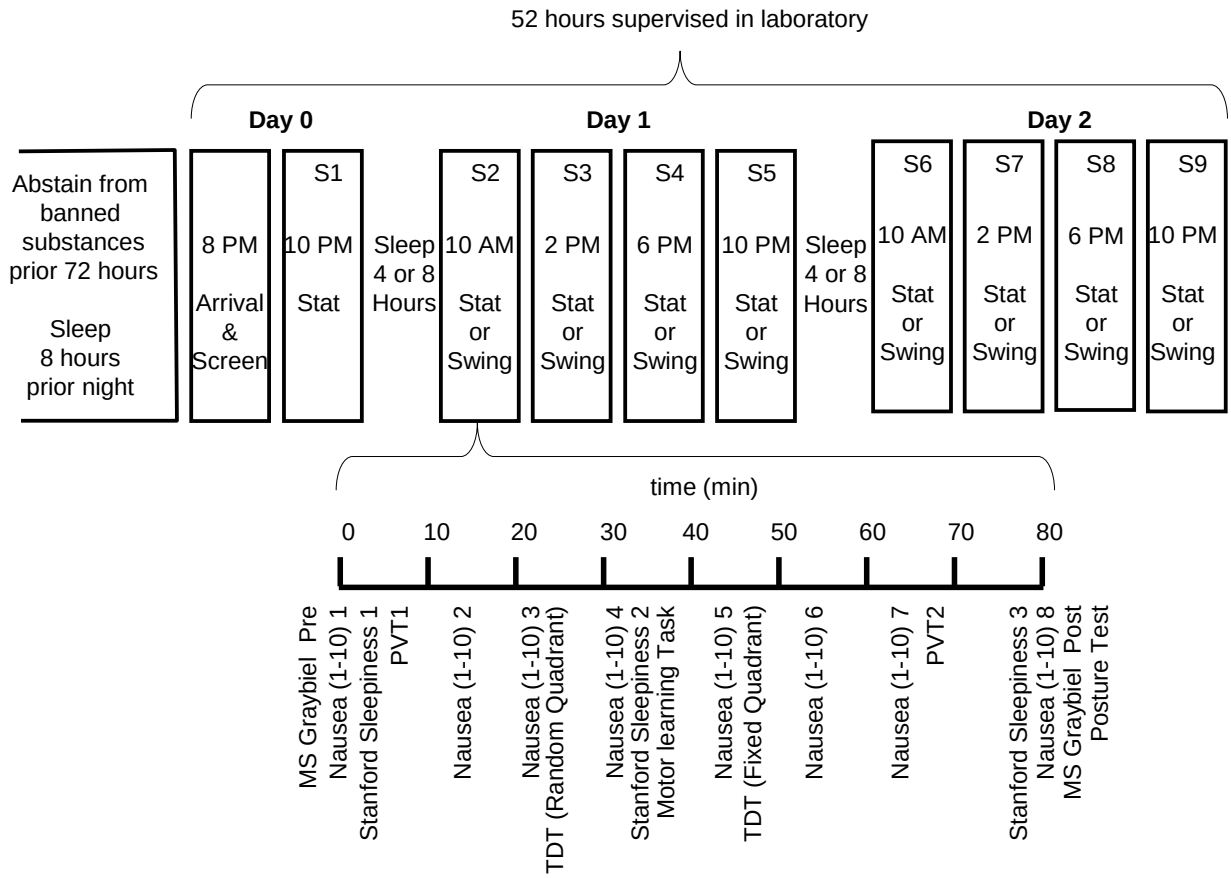

52 hours supervised in laboratory
Day 0
Day 1
Day 2
Abstain from banned substances prior 72 hours
Sleep 8 hours prior night
8 PM Arrival & Screen
S1 10 PM Stat
Sleep 4 or 8 Hours
S2 10 AM Stat or Swing
S3 2 PM Stat or Swing
S4 6 PM Stat or Swing
S5 10 PM Stat or Swing
Sleep 4 or 8 Hours
S6 10 AM Stat or Swing
S7 2 PM Stat or Swing
S8 6 PM Stat or Swing
S9 10 PM Stat or Swing
time (min)
0
10
20
30
40
50
60
70
80
MS Graybiel Pre
Nausea (1-10) 1
Stanford Sleepiness 1
PVT1
Nausea (1-10) 2
Nausea (1-10) 3
TDT (Random Quadrant)
Nausea (1-10) 4
Stanford Sleepiness 2
Motor learning Task
Nausea (1-10) 5
TDT (Fixed Quadrant)
Nausea (1-10) 6
Nausea (1-10) 7
PVT2
Stanford Sleepiness 3
Nausea (1-10) 8
MS Graybiel Post
Posture Test

