The Effect of Cognitive Engagement on Physiological Sleepiness and Simulated Driving Performance during Acute Sleep Deprivation

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Abstract

Driver safety is of utmost importance in the US, a country with approximately 208 million licensed drivers (Our Nation's Highways, 2010). Driving while distracted or drowsy decreases performance and endangers lives. Yet in today's bustling society, driving when distracted and/or sleepy is unfortunately more often the norm than the exception.

In order to construct appropriate countermeasures to drowsy and distracted driving, it is important to understand how distraction and sleepiness affect driving. Therefore, we examined how objective markers of physiological sleepiness and simulated driving performance were influenced by time awake and cognitive distraction (referred to in this thesis as cognitive engagement) by using a 30-min driving simulation during 28-hrs of continuous wakefulness.

Thirty-four healthy subjects (17 males [21.8 ± 3.8 years; mean ± SD) were studied in a modified constant routine protocol. Participants were deemed healthy based on a physical exam, sleep, psychological and medical histories, and blood chemistries. Subjects were also drug free based on urine toxicology and alcohol breath tester. After an 8-hour sleep opportunity, seven driving simulations were given beginning at approximately 1.25 hours awake and every 4 hours thereafter until approximately 25.25 hours of wakefulness. Subjects were randomized into the quiet driving (QD) (18 subjects [10 males]) or cognitive engagement (CE) (16 subjects [7 males]) condition. Subjects in the CE condition completed working memory tasks (*N*-back and serial subtraction) as well as trivia questions during all drives.

Visual identification of markers of physiological sleepiness— slow eye movements (SEMs) and microsleep (MS) event number and duration— allowed for mean calculations of physiological sleepiness for each drive. Also for each drive, simulated driving performance was determined by mean crash events and absolute values of speed deviations (kph) and lane deviations (cm). All variables were analyzed in a mixed model ANOVA, with paired t-tests for planned comparisons, and a modified Bonferroni correction for multiple comparisons.

A significant main effect of hours awake (HA) was observed for all markers of physiological sleepiness (PS) and measures of driving performance. Additionally, effects of condition were seen for all PS markers and speed deviations ($p < 0.048$). Compared to the QD condition, CE subjects showed significantly increased speed deviations at 9.25 and 13.25 HA, and significantly reduced PS markers at 5.25, 13.25, 17.25, 21.25 and 25.25 HA.

In general, increased markers of physiological sleepiness and decreased driving performance were associated with increased time awake. Our results suggest that during extended wakefulness, CE worsens driving performance during the day but reduces markers of physiological sleepiness beginning in the afternoon and through the early morning. Therefore, reducing physiological sleepiness through cognitive engagement may prevent episodes of falling asleep at the wheel and/or catastrophic accidents late at night. These findings support the need for further research regarding the influence of cognitive engagement on sleepiness during driving.

1. Introduction

Driver drowsiness is responsible for approximately 71,000 injuries and 1,500 deaths per year in the US (Drowsy or Fatigued Driving, 2011). It is estimated that approximately 100,000 motor vehicle crashes, or 20% of all collisions, are caused by sleepiness (Drowsy or Fatigued Driving, 2011; Horne and Reyner, 1995). Even though these statistics are astonishing, they probably do not reflect the magnitude of the drowsy driving problem because criteria and formal reporting measures for sleep-related accidents do not exist (Moran, 2007). Additionally, drowsy drivers often inaccurately judge the magnitude of and danger associated with their sleepy states (Howard *et al.*, 2007; Verwey and Zaidel, 2000), and even drivers aware that an accident is sleep-related are unlikely to report it as so (Moran, 2007).

The nonchalant attitudes of legislators, law enforcement and the general public about the safety risks of drowsy driving are conveyed through the few and incomplete state drowsy driving laws, in addition to the failure to implement a law on the federal level. All but one US state have young driver curfews, eight consider drowsy driving to be 'reckless', and vehicular homicide in Washington is considered to be 'sleeping driver homicide' if a sleeping driver caused a fatal accident (State of the States Report on Drowsy Driving, 2008). However, only in New Jersey is drowsiness a basis for reckless homicide if the driver has *not slept* for 24 hours or more (Drowsy or Fatigued Driving, 2011; State of the States Report on Drowsy Driving, 2008). Unlike other legislation, New Jersey's law punishes drivers who have gotten into fatal accidents during sleep deprivation, regardless of if they have been found to be sleeping at the time of the accident. As such, it recognizes the unpredictable transitions to sleep that often occur during sleep loss, and is the best legislative countermeasure to drowsy driving accidents. Additionally, attitudes and driving practices deemphasizing the risks associated with drowsy driving prevail (Verwey and

Zaidel, 2000). This occurs even though cognitive impairment from total sleep deprivation (SD) is comparable to that of legal alcohol intoxication. Specifically, Arendt *et al.* reported that 21 continuous hours of wakefulness increased variability of lane position and speed from posted limits on a driving simulation as much as a blood alcohol level of 0.08 (2001).

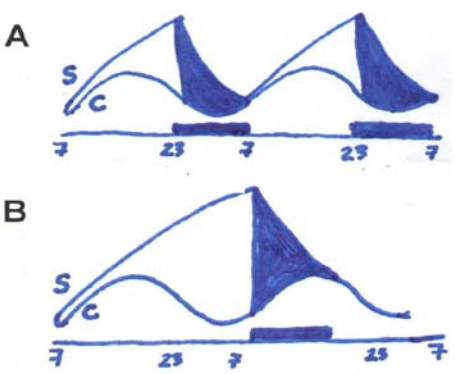


Figure 1. The circadian (C) and homeostatic (S) regulation of sleep and wakefulness. Processes C & S independently impact physiology but interact to produce varying amounts of sleep pressure at different times of day (represented by the solid area between curves). Compared to approximately diurnal sleep-wake patterns (A), extended wakefulness (B) results in increased sleep pressure that promotes sleepiness regardless of circadian phase. Note: solid bars on the X-axis represent sleep episodes.

