Transportation Safety and Operator Sleepiness: Where Biology Needs Technology

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1. INTRODUCTION

Transportation systems have historically appreciated the need to place safety limits on operators relative to two commonly occurring factors that can make driving unsafe. The first factor is consideration of the age of the operator. Those who are too young to drive safely or those who are visually or cognitively incapacitated—commonly from advanced age—are often restricted from driving. The second factor is consideration of ingestion of alcohol and sedating medications. Typically countries place limits on blood alcohol levels and prohibit driving when certain sedating medications are taken, although the former is often enforced much more so than the latter. While enforcing limits on age and alcohol intake has helped improve accident risks, these are not the only common incapacitating risks to driver safety.

In the past decade, there has been a growing awareness that driver sleepiness is another common cause of traffic accidents. In some parts of the world, such as North America and the European Union, the risk factor of sleepy driving is subsumed under the broader umbrella of "fatigue" for those industries with regulated work hours (e.g., commercial truck drivers). As motor vehicle density grows faster than roadway capacity in many countries, more motor vehicles are operated at all hours of the day and night, exposing more people to sleep deprivation prior to driving, and/or to driving during a circadian time when the brain is biologically programmed to fall asleep.

Driving with inadequate sleep and/or during biological night can pose significant risks for fatigue-related driving errors and fall asleep crashes. There is extensive scientific evidence that human behavioural capability to operate a motor vehicle depends upon alertness, and that inadequate sleep (either from sleeping too little or disturbed sleep) can induce performance deficits equivalent of those observed from unacceptable blood alcohol levels. Therefore both the common occurrence of driving sleepy or drowsy driving (which typically have the same meaning) and the risks they pose to safety have highlighted the need to mitigate this third domain of safety risk.

Unlike age and alcohol, most governments that have mitigation strategies for drowsy driving typically do not rely on screening and enforcement, due to the difficulty of identifying when an operator is incapacitated by inadequate sleep or sleepiness when driving. (Unlike age and blood alcohol level, which can be verified when a driver is stopped by a member of law enforcement, inadequate sleep and sleepiness are easily masked by the transient alerting effects of the law enforcement vehicle and officer.) Among those governments in which sleepy driving has been identified as a comm risk, mitigation efforts have focused on education; the use of rest areas along motorway; the implementation of roadway “rumble” or vibration strips to alert drivers of drifting out of lane; and enforcement of reckless driving laws. Although there is some evidence that these measures can help reduce drowsy driving crash risk, the increasingly common occurrence of sleepy drivers on roadways in many countries, such as the United States, has resulted in the need to identify technologies that can detect and warn a driver of sleepiness and its effects on their driving safety. This is an especially critical area for technology development because drowsy drivers are often not fully aware of their sleepiness or its effects on their driving safety. This article reviews the scientific evidence for risks posed by driving sleepy, and evidence of the effects of technology designed to detect sleepy driving and warn drivers of its risks.

2. TRANSPORTATION SYSTEMS INVOLVE CONTINUOUS OPERATIONS

2.1. 24-hour operations in transportation modalities

The global economy depends upon nearly every form of commerce operating 24 hours a day. As the 24-hour pace of industrialized societies continues to spread globally, with technology permitting billions of humans to compress time by multi-tasking, communicating, and travelling across vast distances, time itself has been elevated to among the most precious of commodities. Contributors to human behaviour 24/7 include investment markets and banking; proliferation of around-the-clock industries; widespread use of nonstop automated systems; increases in the amount of night shift work; growing trend toward prolonged work hours; overnight and just-in-time delivery; emergency operations; physical access to entertainment, shopping, etc. day and night; internet access around the clock; early school start times coupled with later bed times; life-styles that rely on chronic sleep restriction; 24-h vigilance by police and military; and increased international commercial aviation and shipping. Every facet of modern life, from transportation, and industrial production, health care and public safety depends upon using the night and stretching the day with artificial light. This fact is most evident in all modes of transportation, where systems are typically operating continuously around the clock, every day in many countries.

2.2. Inadequate sleep has been associated with major transportation accidents

There is extensive US data documenting that fatigue from inadequate sleep can be a risk to safety in general, and to driving in particular (Mitler et al., 1988, Dinges, 1995, Lyznicki et al., 1998, Stutts et al., 2003, Barger et al., 2005). Fatigue is the word that is widely used throughout government, industry, labour, and the public to indicate the effects of working too long, and/or following too little rest, and/or being unable to sustain a certain level of performance on a task (Dinges, 1995). These issues overlap extensively with those that relate to sleepiness and its performance effects, and consequently, sleepiness and fatigue are used interchangeably in this paper.

Efforts to reduce the safety and health risks posed by fatigue from inadequate sleep duration, quality and timing have been the focus of initiatives at the U.S. National Transportation Safety Board, Department Transportation, NASA, Department of Defence, and the National Institutes of Health. The original U.S. federal laws for how long truck drivers could drive are based on a historical (1900 to 1940) understanding of fatigue as being due to the duration of work hours. This concept predates the subsequent extensive scientific literature on the criticality of adequate sleep duration, sleep quality, and sleep timing for effective alertness and performance. We now know—from decades of scientific studies—that sleep need and circadian timing are primary determinants of fatigue/sleepiness, comparable to or greater than the effects of time on task, and that these fatigue-inducing factors potentiate each other (i.e., sleep loss results in more severe time-on-task decrements in performance and safety, although this relationship is also moderated by the circadian timing of sleep and waking).