Figure 3

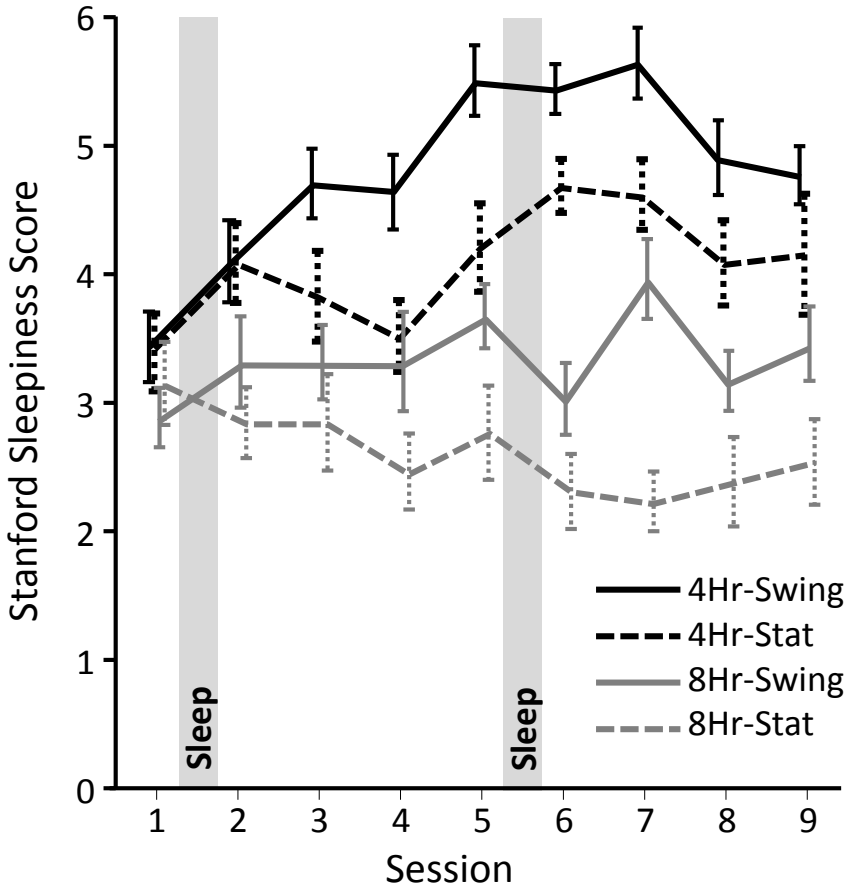

Stanford Sleepiness Score
6
5
4
3
2
1
0
Sleep
Sleep
1
2
3
4
5
6
7
8
9
Session
4Hr-Swing
4Hr-Stat
8Hr-Swing
8Hr-Stat

Figure 4

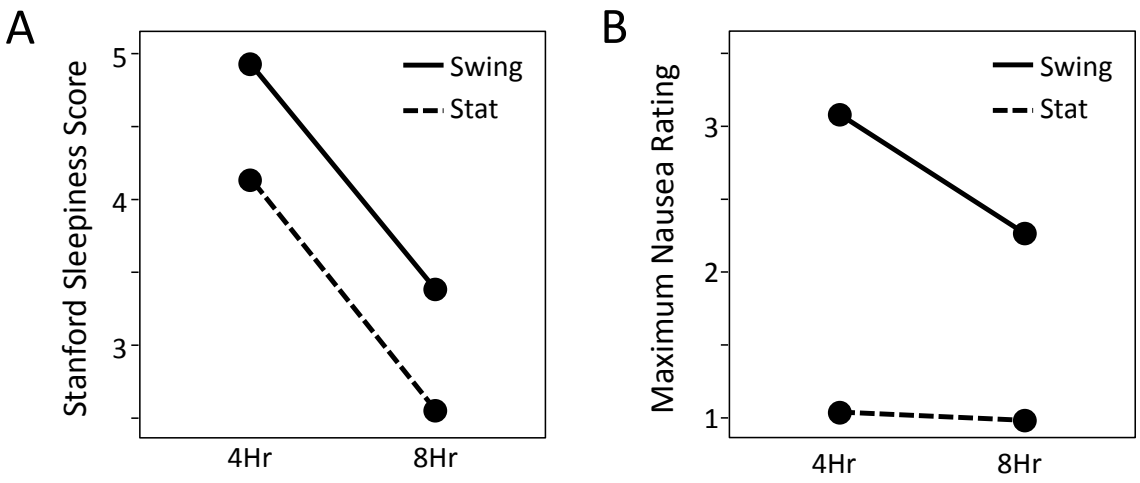

A
Stanford Sleepiness Score
5
4
3
Swing
Stat
4Hr
8Hr
B
Maximum Nausea Rating
3
2
1
Swing
Stat
4Hr
8Hr