There are various causes and contributing factors to drowsiness, including time awake, prior sleep duration, time in the circadian cycle, fatigue and boredom (Borbély and Achermann, 1999; Cajochen *et al.,* 1999; Horne and Reyner; 1995; Jewett *et al.*, 1999; Papadelis *et al.,* 2007). In particular, this study analyzed driver drowsiness due to sleep deprivation, also known as extended wakefulness. Homeostatic regulation of sleep, or Process S, produces a sleep drive that builds in a linear fashion during wakefulness and dissipates in a non-linear fashion at night during sleep (Borbély and Achermann, 1999) (see Figure 1). Opposed to approximately diurnal sleep-wake patterns (see Figure 1A), extended wakefulness (see Figure 1B) promotes much higher sleep pressure (denoted by the greater blue shaded area between the curves in Figure 1B than in Figure 1A). At different times of day, the intrinsically oscillating circadian (C) system may ease or compound feelings of sleepiness caused by accumulating homeostatic sleep drive; the amount of sleep pressure a person feels due to the interaction between circadian phase and homeostatic sleep pressure is depicted at different points in time by the area between the C & S curves in Figure 1 (Borbély and Achermann, 1999). Yet

regardless of circadian phase, high sleep pressure will usually produce extreme sleepiness that often results in unwanted transitions to sleep.

High sleep pressure resulting from sleep deprivation has been hypothesized to compromise the 'flip flop switch,' a model of neural circuitry in the brain that normally produces separate sleep or wake states and promotes rapid and complete transitions between the two (Saper *et al.*, 2010). Resembling an electrical circuit it many ways, the switch is turned 'on' to produce the waking state and 'off' to induce sleep (see Figure 2). Wakefulness is largely maintained by the double-branched ascending reticular activating system (ARAS) (see Figure 2A). ARAS neurons fire quickly to increase cortical activation in the waking state (Saper *et al.*, 2010), less during reduced arousal (in extended wakefulness or sleep deprivation) (Stecker *et al.*, 2000), and slowest during sleep (Takahaski *et al.*, 2010). On the other hand, sleep is initiated and maintained by inhibitory projections from the median preoptic and ventrolateral preoptic areas (MnPO and VLPO, respectively) (Gong *et al.*, 2004; Guzman-Marin, 2000) (see Figure 2B). Mutual inhibition between these two state networks normally prevents intermediate sleep-wake states (Saper *et al.*, 2010) (see Figure 2C). During sleep deprivation, however, unwanted

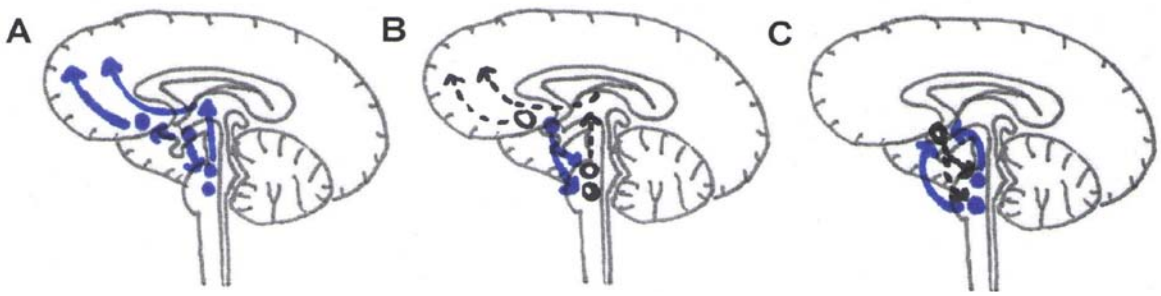


Figure 2. The 'flip flop switch' model of sleep and wakefulness.
During wakefulness (A), projections originating from ARAS nuclei in the mesopontine junction (bottom blue dots) innervate the thalamus and hypothalamus, and projections from the basal forebrain (left blue dot) innervate the cerebral cortex. Orexin neurons in the lateral hypothalamus (middle blue dot) stimulate these centers to augment and maintain the waking state. On the other hand, waking nuclei are inhibited in the transition to and during sleep (B) by the MnPO and VLPO, respectively (active sleep centers are denoted by the middle blue dot, and inactive ARAS nuclei and their projections are denoted by black open circles dotted lines). Also during wakefulness (C), these wake-promoting nuclei (lower blue dots) inhibit sleep centers. This mutual inhibitory relationship produces rapid and complete state transitions during normal sleep and wakefulness. Yet under conditions of high sleep pressure, mutual inhibition of sleep-wake circuits is compromised, resulting in unpredictable transitions to sleep.

transitions to sleep often occur. One hypothesized physiological explanation for these intermittent transitions to sleep in animal models is the buildup of adenosine during sleep deprivation. Adenosine is a marker of sleep homeostasis, and is the byproduct of normal metabolism in neuronal astrocytes (Nehlig *et al.*, 1992; Saper *et al.*, 2001). Adenosine buildup in sleep-wake brain centers is predicated to "bias" activity of the neural circuits in Figure 2 toward the sleep state (Saper *et al.*, 2001; Stecker *et al.*, 2000), producing unwanted transitions to sleep during extended wakefulness.

A compromised 'flip flop switch' and the unwanted sleep transitions it may cause are hypothesized to be associated with markers of physiological sleepiness (PS). Slow eye movements (SEMs) and microsleep (MS) events are two widely accepted markers indicative of drowsiness that can be identified in the waking electrooculogram (EOG) and electroencephalogram (ECG) (Poudel *et al.*, 2010; Torsvall and Åkerstedt, 1988; Ogilvie *et al.*, 1988; Snider and Wright, unpublished; Tirunahari *et al.*, 2003). Specifically, SEMs are slow binocularly synchronous rolling eye movements that occur in a drowsy state, before sleep and just after sleep onset (De Gennaro *et al.*, 2000 & 2001; Ogilvie *et al.*, 1988; Porte *et al.*, 2004). MS events are brief transitions to sleep that result in "short bursts of psychomotor unresponsiveness secondary to behavioral lapses in alertness" (Kecklund and Åkerstedt, 1993). To assess drowsiness in the current study, SEM occurrence and MS event number and duration will be quantified.