Transportation systems never sleep, but the humans that operate them are programmed biologically to sleep nearly a third of every 24-hour period. Sleep need and circadian timing are often in conflict with the work demands of transportation systems. There is extensive scientific evidence demonstrating that fatigue associated with sleepiness (Roehrs et al., 2011) occurs as a result of the physiological consequences of inadequate sleep, prolonged wakefulness, and being awake at a circadian time that the brain is programmed to sleep (Dinges et al., 1997, Belenky et al., 2003, Van Dongen et al., 2003, Banks et al., 2010, Banks and Dinges, 2011). These factors can co-occur to produce and amplify fatigue and its adverse effects on behaviour, including sleepiness, slowed reactions, and involuntary sleep onsets (Dinges et al., 1997, Jewett et al., 1999, Belenky et al., 2003, Banks et al., 2010, Mollicone et al., 2010, Banks and Dinges, 2011, Goel et al., 2011b).

An evaluation of the extent to which fatigue is likely to have contributed to an accident therefore requires evaluation of information on the timing of sleep and wakefulness, rather than merely a focus on the duration of work hours or driving time. In addition to identifying whether the antecedents of fatigue were present relative to an accident, the behaviour of someone involved in an accident must be evaluated for the extent to which it is consistent with scientific knowledge on the manner in which sleep and circadian biology affect the ability to perform certain tasks. There is extensive scientific evidence that fatigue resulting from lost sleep can make it difficult to remain awake, alert and attentive for sustained periods of time (Lim and Dinges, 2008, Lim and Dinges, 2010, Basner and Dinges, 2011, Roehrs et al., 2011). In addition, sleep loss can induce performance deficits equivalent to alcohol limits (Dawson and Reid, 1997, Williamson and Feyer, 2000, Williamson et al., 2001, Roehrs et al., 2003).

Driving drowsy has been discovered to common among many countries (McCartt et al., 1996, Sagberg, 1999, Lloberes et al., 2000, Masa et al., 2000, Flatley et al., 2004, Abe et al., 2012). Driving drowsy motor vehicle crashes have been found to have a high risk of bodily injury and fatality (Pack et al., 1995, Philip et al., 2001, Connor et al., 2002, Flatley et al., 2004). The inability to stop the occurrence of sleepiness-related performance lapsing, or frank sleep onsets while driving, is the reason that motor vehicle crashes associated with sleepy driving are often (1) single vehicle, (2) roadway departure at highway speed, and (3) lacking evidence of corrective action before the vehicle impacts another object. These factors may explain why the fatality rate for sleep-related crashes has been found to be near to that for alcohol-related crashes in the U.S. In addition, research sponsored by the National Highway Traffic Safety Administration (NHTSA) has found that driving drowsy results in a four- to six-times higher near-crash/crash risk relative to driving alert, and drowsy driving had a higher crash risk than distracted driving (Klauer et al., 2006).

Excessive sleepiness as a course of risky driving is a common and serious problem due primarily to life style decisions and secondarily to medical disorders and medications. Most common cause of sleepiness is insufficient sleep syndrome. This is a medical concept because there are many epidemiological studies from around the world, showing that as sleep gets reduced below 6-7 hours by lifestyle, people are more likely to be obese, have cardiovascular disease, and an elevated risk of dying—all-cause mortality (Ayas et al., 2003, Gottlieb et al., 2005, Gottlieb et al., 2006, Kaneita et al., 2008, Marshall et al., 2008, Wolff et al., 2008). Shift work and jet lag disorders can be profound physiological stressors and produce deficits in cognitive functions. The World Health Organisation currently lists night shift work as a carcinogenic activity, because of the elevated rates of breast and prostate cancer observed among night shift workers (Davis et al., 2001, Schernhammer et al., 2001, Kubo et al., 2006, Pukkala et al., 2009). Obstructive sleep apnea syndrome, one of the most common sleep disorders in many countries, involves chronic fragmentation of sleep from disturbed breathing that occurs only during sleep. In addition, it causes excessive sleepiness from the lack of physiological sleep continuity and duration, and thereby promotes the risk of sleepiness while driving. Narcolepsy and other hypersomnolence syndromes, and other sleep disorders can also be a cause of excessive sleepiness.

2.3. The commute conundrum: Time spent driving can affect sleep time

Time spent driving can also affect sleep time, creating a circular effect: less sleep can contribute to more sleepy driving, and more driving time can reduce sleep time. The American Time-Use Survey (ATUS) annually samples how US citizens from ages 4 years and older use their time. Analyses of ATUS data from 47,731 respondents during the years 2003-2005 revealed that work time, travel time, and time for socializing, relaxing, and leisure are the primary activities reciprocally related to sleep time among US citizens (Basner et al., 2007, 2009). The largest reciprocal relationship to sleep was found for work time, followed by travel time (Figure 1). Travel time included time to commute to and from work. Commute time accounted for 26.8% of travel time on weekdays and for 44.7% of travel time in those who worked on the ATUS interview day.