Figure 5

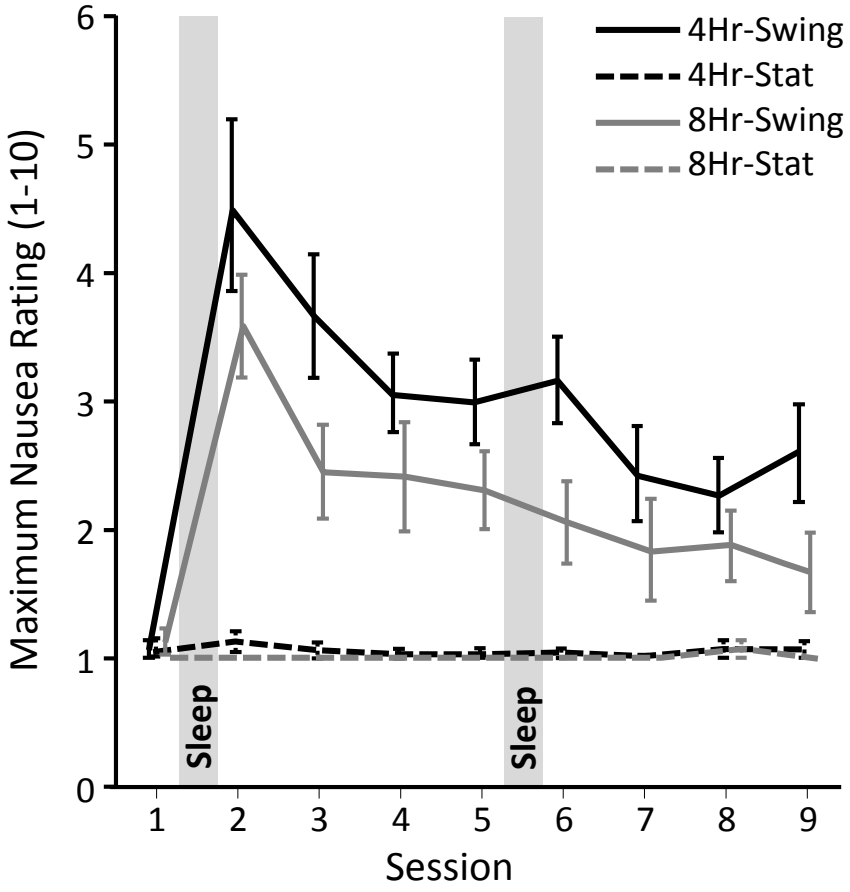

Maximum Nausea Rating (1-10)
Session
4Hr-Swing
4Hr-Stat
8Hr-Swing
8Hr-Stat
Sleep
Sleep
0
1
2
3
4
5
6
1
2
3
4
5
6
7
8
9