SEMs and MS events are correlated markers of physiological sleepiness that are sensitive to sleep loss and associated with poor driving performance (Gillberg and Åkerstedt, 1996; Banks *et al.*, 2004 & 2005; Desai *et al.*, 2006 & 2007; Risser *et al.*, 2000; Vakulin *et al.*, 2007; Boyle *et*

al., 2007; Paul *et al.*, 2005). Both may occur before and during behavioral lapses of attention[1] (Anderson *et al.*, 2010; Poudel, 2010; Torsvall and Åkerstedt, 1988). For instance, drowsy drivers that perceive themselves to be awake and alert may experience MS events during which they are "perceptually blind" and "often unaware of having fallen asleep" (Why do we sleep?, 2000). Because microsleep EEG theta activity has been shown to be associated with SEMs (Gillberg and Åkerstedt, 1996; Torsvall and Åkerstedt, 1987 & 1988), experiencing either marker of physiological sleepiness during the waking state is indicative of extreme, often dangerous drowsiness. For example, Papadelis *et al.* reported significant decreases in waking and increases in slow EEG activity before traffic accidents in a driving simulation (2007), and Boyle *et al.* found that lane-keeping behavior is diminished during MS events (2008). Additionally, Shin and colleagues found that 85% of all simulated traffic accidents occurred during dense periods of SEMs, and that subjects alerted during SEMs avoided head-on collisions (2010). Based on prior sleep deprivation, physiological sleepiness and driving performance research, we hypothesize that SEM occurrence and MS event number and duration will increase during SD while performing a driving simulation, and that increased markers of physiological sleepiness will be associated with decreased driving performance.

Similar to the effect of sleepiness, a distracted driver experiences decreased driving performance (with significantly longer reaction times and more crash events) to approximately the same degree as a driver with a blood alcohol content of 0.08 (Stayer *et al.*, 2006). Previous research has shown that physical and/or cognitive distractions (such as talking on a hand-held or

[1] Note that a lapse can occur without a MS and visa-versa (Anderson *et al*., 2010). To minimize visual scoring error (Blavias *et al.*, 2007), the widely accepted definition of a microsleep requires the event to be 3 seconds in length. This is much longer than the 500ms lapse, which may or may not occur anytime during the duration of a MS event (Anderson *et al*., 2010). Furthermore, lapses can also occur during bursts of EEG theta less than 3 seconds. So although lapses and MS events are associated, they are not always correlated.

hands free cell phone, text messaging, and engaging conversations) worsen driving performance (Drews *et al.*, 2004; Young and Regan, 2007; Questions on Distracted Driving, 2010). This conclusion is supported by the nearly 6,000 deaths and half a million recorded injuries caused by inattentive or distracted drivers in 2002 (Questions on Distracted Driving, 2010). The National Highway Traffic Safety Administration (NHTSA) claims that even cognitive engagement during driving, or simply removing one's attention from the road, significantly degrades driver performance because drivers are more likely to ignore key visual and audio cues needed to avoid a crash (Questions on Distracted Driving, 2010). During daytime driving, Harbluck *et al.* reported reductions in scanning and time checking instruments as well as increases in hard braking when subjects solved arithmetic problems (a cognitive distraction) through hand-held cell phones (a primarily physical one) (2002). These findings demonstrate that both types of distractions can amount to distract drivers, which is perhaps why injury and death rates resulting from distracted driving accidents are so high.

Also regarding cognitive distractions, behavioral and brain imaging studies provide physiological evidence supporting NHTSA's claims. Analysis of fMRIs during a daytime simulated driving task has indicated that visuospatial processing in the parietal lobe is reduced and driving accuracy impaired when participants listen to statements of common knowledge (Just *et al.*, 2008). This shows that engaging in a secondary task while driving, even if it is not particularly engrossing, results in formidable cognitive distraction that decreases spatial processing and driving performance.

In the current investigation, subjects in a cognitive engagement (CE) condition were cognitively distracted during simulated driving with trivia questions and working memory (WM) tasks. WM tasks facilitated cognitive engagement such that WM is an, "integral component of

many cognitive operations, from complex decision making to selective attention" (Baddeley, 1986). Tasks used were the *N*-back (1 and 3-Back, to provide varying cognitive loads) and serial subtraction test. These tasks that have been observed to place demands on WM by requiring on-line monitoring, updating, and manipulation of information in short-term memory (Drummond *et al.,* 2010; Jaeggi *et al.,* 2010; Owen *et al.,* 2005). CE subjects also solved trivia questions, which facilitated social interaction that has been shown to be distracting in previous studies of daytime driving (Drews *et al.,* 2004).

Interestingly enough, past studies have only analyzed driving performance during separate periods of CE or sleep loss, so this investigation aims to observe the effect on driving performance when cognitive engagement and sleepiness and are experienced simultaneously. Therefore, the primary aim of this honors thesis is to understand if specific cognitively engaging tasks affected physiological sleepiness and/or driving performance during sleep deprivation. Literature on distracted driving and sleepiness as separate entities conveys that both impair driving performance comparable to intoxicated states, so we predict that physiological sleepiness will increase and driving performance will worsen when the two are experienced together. Moreover, general neurobehavioral function, WM capacity (Drummond *et al.,* 1999; Thomas *et al.,* 2002), attention and vigilance are diminished during sleep deprivation (Lim and Dinges, 2008), so we hypothesize that cognitive engagement at this time will require increased effort and draw mental resources away from driving. As such, we predict that CE during sleep deprivation will increase physiological sleepiness and reduce driving performance.

In summary, we hypothesize that while performing a driving simulation under sleep deprived conditions, SEM occurrence and MS event number and duration will increase. Additionally, we predict that increased markers of physiological sleepiness will be associated

with decreased driving performance. These predictions are consistent with past research on sleep homeostasis and driving performance.

Also, we predict that SEMs and MS event number and duration will increase in sleep deprived subjects who are cognitively engaged during driving, indicating increased cognitive effort at a time when neurobehavioral capacity is already diminished. Likewise, we hypothesize that distraction will worsen driving performance at this time, reflecting the sleepy brain's increased difficulty to attend to the driving task.