As shown in Figure 1A, work time and travel time are the primary activities that are reciprocally related to sleep time among U.S. citizens (Basner et al., 2007). Average sleep time for adults who worked ≥ 8 hours per day was 7 hours 32 minutes per day, while those who worked less than 8 hours per day slept 8 hours and 7 minutes per day in bed, and those who did not work slept 8 hours and 50 minutes per day (Basner et al., 2007).[1] Figure 1B illustrates the distribution of bedtimes for 21,475 Americans from the years 2004-2006. Figure 1C illustrates the distribution of wake times for those same years. Adults who worked ≥ 8 hours terminated bed time an average of 0.68 hours (41 minutes) earlier than those who worked less than 8 hours, and 1.31 hours earlier than individuals that were not working. It is noteworthy that many of them are awakening to begin their commute to work between 05:00 and 06:00 clock time—which for most humans coincide endogenous circadian phases of elevated sleep pressure (Doran et al., 2001; Lim and Dinges, 2008). However, there were no reliable differences between among the three work categories relative to bedtime. Watching television was the primary activity people engaged in before going to bed, while the timing of commute to work appeared not to be as flexible. (Basner and Dinges, 2009). These data suggest that those who work longer hours for compensation also obtain less sleep due to awakening earlier, primarily for reasons related to commuting to work.

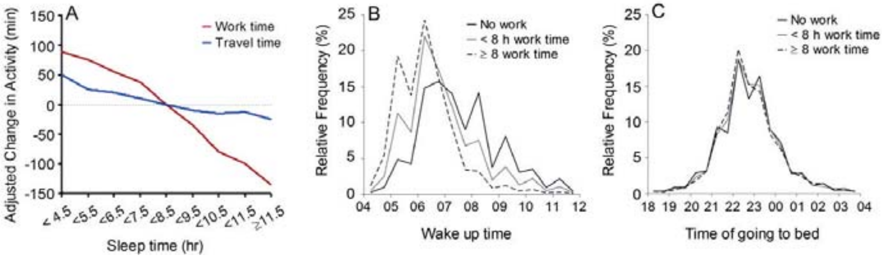

Figure 1 Panel A shows average change in weekday work time and travel time depending on sleep time category based on multiple linear regression models adjusting for age, gender, ethnicity, educational attainment, income, presence of partner, and presence of children. The 7.5 hours to less than 8.5 hours sleep time category served as reference (reprinted with permission from Basner et al., (2007)). Panels B and C show distributions of time of getting up in the morning (B) and time of going to bed at night (C) for three subgroups: respondents who did not work; those who worked less than 8 hours; and for those who worked 8 hours or more (reprinted with permission from Basner & Dinges (2009)).

The vast majority of U.S. workers commute to and from work primarily by driving a motor vehicle alone. Data from the U.S. Census Bureau for the year 2010 revealed that an estimated 76.6 percent of Americans (51.7 million people) regularly drove to and from work alone in the year 2010.[2] Only 9.7 percent carpooled (i.e., more than 1 person in the vehicle), while only 4.9 percent used public transportation. Another 2.8 percent walked to work and 1.7 percent commuted to work in other ways (e.g., bicycle, motorcycle, taxicab). The overall estimated average commute travel time for U.S. workers 16 and older was 25.3 minutes. An estimated 4.3 percent worked at home.

Collectively the ATUS and U.S. Census Bureau data highlight the extent of the reciprocal relationship between sleep time and commute time in the U.S. It is not know if this relationship would be found in other industrialized countries.

[1] It is noteworthy that average ATUS sleep times were longer than those reported in many other population-based stud¬ies of Americans (Basner et al., 2007). This was attributed to the ATUS “sleep” category including other terms that may not involve physiological sleep (e.g., falling asleep, dozing off, nap¬ping, getting up, waking up). Thus, the ATUS sleep times are overestimates of actual physiological sleep obtained by U.S. respon¬dents per 24 hours. This overestimate was a constant across sleep times, and therefore should not have affected the relationship between sleep time and other activities.

[2] http://www.census.gov/newsroom/releases/archives/american_community_survey_acs/cb11-158.html

3. HEALTHY SLEEP IS ESSENTIAL TO OPERATE A MOTOR VEHICLE SAFELY

Sleep has not been eliminated by evolutionary adaptation. It is ubiquitous in the animal kingdom when defined by the following behavioural criteria: behavioral quiescence; stereotypical body posture; reduced response to stimulation; spontaneously reversed in less than 24 hours; resists deprivation; and increases following deprivation. On the basis of these criteria, we can conclude that sleep is present throughout the animal kingdom. There is also extensive scientific evidence in virtually all species that have been studied that sleep continuity, intensity and duration collectively provide the "recovery" that restores alertness. Sleepiness increases when any of these aspects are denied.

3.1. Acute and chronic sleep loss affect alertness and performance

A meta-analysis investigating 70 published scientific studies of acute sleep loss involving 147 cognitive tests revealed that both cognitive speed and accuracy were adversely affected by sleep deprivation (Lim and Dinges, 2010). Effect sizes were largest for lapses in simple attention and smallest (nonsignificant) for reasoning accuracy. This result, and a great deal of other research summarized briefly below, supports the conclusion that deficits in ability to sustained attention and respond quickly—elements required for safe operation of motor vehicles and many other transportation modalities—are among the primary effects of inadequate sleep on human performance, and therefore represent the most parsimonious explanation for real-world errors and accidents associated with sleep deficits (whether from life style or medical conditions).