Figure 6

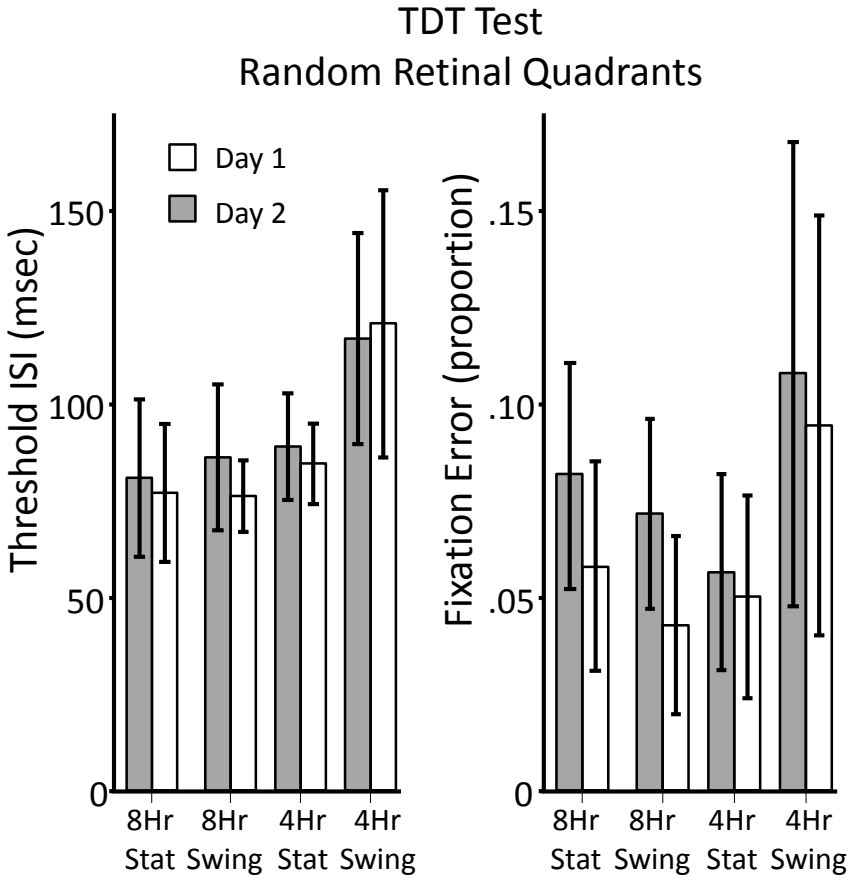
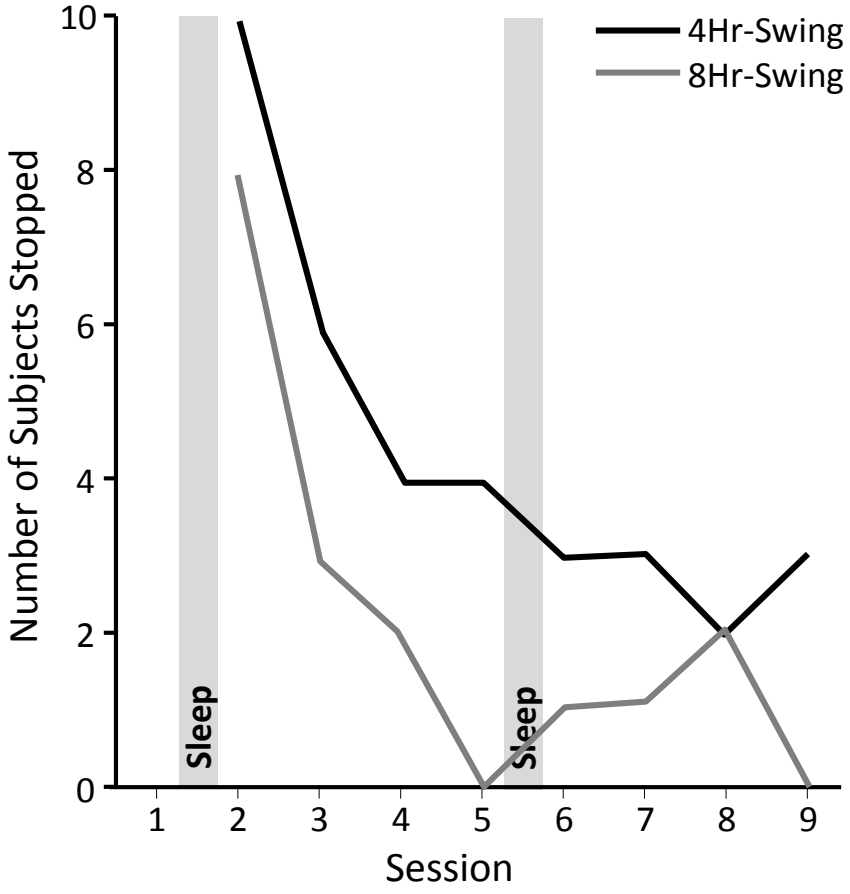

TDT Test
Random Retinal Quadrants
Day 1
Day 2
Threshold ISI (msec)
150
100
50
0
8Hr Stat
8Hr Swing
4Hr Stat
4Hr Swing
Fixation Error (proportion)
.15
.10
.05
0
8Hr Stat
8Hr Swing
4Hr Stat
4Hr Swing

Figure 7


4Hr-Swing
8Hr-Swing
Number of Subjects Stopped
Session
Sleep
Sleep
0
2
4
6
8
10
1
2
3
4
5
6
7
8
9