2. Methods:

2.1 Subjects

Thirty-four healthy subjects (17 males [21.8 ± 3.8 years; mean ± SD) participated in a 28-hour sleep deprivation protocol. Exclusion criteria included any current or chronic medical or psychiatric conditions, current smokers, known sleep problems, use of prescription medications, shift work in the past 3 months, travel across more than one time zone in the past 3 weeks, or BMI outside the normal range of 18.5 to 24.9. Self-reported consistent sleep schedules of 7-9 hours per night (mean 8.2 ± 0.6 hours) were verified with ambulatory recordings of wrist-actigraphy (Mini Mitter Respironics, Actiwatch-L, Bend, OR), call-ins to a time stamped voicemail system, and sleep-wake logs. Consumption of alcohol, caffeine, tea, chocolate and any medications were prohibited for 3 days prior to the laboratory protocol to control for withdrawal and acute effects on our primary outcome measures. Subjects were deemed drug and alcohol free at screening, medical evaluation at the Clinical and Translation Research Center (CTRC) at the University of Colorado-Boulder, and upon admission to the laboratory (6.5 hours prior to scheduled bedtime).

Study procedures were approved by the University of Colorado at Boulder Investigation Review Board and the Scientific Advisory Committee of the Colorado Clinical and Translation Sciences Institute (CCTSI). Subjects provided written informed consent and received monetary compensation upon study completion.

2.2 Data Collection

After admission to the laboratory, gold F-EGH Grass SAFELEAD electrodes (152cm) were placed according to the international 10-20 system (F3xA2, C3XA2, C4xA1, O1xA2) for EEG recordings. These electrodes were also used for EOG recordings, and were offset 1cm from the outer canthi of the eyes with the left EOG placed lower and right higher than the eye midline.

Upon awakening from an 8-hour sleep opportunity (which ensured that subjects were not sleep deprived prior to our investigation), subjects began a 28-hour period of continuous wakefulness in modified constant routine conditions (Duffy and Wright, 2005) to control for the influence of environmental and behavioral factors on our primary outcome measures. Specifically, subjects were studied in a sound-attenuated room in a semi-recumbent posture with the head of the bed raised to ~35 degrees, ambient temperature controlled at a thermoneutral range, and artificial lighting maintained at dim levels (~1.5 lux). Wakefulness and compliance with modified constant routine procedures were verified via continuous monitoring of behavior and/or EEG by laboratory staff. If subjects showed signs of sleepiness, research assistants engaged subjects in various activities (i.e. talking or playing games).

Seven 30-minute simulated drives were performed beginning 1.25 hours after awakening and every 4 hours thereafter (at 5.25, 9.25, 13.25, 19.25, 21.25 and 25.25 hours post-wake time). During each drive, polysomnography was performed using Siesta System digital sleep recorders

(Compumedics USA Ltd., Charlotte, NC). All impedances were <10kΩ and recordings were stored at 256 samples per second per channel with a 12-bit A-D board. Visual scoring of physiological markers of sleepiness occurred in 30-second epochs with Profusion PSG 2 V2.1 Build 101 (Compumedics USA Ltd., Charlotte, NC). Driving performance data were collected from the AusED™ simulator (Woolcock Institute of Medical Research, Syndney, Australia).

2.3 Experimental Conditions

Subjects were randomized into a quiet driving (QD) or cognitive engagement (CE) condition. Subjects in the QD condition (18 subjects [10 males]) drove without speaking and were able to focus on the driving task. In the event that a subject fell asleep, they were awoken by an experimenter and asked to continue until the drive's completion.

Cognitive Engagement Activity	Time (min)
Quiet driving	3
WM: Serial subtraction	4
Trivia	5
WM: 1-Back	6*
Trivia	2*
WM: 3-Back	6*
Trivia	4*
Total drive	**30**

Table 1. CE driving task schedule Subjects participated in a mixture of *N*-back and trivia during all seven 30-minute drives. Asterisks denote approximate times.

In the CE condition, 16 subjects [7 males] were cognitively engaged with verbal working memory tasks (WM) (serial subtraction and *N*-back paradigms) and trivia questions during all drives (see Table 1). The serial subtraction task required subjects to subtract subsequent integers (counting down from 9) from their answers after they began with a randomly assigned three-digit integer. For example, subjects were instructed to, "Start with 917 and first subtract the number 9, then the number 8 from the resulting number, then the number 7 and so on. After you subtract 1, start over at 9." In the *N*-back task, letters were vocalized every three seconds by experimenters, and subjects were asked to indicate with a 'yes' when a current letter was the same as one presented in *n*-previous trials. In this investigation, 1*N*- and 3*N*- tests were utilized. Additionally, trivia

questions on popular culture, common knowledge and interesting facts were asked between WM tasks. Trivia was interspersed to provide subjects with mental respites and also to produce an interesting, varied CE protocol that did not bore subjects. CE activities lasted for the entire drive.

Subjects in both conditions used the PC-based AusED™ Driving Simulator, a simulation of a quiet rural drive at night (Woolcock Institute of Medical Research, Syndney, Australia). The simulation consisted of alternating portions of chicane/curvy (2min) and straight (5min) road; upon completion of the drives, subjects had driven a total of five chicane sections (10 min total) and four straight sections (20 min total). Also to facilitate a rural driving experience, Logitec speakers emitted pink noise from both sides of the monitor (Logitec, Fremont, CA). Finally, the simulation used a Logitec MOMO Racing wheel and pedals (Logitec, Fremont, CA), and a 19' Viewsonic VG901b LCD Monitor.

Subjects conducted three to five practice drives to account for learning effects (Ivancic and Hesketh, 2000) prior to their sleep opportunity, and before each drive (practice or test) laboratory staff reinforced the simulation directions. Subjects were told to keep the vehicle in the center of the right-hand lane, and that speed should be maintained within a 60-80 kph zone.[2] Additionally, subjects were instructed to brake immediately at the appearance of trucks on the road (approximately 10 intermittently appeared per 30-minute drive). After braking, the truck would disappear and subjects were told to accelerate to their previous speed.

2.4 Measurements

Simulated full-drive performance was assessed using three output variables: lane deviation (absolute value in cm from the center of the vehicle to the median of the road), speed

[2] The speedometer in the left-hand corner of the screen turned red when subjects drove <60 kph or >80 kph, yet was otherwise green.

deviation (absolute value in kph of speed deviations outside the 60-80 kph speed zone), and mean crash events. These variables have been previously shown to be sensitive to sleep deprivation by the AusED™ simulator (Banks *et al.,* 2004 & 2005; Desai *et al.,* 2006).