The Psychomotor Vigilance Test (PVT), which is based on probing the ability of the brain to sustain attention and respond quickly (i.e., behavioral alertness), has proven to be one of the most sensitive performance assays for detecting wake state instability and elevated neurobehavioral pressure for sleep (Dinges and Powell, 1985, Doran et al., 2001, Lim and Dinges, 2008; Basner and Dinges, 2011). Wake state instability refers to moment-to-moment shifts in the relationship between neurobiological systems mediating wake maintenance and those mediating sleep initiations (Doran et al., 2001, Banks and Dinges, 2007; Lim &

Dinges, 2008). Figure 2 shows all the sequential 10-minute PVT reaction times (RT) for a single subject at 20:00 hour clock time following 12 hours awake (Figure 2A) and 60 hours awake (Figure 2B). Fast, stable responding was possible at 12 hours awake (Figure 2A). However, after 60 hours awake, reaction time fluctuated wildly from response to response as time on task proceeded (Figure 2B). Latency to the loss of stable performance decreased with increasing sleep deprivation. The duration of longer reaction times (i.e., lapses in attention) also increased. In addition, the presence of false starts (i.e., pressing the response key when no stimulus was present) can be seen in Figure 2 B (down arrows) together with frequent long-duration lapses. The changes in behavioural alertness are the hallmarks of inadequate sleep and they can be detected even when sleep deprivation is relatively modest but chronic (Lim and Dinges, 2008), which can occur when people habitually restrict their sleep to 4-6 hours a night during work weeks.

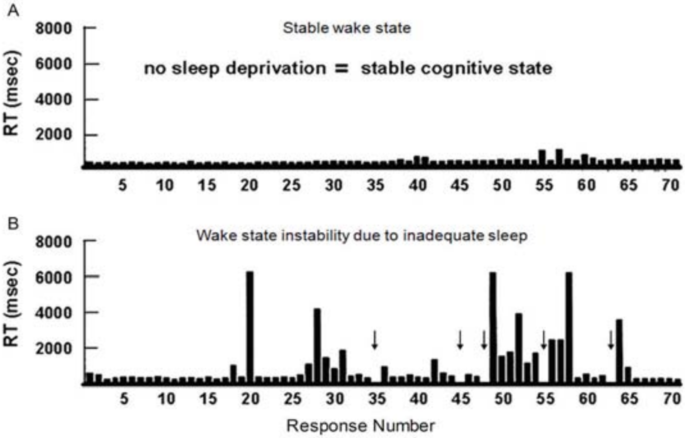

Figure 2 A healthy adult's consecutive response times (ms) across 10 minutes of Psychomotor Vigilance Test (PVT) performance at 12 hours awake (panel A) and 60 hours awake (panel B).

The adverse effects of sleep loss on the tendency to fall asleep, on lapses in attention, and on slowing of psychomotor and cognitive speed are cumulative and people are often not aware of how much it is affecting alertness and performance (Dinges et al., 1997). Two large-scale experimental studies described dose-related effects of chronic sleep restriction on neurobehavioral performance measures (Belenky et al., 2003, Van Dongen et al., 2003). In one study, subjects were randomized to 7 nights of 3, 5, 7 or 9 hours of time in bed for sleep per night (Belenky et al., 2003). In the other study, subjects were restricted to 4, 6, or 8 hours of time in bed per night for 14 nights (Van Dongen et al., 2003). These studies showed that vigilance lapses and response slowing occurred more frequently with each day of sleep duration below 7 hours. In addition, vigilance lapses increased across days of sleep restriction, but ratings of fatigue and sleepiness changed very little, indicating that the more impaired subjects became from chronic partial sleep loss, the less accurately they estimated their fatigue and sleepiness (Van Dongen et al., 2003).

Although people are not always able to estimate accurately how sleepy they are when sleep-restricted, there is no question that they experience sleepiness and its effects on their performance. Consequently, sleepy drivers experience sleepiness and often struggle with it (Reyner and Horne, 1998, Horne and Baulk, 2004), but they are not always able to accurately judge the severity of the sleepiness relative to the risk it poses to their performance (Van Dongen et al., 2003). That is, they come to believe they can overcome the sleepiness by force of will or certain behaviours (e.g., signing, listening to music, etc.), but these attempts at alerting one's self have a very short time constant, and quickly give way within a few seconds or minutes to reduced alertness, degraded response times, and lapses of attention.

Even a brief lapse of attention can be catastrophic when operating a motor vehicle. A drowsy driving crash requires a lapse of only a few seconds to result in a crash. As sleepiness overtakes a driver's brain and behaviour, causing a reduction in steering control that typically leads to a shallow drift out of lane, a crash is imminent within seconds. Thus, a 2-second lapse in which the angle of drift is 4 degrees and speed is at 60 miles per hour ph (i.e., 96.6 km per hour) results in a vehicle leaving the lane of traffic. A major video-camera-based study of naturalistic driving by the U.S. National Highway Traffic Safety Administration found that eyes-off-road durations of greater than 2 seconds significantly increased individual near-crash/crash risk (Klauer et al., 2006).

3.2. Sleep loss can pose a performance risk equivalent to alcohol

Scientific studies have equated performance deficits induced by varying degrees of sleep loss to the deficits induced by varying blood alcohol concentrations (Dawson and Reid, 1997, Williamson and Feyer, 2000, Williamson et al., 2001, Roehrs et al., 2003). For example, 18 hours of wakefulness in healthy adults produced psychomotor performance deficits equal to those present when blood alcohol concentration (BAC) was 0.05%. Twenty-two hours of wakefulness produced psychomotor performance deficits equal to 0.08% BAC (Dawson and Reid, 1997). Other studies also equate prolonged wakefulness with BAC > 0.04 g%. Such data have increased public awareness of the risks posed by operating a motor vehicle with inadequate sleep, and they have led to public policy debates regarding ways to prevent or discourage drowsy driving.