Physiological markers of sleepiness were visually scored on the waking polysomnogram during each full drive. Variables included: SEM number, MS number and MS duration (total seconds). Horizontally binocularly synchronous SEMs were defined as EOG events with an amplitude >50 microvolts lasting longer than one second (Ogilvie *et al.,* 1988; DeGennaro *et al.,* 2000 & 2001; Shin *et al.,* 2010; Torsvall and Åkerstedt, 1987 & 1988). SEMs were primarily scored in LOC which was visually high-pass and low-pass filtered at 0.1 and 0.5 Hz, respectively. They were then secondarily scored under visual high-pass and low-pass filters of 0.1 and 30 Hz and SEMs with vertical inflections of < 0.5 second were excluded from analysis. The investigator was blind to EEG signals when scoring SEMs, but records were double-checked and SEMs verified so that they were not scored during visible EEG artifacts.

MS events were defined as 3-15 second bursts of synchronous 4-7 Hz theta EEG activity replacing the background beta or alpha rhythm (Banks *et al.,* 2004 & 2005; Blaivas *et al.,* 2007; Boyle *et al.,* 2008; Moller *et al.,* 2006). They were scored using C3xA2 (or C4xA1 when necessary) under visual high and low-pass filtering of 0.1 and 30 Hz, respectively. The EEG was visually low-pass filtered at 15 Hz in records with excessive artifact.

2.5 Statistical analysis

For each full drive, the mean and standard deviation was calculated for all electrophysiologic variables of sleepiness. Markers of physiological sleepiness and full-drive performance measures were analyzed for differences across hours awake and between conditions

(CE or QD) using the Statistica 6.0 data package. A mixed model ANOVA was performed with subject as a random factor, and hours awake and condition as fixed factors. Paired t-tests were used to determine which planned comparison data points significantly differed, in conjunction with a modified Bonferroni correction that reduced probability of type I errors.

3. Results

Significant main effects of hours awake (HA) and condition (CE or QD) were observed for all physiological markers of sleepiness (see Figure 3 on pg. 15). Mean SEM number differed with increasing hours awake (F=7.464), between subjects (F= 2.571), and between the CE and QD conditions (F=5.958). However, only at 21.25 HA was the mean SEM number significantly higher in the QD condition (see Figure 3A). Mean MS events significantly differed with increasing hours awake (F=7.213), between subjects (F=4.641), and between the CE and QD conditions (F=8.421). Significantly more MS events were observed in the QD condition at 5.25, 13.25, 17.25, and 21.25 HA (see Figure 3B). Finally, MS duration significantly differed with increasing hours awake (F=6.555), between subjects (F=4.344), and between conditions (F=8.952). Significantly longer MS durations were observed in the QD condition at 13.25, 17.25, and 21.25 HA (see Figure 3C). Additionally, there was a HA x Condition interaction for sum MS durations (F=2.294). Significant difference was found at $p < 0.048$ in all cases (modified Bonferroni correction).

All variables of simulated driving performance showed HA and between subject main effects. Although LD (F=11.118 for HA and F=24.745 between subjects), SPDEV (F=3.748 for HA and F=6.779 for between subjects) and crashes (F=4.388 for HA and F=4.882 for between subjects) showed this variation, only the planned comparison for SPDEV significantly differed

between the QD and CE conditions at 9.25 and 13.25 HA (see Figure 3D). Significant difference was found at $p < 0.048$ (modified Bonferroni correction). Mean crash events visibly increased beginning at 17.25 HA in the CE condition, but were not significantly more numerous than in the QD group (see Figure 3E). Lane deviations were never significantly different between groups (see Figure 3F).

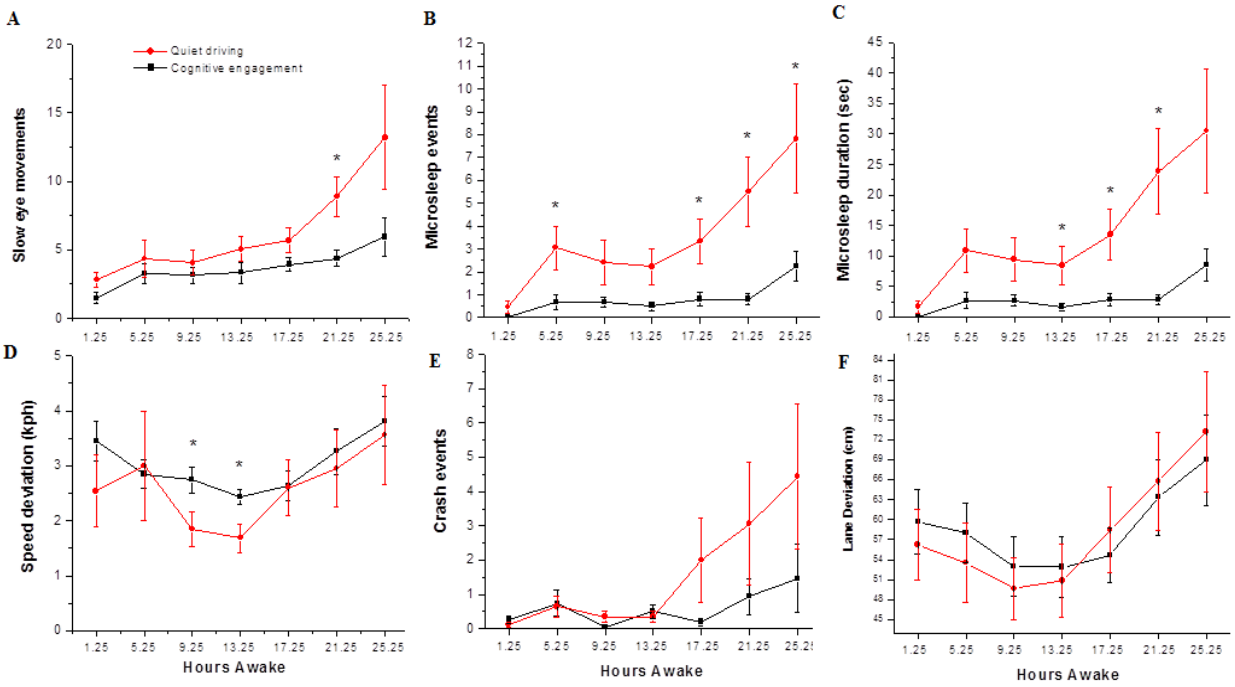


Figure 3. Markers of physiological sleepiness (A-B) and driving performance (D-F) during sleep deprivation. Mean slow eye movements (per drive) and microsleep number (per drive) and duration (total seconds per drive) increase throughout a period of 28-hour total sleep deprivation. Cognitive engagement reduces physiological markers of sleepiness, significantly so during periods of increased sleep pressure at night. All measured of driving performance generally worsened throughout the sleep deprivation protocol, but only speed deviations were significantly worse while cognitively engaged during the afternoon and evening. * = $p < 0.048$.

4. Discussion

4.1 Physiological Sleepiness

In agreement with previous literature on sleep deprivation and physiological sleepiness, our hypothesis that SEMs and MS events would increase in incidence and duration during sleep deprivation (i.e. with increasing hours awake) was supported. Physiologically, this effect may

have been due to adenosine buildup in sleep-wake brain regions serving to depress the neuronal firing of wake-promoting neurons. Depression of firing rates most likely resulted in sudden and unwanted transitions to sleep during the waking state, which most likely were seen in our investigation as MS events surrounded by SEMs. This effect is an example of the powerful influence of the homeostatic sleep drive on sleep-wake regulation.

Mean SEM occurrence was significantly decreased in the CE group at 21.25HA (0415h the next day in a subject with a 0700h wake time), but did not continue to be significantly different after that point in time (i.e. SEMs were not significantly more numerous during drive seven, or at 0815 the next day for a subject waking at 0700h). This is may have been due to formidable interindividual differences in coping with sleep deprivation (Van Dongen, 2006) that produced substantial variance in SEM occurrence at this time (mean=13.18, SD=15.65) (see Figure 3A). MS event number and duration in the QD condition were significantly greater than the CE condition beginning at 17.25 HA (2415h in a subject waking at 0700h) and continued to be higher for the remaining simulated drives (see Figure 3B).

MS event duration was significantly lower in CE subjects beginning at 13.25HA (or 2015 in a subject waking at 0700h). Yet similar to SEMs, MS event duration was no longer significantly different between conditions at 25.25HA (0815h the next day for a subject waking at 0700h). Comparably, this may have occurred due to the interindividual variation in responses to sleep deprivation at this time (mean MS duration=30.49s, SD=40.69). Interestingly, MS durations in the QD group were significantly higher earlier in the sleep deprivation period than any other marker of physiological sleepiness (at 13.25HA or approximately 1615h in a 0700 early riser) (see Figure 3C). This finding, along with significantly higher microsleep events in QD subjects early in the sleep deprivation period (at 5.25HA, or 1215 hours when waking at

0700) conveys that microsleep events may be a more sensitive and/or reliable polysomnographic marker of PS during open-eyed wakefulness (as compared to SEMs). This conclusion supports those by Marzano *et al.* (2007), who claimed that SEMs are not reliable markers of physiological sleepiness when eyes are open (2007), and discussion by Shin *et al.*, who found that even though the SEM is a useful marker of physiological sleepiness, it is often mistaken with movement, the vestibuloocular reflex, or eye movements that occur during yawning (2010).

It should also be noted that increased variation in variables of physiological sleepiness in QD subjects (particularly in SEMs and MS duration during drive 7) may have also been due to lack of cognitive engagement in this group. It is possible that our CE protocol provided subjects with a point of focus during their drives, so their minds did not wander to their overwhelming feelings of sleepiness. Homeostatic drives have powerful physical and psychological effects on the body, so that it is difficult to focus on anything else until whatever a certain drive regulates is obtained. For example, when hungry, thirsty, or in this case sleepy, it is often hard to think of anything else but eating, drinking, or sleeping. Thus, even though we thought that the QD group would be better able to focus their energy on the driving task itself, they may have actually been *distracted* from the driving task by their overwhelming feelings of sleepiness. In the CE group, on the other hand, our WM and trivia protocol may have preoccupied sleepy drivers, reducing their subjective and physiological sleepiness. In so doing, the variability in PS measures in CE subjects may have decreased because they were not permitted to ruminate on or be as influenced by their sleepy states (unlike the highly variable QD group).

Our second hypothesis regarding physiological sleepiness was not supported, because SEM occurrence and MS event number and duration did not increase in sleep deprived CE subjects. We originally predicted that these markers of PS would increase in sleep deprived

subjects because mounting sleep pressure comprises the ability to manipulate and store information in working memory (WM). Because our CE protocol involved WM tasks, we thought that CE during sleep deprivation would be extremely difficult and result in higher physiological sleepiness. In all, more SEMs and MS events would reflect the decreased ability of the brain to engage in its sleep deprived state.

Instead, we found that SEM occurrence and MS event number and duration actually decreased in CE subjects. A possible explanation for this unexpected finding may lie in the residual activation, albeit reduced, of the prefrontal cortex (PFC) during sleep deprived WM activation. Multiple studies have found that working memory *capacity* is reduced during SD, and this fact is most likely associated with a large reduction inactivated PFC area during WM tasks in sleep deprived subjects (Thomas *et al.,* 2000; Drummond *et al.,* 1999). Yet unlike in rested controls, WM activation during SD produces activity in the left premotor region of the PFC and lateral occipital gyrus (Drummond *et al.,* 1999). This conveys that WM activation still occurs during SD, even though not as many common PFC regions or as much cortical area is involved. Additionally, the distinct PFC areas activated by WM tasks during SD alludes to a more visually-based strategy at this time, one that is apparently less accurate than the primarily language-based strategies used when subjects are well rested (Drummond *et al.,* 1999). Therefore, WM strategies may be different, accuracy reduced and total activated cortical area diminished, but activation nevertheless occurs during SD.