4. DRIVING SLEEPY IS COMMON AND A RISK TO TRANSPORTATION SAFETY

4.1. Driving sleepy is common even in daylight in urban areas

Operating a motor vehicle while fatigued, sleepy, drowsy, or while falling asleep has been discovered to be a more common than previously assumed (McCartt et al., 1996, Sagberg, 1999, Lloberes et al., 2000, Masa et al., 2000, Flatley et al., 2004, Klauer et al., 2006, Abe et al., 2012). Contrary to previous assumptions that boredom and monotony produce drowsy driving, the phenomenon has been found to be quite common urban areas, on busy roadways, and in the daytime. Both laboratory and field scientific studies have revealed that the biology that initiates sleep can do so even when there is stimulation and risk.

The U.S. National Highway Traffic Safety Administration asked for volunteers living in the Washington D.C. metropolitan area to allow their cars to be specially instrumented with recording systems for one year. They instrumented the cars of 100 volunteers with cameras looking forward, looking at the driver's face, looking at the driver's lap and the console, looking in the rear-view mirrors and looking off to the side. The participants then used their motor vehicles as they normally did for a year. The National Highway Traffic Safety Administration did no intervention, but simply acquired naturalistic data on driver and vehicle behaviours. The results definitely demonstrated that drowsy driving in metropolitan Washington D.C. was as common as distracted driving, and it occurred more often during daylight/lighted conditions (Klauer et al., 2006). In fact, a majority of the drowsiness-related crashes in this study occurred during the daytime in heavy traffic (during morning and evening commutes). Thus, the risks of driving drowsy during the day may be slightly higher than at night due to higher traffic density, at least in metropolitan areas.

Figure 3A from Klauer et al. (2006) shows the percentage of crashes and near-crashes in which three types of inattention were identified as a contributing factor in the Washington D.C. naturalistic driving study. The baseline epochs show similar or lesser percentages to crashes or near-crashes in the secondary tasks and driving-related inattention. In contrast, it is an interesting finding when comparing drowsiness's low baseline-epoch percentage to the much higher percentage in crashes and near-crashes. This indicates that driver drowsiness significantly increases near-crash/crash risk.

Figure 3B from Klauer et al. (2006) presents the baseline data percentages for secondary task-related epochs, drowsiness-related epochs, and total number of epochs for each level of lighting. They indicate that there was a considerable amount of distracted driving risk in daylight. The majority of secondary task-related events and total epochs occurred during daylight hours. While it is commonly thought that most drowsy driving occurs at night, this figure shows that driving drowsy during the daylight may be slightly riskier than driving drowsy in the dark due to higher traffic density.

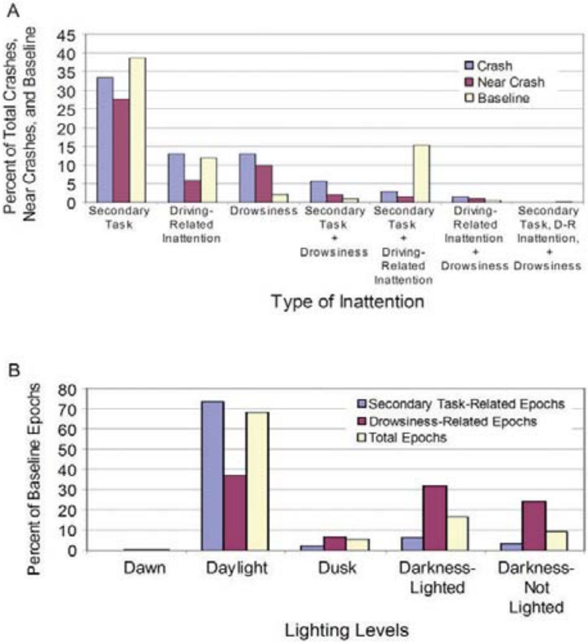

Figure 3 (Panel A) The percentage of crashes and near-crashes in which three types of inattention were identified as a contributing factor (N = 69 crashes, 761 near-crashes, and 19,827 baseline epochs). (Panel B) Percentage of secondary-task-related, drowsiness-related, and total baseline epochs for the different lighting levels observed. Figure from Klauer et al. (2006) naturalistic study of U.S. drivers in metropolitan Washington DC.

Although the Klauer et al. (2006) study did not provide a good estimate of the prevalence of drowsy driving in the U.S., a 2002 Gallup survey conducted for the U.S. National Highway Traffic Safety Administration on the distracted and drowsy driving attitudes and behaviours found that 37% of the driving population indicated they had nodded off for at least a moment or fallen asleep while driving at some time in their life and 4% within the past month (National Survey of Distracted and Drowsy Driving Attitudes and Behaviors, 2002, Centers for Disease Control and Prevention, 2013). Male drivers were almost twice as likely to report having nodded off while driving (49%) than were female drivers (26%). Approximately 22% of male drivers who reported falling asleep while driving indicated it was within the past month, compared to 19% of females. Sleep loss was also found to common among U.S. drivers who experienced drowsy driving. Reduced sleep time was also common among those reporting drowsy driving: 24% who reported a recent drowsy driving episode also reported having 4 or fewer hours of sleep the night drowsy driving, while 26% reported receiving about approximately 6 hours of sleep the night prior to drowsy driving. Interestingly, relatively few drivers who reported driving sleepy indicated they had consumed alcohol (2%) or sedating medications (12%) prior to driving.

This survey study estimated that it approximately 292,000 U.S. drivers were involved in some type of crash within the past six months as a result of falling asleep at the wheel (National Survey of Distracted and Drowsy Driving Attitudes and Behaviors, 2002). This U.S. report concluded that in recent years there have been about 56,000 crashes annually in which driver drowsiness/fatigue was cited by police. Annual averages of roughly 40,000 nonfatal injuries and 1,550 fatalities result from these crashes. It is widely recognized that these statistics underreport the extent of these types of crashes.