Thus, cognitive engagement that activates the PFC and parietal lobes may lead to increased waking brain activity during sleep deprivation. This is evidenced by Thomas *et al.*, who discovered the alpha waveform (or relaxed wakefulness) emanating from the sleep deprived PFC during WM tasks (2002). Jensen *et al.* added to these findings by noticing that alpha

activity is proportional to increasing cognitive stimulation in this brain region during a WM task (2002). Moreover, because the prefrontal cortex is shown to be particularly vulnerable to sleep loss (Thomas *et al.,* 2000; Drummond *et al.,* 1999), WM activation may actually help to induce alertness in a cortical region where SD reduces brain activity. In other words, CE during SD may activate ascending arousal systems in areas of the brain where activity is lacking. At a time when unstable sleep-wake state circuitry induces unwanted sleep transitions (recall the model of increased sensitivity of the 'flip-flop switch'), WM tasks may act as quick fix countermeasures to physiological sleepiness.

Nevertheless, it must also be recognized that SEMs and MS events may have been reduced due the social interaction between subject and experimenter. In addition to time of day, Eriksen and colleges have emphasized the importance of environment and activity on sleepiness, reporting that social interaction was associated with reduced subjective drowsiness (2005). Therefore, trivia used between WM tasks may have facilitated social interaction between the sleepy subject and experimenter, effectively arousing the subject and reducing markers of physiological sleepiness.

4.2 Driving performance

In support of the conclusion that driving performance is significantly worsened during SD (Arnedt *et al.,* 2001), we found significant main effects for hours awake (HA) in each driving performance measure. These findings reflect Doran *et al.'s* state instability hypothesis, a well-known postulate on the effects of sleep deprivation (2001). Doran and colleagues claim that mechanisms controlling sleep and alertness become progressively disrupted with mounting homeostatic sleep drive, which ultimately increases variability in neurocognitive performance

(2001). In this investigation, neurocognitive variability and decreased performance were seen through increased speed deviations, lane variability and crash events as sleep pressure mounted throughout the 28-hr period of extended wakefulness.[3] Based on these and previous findings, the danger of operating heavy machinery during sleep deprivation, a period of reduced vigilance and alertness (Lim and Dinges, 2008), is apparent.

Even though sleepiness and distraction *separately* reduce driving performance comparable to severely intoxicated states, no compound performance decrements were witnessed when drivers were distracted and sleep deprived simultaneously. We hypothesized that the sleep deprived brain's already-reduced neurocognitive performance would be challenged by cognitive engagement, and that decreased driving performance at this time would reflect the sleepy brain's difficulty at attending to the driving task.

Rather, we discovered that driving performance between the CE and QD groups was not significantly different during late nighttime or early morning hours (i.e. during sleep deprivation). Mean crash events in the CE group at night appear to decrease (see Figure 3E), but this effect was not significant due to large variability in the QD group's mean crashes during the last three drives (17.25HA: mean=2, SD=5.11; 21.25HA: mean=3.06, SD=7.39; 25.25HA: mean=4.44, SD=8.40). However, it is essential to understand that even though mean crashes in the CE group did not decrease significantly, they were certainly not as numerous. Even though not *statistically significant* in this investigation, reduced crashes in the CE group may be *meaningful* in the real world. One less crash may translate to one less death from a catastrophic drowsy driving accident.

[3] This investigation did not analyze the AusED reaction time (RT) output because the simulator has not consistently shown sensitivity to the measure during SD (Banks *et al.*, 2004; Vakulin *et al.*, 2007).

The large variability in mean crashes in the QD group may have been due to interindividual differences in how subjects were able to cope with sleep deprivation (Van Dongen, 2006), but it is likely that it also resulted from lack of a routine CE protocol. To demonstrate this point, the consistently *decreased* variability in mean crash events in the CE group may have resulted from the engaging protocol that did not allow subjects ruminate on their sleepy states. Thus, CE may have focused their attention away from their sleepiness and onto the driving task, which consistently aroused them enough to avoid unwanted transitions to sleep and catastrophic crash accidents. In contrast, the QD group did not have a routine while driving, showed higher unwanted transitions to sleep (as seen through significantly higher physiological sleepiness during SD), and higher mean crash events.

Yet in line with previous research on cognitive distractions during daytime driving, we did find that CE during the afternoon and evening (at 9.25 and 13.25HA, or 1615h and 2015h if rising at 0700h) significantly impaired sensitive measures of driving performance. Evidence of this effect can be seen through increased speed deviations at these times (see Figure 3D). However, CE did not significantly increase crash events at this time. This is not surprising, however, because the majority of catastrophic accidents (i.e. off-road crash incidents) occur during late night driving (Desai *et al.* 2006). Moreover, Desai and colleagues' observation upholds the validity of the main effect of time on crash events witnessed in this investigation.

In all, performance outcomes in the CE condition convey that driving performance may not be inarguably worsened by *all* forms of 'distractions' at *all* times. Consistent with previous research, our results emphasize that CE is distracting during the day, a time when sleep pressure has not accumulated and when neurocognitive performance is still high. But when the brain's neurocognitive capacity is already reduced at night, CE may engage the cortex just enough to

activate ascending arousal systems that reduce markers of physiological sleepiness, unwanted transitions to sleep, and catastrophic crash accidents. Moreover, CE did not *worsen* sensitive measures of driving performance (i.e. speed deviation or lane position) or overly-distract subjects from the driving task at night (as was the case during the day). This may reflect subjects' underlying reduced cognitive capacities at this time, which may have allowed them not to be influenced by CE in the same way. However, in order to assess subjects' cognitive capacities during SD, WM tests must be evaluated for accuracy (a future direction of this study that may help us further decipher our findings). Nevertheless, it appears that our CE protocol may have 'woken up' subjects' drowsy, sleep deprived cortices and may be useful during night driving.

In addition to the WM tasks, social interaction during night driving may have also altered subjects' states of alertness and resulted in them not having further impaired driving performance. In line with findings that speaking on a hand-held or hands-free cell phone during the day increases distraction levels (Questions on distracted driving, 2010), Young and Regan note that the degree of cognitive distraction associated with an engaging conversation is often enough to decrease performance in the execution of simultaneous tasks (2007). Nevertheless, increasing social interaction that is not overly engrossing may help to alleviate feelings of sleepiness (Erickson *et al.,* 2005) and engage a sleepy driver. This may alert subjects enough to avoid unwanted transitions to sleep, but not so much that their driving performance is decreased. Therefore, the degree of cognitive engagement during night driving is of utmost importance.