4.2. Driving sleepy is a common crash risk

In the U.S., Japan, Europe, and elsewhere, fall-asleep crashes have been associated with insufficient sleep due to both lifestyle (e.g., chronic insufficient sleep to accommodate longer work hours and/or longer commute times), and medical conditions (i.e., untreated hypersomnolence disorders) (George et al., 1987, McCartt et al., 1996, Sagberg, 1999, Lindberg et al., 2001, Connor et al., 2002, Nabi et al., 2006, Powell et al., 2007, Gnardellisa et al., 2008, Mulgrew et al., 2008, Papadakaki et al., 2008, Abe et al., 2010, Sagaspe et al., 2010, Pizza et al., 2010, Abe et al., 2011a). Driver fatigue and sleepiness has been estimated to contribute to 10-20% of motor vehicle crashes, and 15-50% of motor vehicle fatalities on busy motorways (Horne and Reyner, 1995, Maycock, 1995, Sagberg, 1999, Philip et al., 2001, Flatley et al., 2004).

Driving sleepy has been found to be a significant factor in injury-related and fatal crashes in many countries (Philip et al., 2001, Connor et al., 2002, Flatley et al., 2004; Klauer et al., 2006). In New Zealand, an eightfold increased risk was observed if drivers reported sleepiness. In addition, almost a threefold risk was reported for drivers who were driving after five hours or less of sleep (Connor et al., 2002). In France, a survey of 67,671 crashes in France determined 10% were fatigue related (Philip et al., 2001). In United Kingdom, a recent study that examined 1,828 crashes in the U.K. reported that 17% of the accidents resulting in injury or death were sleep related (Flatley et al., 2004). The U.S. National Highway Traffic Safety Administration estimates of driver fatigue/sleepiness annual costs to be $12.5 billion, 100,000 police-reported crashes, 1,550 deaths (4% of fatalities) and 71,000 injuries.

4.3. Sleep-related driving crashes have a temporal profile

Figure 4 shows the time of day profile of fall-asleep crashes from the North Carolina database in the United States over the years 1990-1992 (Pack et al., 1995). This study investigated time of day of 4,333 highway crashes (primarily rural roadways) in which the driver (all ages) was judged by law enforcement to be asleep but not intoxicated. It shows that drowsy driving crash risk varies across the day in a manner reflecting (nonlinear) circadian and sleep need dynamics. Crashes peaked in the morning between 06:00 and 09:00 clock time, and again in mid-afternoon. Both of these periods are biological times of elevated sleepiness (Doran et al., 2001). Moreover, the increased likelihood of sleepiness-related crashes in the morning, often after sunrise, which is consis tent with the higher number of crashes in daylight in the Klauer et al. (2006) study, likely reflects both the elevated sleep pressure at this time—particularly when sleep has been restricted the day before—and the occurrence of more motor vehicles on the roadway due to commuting. This indicates how the biological dynamics of sleep drive that can impair driving performance interact with the environmental factors of exposure (i.e., traffic density) to yield a nonlinear profile for sleepiness-related crashes.

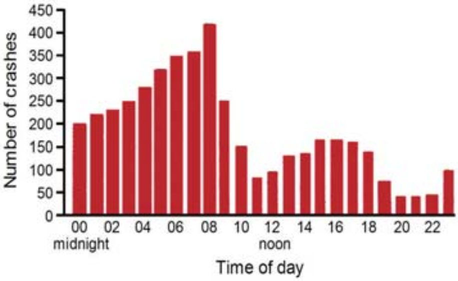

Figure 4 Time of day profile of fall-asleep crashes from the North Carolina database in the United States over the years 1990-1992. Reprinted with permission from Pack et al. (1995).

Figure 5 displays the time of occurrence of falling asleep crashes in drivers of different ages. Drivers 25 years of age or younger were most at risk for fall asleep crashes overall and for night time into early morning crashes, in particular. This is consistent with both the increased risk-taking among younger drivers, and evidence that adolescents and young adults are more vulnerable to the neurobehavioral effects of sleep loss. At the opposite end of the spectrum, drivers over 65 years of age were least at risk for sleep-related accidents overall, but most at risk for mid-afternoon crashes. Their profile likely reflects the fact that few of them drive at night due to deficits in nocturnal vision. In addition, there is possibility that older drivers stop driving at night because of the loss of night vision.

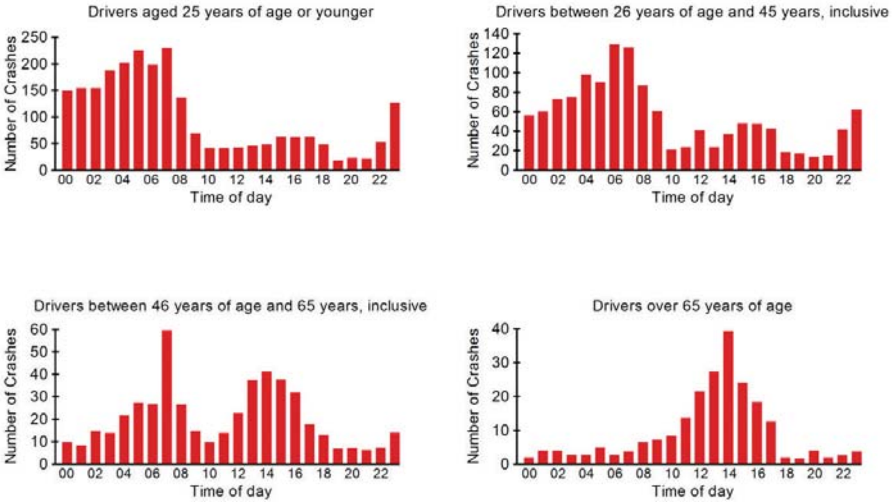

Figure 5 Time of occurrence of crashes from the North Carolina database in the United States over the years 1990-1992. Data are shown for drivers of different ages in which the driver was judged to be asleep but not intoxicated. Reprinted with permission from Pack et al. (1995).

5. DRIVER INCAPACITATION FROM SLEEP LOSS REQUIRES NOVEL SOLUTIONS

Limitations in current transportation systems (e.g., inadequate numbers of safe roadway safe rest to nap or ingest caffeine) can increase the likelihood of people driving sleepy. Despite a wide range of roadway and vehicle technologies to make driving safer and crashes less likely to be lethal, driver incapacitation from insufficient sleep appears to a common occurrence that is associated with both an elevated crash risk and a serious bodily injury risk. There is no evidence that driving drowsy will decrease without solutions to prevent its cause and mitigate its occurrence. Safety technologies are increasingly available in motor vehicles (e.g., from anti-locking brakes to proximity-warning systems) that reduce crash risk. However, there is a need to develop validated safety technologies for detecting when a driver is increasingly unfit to operate a vehicle safely. The need is especially great in the area of drowsy driving given its prevalence and crash risk, and the inability to detect these risks with a breath test or a traffic stop by a law enforcement officer. A recent review of technologies for managing driver fatigue and sleepiness—especially in federally-regulated industries such as commercial trucking in the U.S.—concluded that there are significant challenges and opportunities for technological approaches to fatigue management (Balkin et al., 2011). There is need to establish their validity, safety value, acceptance and use adherence by the motor vehicle operator, and abuse potential (Dinges and Mallis, 1998).

5.1. Sleepiness/fatigue prediction technologies

Human performance (e.g., alertness, attention, working memory, problem solving, reaction time, situational awareness, risk taking, etc.) is dynamically controlled by the interaction of waking biological processes sensitive to time awake, sleep quantity, and circadian phase near-linear processes within and between days, the circadian interaction with these processes makes the prediction of performance nonlinear. For example, when remaining awake for 40 hours, it is a counterintuitive fact that fatigue and performance deficits are worse at 24 hours than at 40 hours awake. It is this nonlinearity that makes inadequate and imprecise many work-hour limits based solely on a linear model of fatigue (i.e., the longer one works the more fatigued one will become). This nonlinearity in the brain's performance capability over time is the reason that developing mathematical models that predict performance is increasingly regarded as essential. Mathematical models of sleepiness/fatigue prediction are the fatigue management technologies that have received the most attention in the past two decades (Borbély, 1982, Mallis et al., 2004, Van Dongen et al., 2007, McCauley et al., 2009). Based on the dynamic interaction of human sleep homeostatic drive and circadian rhythms, some of these mathematical models have advanced to the critical point of integrating individual differences into the modeling predictions for a more accurate estimate of the timing and magnitude of fatigue effects on individuals (Van Dongen et al., 2007), which should facilitate more precise use of countermeasures (e.g., naps, recovery sleep, caffeine intake). There is recognition, however, that mathematical models developed to predict and prevent fatigue risks have limitations (e.g., they cannot predict a given individual's dynamic profile of fatigue/sleepiness), and as such they may be only one element in a fatigue risk management system. On the other hand, sleepiness-detection technologies that monitor an individual's momentary level of alertness hold the promise of helping to mitigate drowsy-driving risks more precisely.

5.2. Sleepiness Detection Technologies

There are three scientifically-based reasons why objective sleepiness-detection technologies are needed in safety-sensitive operations such as transportation. (1) Humans are often unable to accurately estimate how variable or uneven their alertness and driving performance may have become due to inadequate sleep, working at night, or a sleep disorder. When fatigued they tend to estimate their alertness based by their best responses and ignore their worse responses. This may be why sleepy drivers may continue to drive despite the obvious risk to themselves and other vehicles as well as pedestrians. (2) Performance deficits from sleep loss accumulate over days to high levels when recovery sleep is chronically inadequate (Belenky et al., 2003, Van Dongen et al., 2003). Awareness of these cumulative deficits appears to be less accurate as performance declines (Van Dongen et al., 2003). (3) While everyone eventually develops performance deficits from sleep loss, some people do so very rapidly while others take much longer, and these differences appear to be stable characteristics of people (Van Dongen et al., 2004) and therefore they may reflect biological differences among them (Viola et al., 2007, Goel et al., 2009, Goel et al., 2010, Goel et al., 2011a, Kuna et al., 2012). There are currently no reliable biomarkers for one's performance vulnerability to sleep loss, making detection of sleepiness while driving a primary goal.