In terms of this investigation, our CE protocol was socially engaging and alerting to an acceptable degree in that it did not decrease driving performance *but* reduced physiological sleepiness. Thus, benign social interaction resulting from trivia questions and/or working memory tasks that do not produce cognitive overload at this time may be facilitate alertness

without being overly distracting. Thus, certain CE protocols may effectively prevent drivers from incurring unwanted transitions to sleep during night driving. These are important findings even for drivers who drive alone, who may be able to reap the same benefits by engaging their brain through recorded trivia or WM tasks (a hypothesis that requires additional research).

4.3 Applications and future directions

Our findings challenge the prevailing view that cognitive engagement is synonymous with distraction during driving. However, our results are specific to prior time awake and must not be taken out of context. Namely, we do not promote that CE during sleep deprived driving makes operating a motor vehicle safe. Driving while sleep deprived is reckless to oneself and other drivers, and CE during driving in these conditions may only temporarily mask sleepiness. Much like caffeine temporarily inhibits the effects of the somnolent adenosine, a marker of the homeostatic sleep drive (Nehlig *et al.*, 1992), CE will only reduce *manifestations* of physiological sleepiness. Eradication of the homeostatic drive that *causes* sleepiness during sleep deprivation can only be achieved by sleeping (Dijk *et al.*, 1995). Nevertheless, the masking effect CE has over markers of physiological sleepiness may be useful for sleepy drivers who cannot pull to the side of the road at night. Even though driving during SD is a dangerous activity and should be avoided if possible, it important to recognize that cognitive engagement in this state may make driving safer than sleep deprived driving alone.

Yet for many, night driving is unavoidable and drowsy driving common despite attempts to regulate its occurrence. Of 184 Finnish long haul truck drivers interviewed, 13% admitted to violating their contractual maximum hours of service, adding that they received lower pay rates when driving less, along with criticism and the risk of losing their jobs in the event of a late

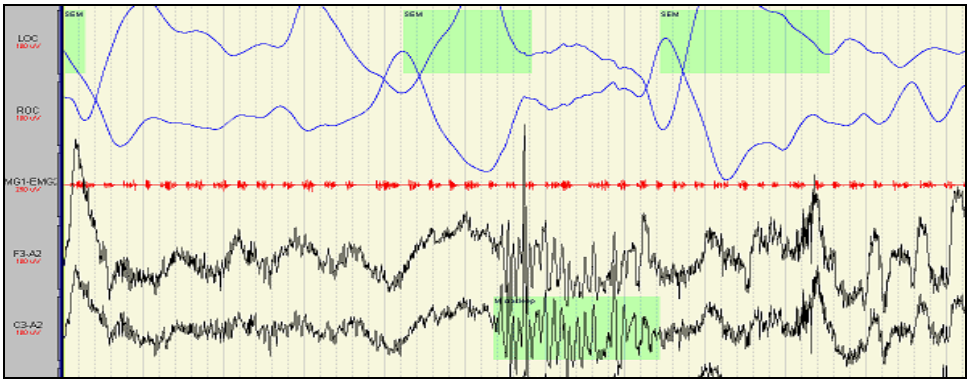
delivery (Häkkänen and Summala, 2000). Even in drivers who did not violate their driving quotas, 40% admitted to having problems staying alert during drives at night, 20% to dozing off at least twice in the last three months, 17% to near-misses and 11% to accidents during periods of reduced alertness (Häkkänen and Summala, 2000). Jargon of physiological sleepiness is not used in these industries, but dozing events can be reasonably associated with EEG microsleeps and SEMs. Ultimately, our finding that CE may be an immediate solution to extreme sleepiness and catastrophic accidents during night driving may benefit people (truck drivers, emergency workers, shift workers, etc.) who must drive when the risk for drowsy driving accidents is high.

The outcomes of the current investigation create the necessity for future studies on sleep deprivation and cognitive engagement during driving at different times of day. Upcoming studies should investigate the effect of trivia/social interaction separately from working memory tasks, in addition to employing multiple types of WM paradigms (i.e. verbal and/or visual) at different cognitive loads (i.e. different *N*-Back versions). Additionally, different driving simulations should be used to verify the consistency of our findings. Yet findings in the current investigation may be more accurate than other studies using exciting, life-size simulations that often produce increased states of alertness. This is because subjects are usually not enthusiastic about operating the simple AusED™ simulator, in that it mimics boring, non-alerting night driving conditions so well. However, our results can only be applied to the context in which they were collected—a simulated, rural road at night. Investigations on CE during driving should be done on other simulators in distinct driving environments, such as urban drives that include changing speed limits and other traffic. Also, cognitive engagement during real driving (involving a car with dual controls and driving instructors who are ready to take over if necessary) should be completed to apply our findings to more realistic situations.

Lastly, it must be recognized that subjects uncomfortable and/or unfamiliar with video-game like tasks, or subjects who did not drive regularly, may have altered our results. Our subject pool consisted of younger individuals who held drivers licenses; consequently, future research is needed to address if our observations are universal among different ages and populations with differing amounts of driving experience, such as professional drivers.

Appendices

Appendix A. SEMs surrounding a MS episode in a sleep deprived subject
A polysomnogram screenshot from this investigation picturing slow eye movements (LOC or left oculogram at top [high pass and low pass filtered at 0.1 and 0.5 Hz]) surrounding a microsleep episode (C3 or central zone three at bottom [high pass and low pass filtered at 0.1 and 30 Hz]). Fast EEG activity after the microsleep makes it appear as if the event caused an episode of behavioral nodding off, after which the subject may have jerked awake. This screenshot was taken at approximately 25.5 hours of wakefulness.



Appendix B. Subject view of the AusED™ driving simulation
The simulator view is of a dark rural road at night with margins marked by cat-eye posts. Area between the 60 to 80 kph speedometer tick-marks (at left) turns green if the subject is driving in the 60-80 kph speed zone and red (pictured) if they are not. Subjects drove in the right-hand lane and braked when they saw trucks (pictured) on the road.

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