Laboratory validation trials. The following is an example of one approach to detecting sleepiness/drowsiness while driving. It illustrates the criticality of the validation science that must be undertaken as an initial first step toward devel oping a reliable unobtrusive measure of sleepiness while driving. We systematically evaluated the validity of a number of the more promising sleepiness detection technologies, which included brain wave (EEG) measures, eye blink devices, a measure of slow eyelid closures (called PERCLOS), and a head position sensor, as well as individuals' own ratings of their sleepiness. In a series number of tightly controlled, double-blind experiments, we evaluated the extent to which each technology detected the alertness of subjects over a 40-hour period, as measured by lapses of attention on the well-validated (to sleep loss) Psychomotor Vigilance Test (PVT). We time-locked each technology to PVT performance in a manner that permitted precise determine of whether a given technology could reliably track minute-by-minute, the waxing and waning of alertness and psychomotor speed across a normal day and during nocturnal and diurnal periods of sleep deprivation. The evaluation was done double-blind such that each technology readout was done by its developer blind to PVT performance, and the latter was scored blind to each technology readout. A professional biostatistician then fit the prediction of alertness from each technology to the PVT performance data for each subject across a 42-hour period of evaluation. This resulted in a measure of statistical coherence for each technology for each subject. The initial study results reported in Dinges et al. (1998) were subsequently replicated for a retinal reflectance measure of (Dinges et al., 2002). As shown in Figure 6, only PERCLOS reliably and accurately tracked PVT lapses of attention in all subjects, outperforming not only all the other technologies, but also subjects' own ratings of their fatigue and alertness in both validation trials (Dinges et al., 1998, Dinges et al., 2002). A more recent study also found that PERCLOS was the most effective indicator among several ocular variables (saccade, slow eye movement, pupil, blink, or eyelid closure) for detecting deteriorated vigilance (Abe et al., 2011b). We are now developing a technique that involves precise unobtrusive tracking of PERCLOS in real time using optical computer recognition (Dinges et al., 2005b, Dinges et al., 2007).

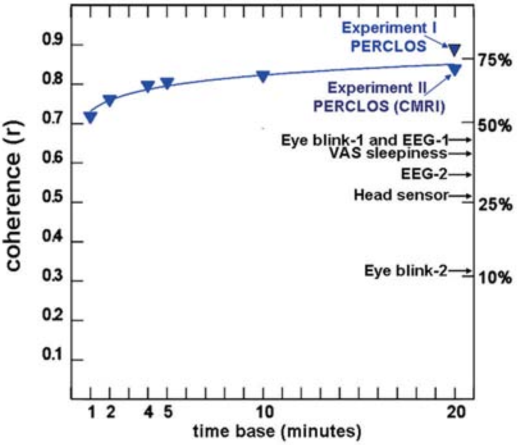

Figure 6 Mean PERCLOS coherence for lapse frequency across 42-hr of waking, as a function of the time base used to define an epoch. A distance-weighted least squares function was fit to the data. Figure from Dinges et al. (2002). In both the 1998 and 2002 experiments, PERCLOS as measured by a human scorer of slow eyelid closures in 1998 and as measured by infrared retinal reflectance in 2002 had much higher coherence with PVT performance lapses of attention—a very sensitive objective measure of sleepiness—than any other technology (i.e., EEG-1, EEEG-2, Eye blink-1, Eye blink-2, Head sensor). PRCLOS was also a better predictor of alertness performance than subjects self-reports of their sleepiness by visual analogue scale (i.e., VAS sleepiness). The accurate of PERCLOS predictions of performance degraded by sleepiness increased as the time base for integrated assessment increased from 1 minute to 20 minutes. More recent work also supports the accuracy of PERCLOS for unobtrusive detection of sleepiness while performing (Abe et al., 2011b).

Field study of commercial truck drivers. In an over-the-road study of the effects of feedback from fatigue-detection technologies on commercial truck drivers we evaluated a group of technologies that included an infrared-based retinal reflectance measure of PERCLOS to determine whether feedback from fatigue detection technologies would help truck drivers maintain their alertness in actual working conditions (Dinges et al., 2005a). We found that the drivers felt the fatigue detection devices (and the PVT test they performed in the middle and at the end of each trip) informed them of their fatigue levels and prompted them to acquire more sleep on their days off duty. The wrist actigraphy data we acquired on the drivers confirmed that they increased their sleep by an average of 45 minutes on days off duty (Dinges et al., 2005a). This is a remarkable and unexpected outcome, and it suggests another purpose for fatigue detection technologies in the workplace—namely to urge operators to sleep more during off-duty periods. Recent research we have conducted on recovery sleep following a period of sleep restriction reveals that getting extra sleep during off-duty periods and days off work is one of the most important fatigue countermeasures-but it will only be effective if sufficient time is permitted for sleep off duty (Banks et al., 2010). If we could use fatigue management technology to warn drivers when they are getting sleepy and to encourage them to get off the roadway, it may be possible to reduce the risk of sleepiness-related motor vehicle crashes.

6. CONCLUSIONS

There is extensive scientific evidence that insufficient sleep can make it difficult to remain awake, alert and attentive. Moreover, performance deficits from prolonged wakefulness have been equated to those from high blood alcohol concentrations. Studies reveal that drowsy driving is increasingly common. Moreover, a naturalistic driving study in the U.S. found that video-documented driving drowsy resulted in a four- to six-times higher near-crash/crash risk relative to driving alert, and that drowsy driving had a higher crash risk than distracted driving. This is because sleep loss reduces the ability to sustain attention, react quickly, and take action to avoid an accident before it is too late. These involuntary lapses of attention and slowed reaction times can be frequent, prolonged and uncontrollable, depending on the degree of sleep loss within and between days. Research has also shown that drivers experience sleepiness and struggle with it, but they are not always able to accurately judge the severity of the sleepiness relative to the risk it poses to their performance. A search for ways to reliably detect and warn or alert drivers who are experiencing sleepiness has led to a search for technologies that can validly, reliably and unobtrusively track fluctuations in driver alertness-sleepiness while driving. Prevention of drowsy-driving risks and crashes with validated technologies is an achievable goal that could reduce accidents associated with inadequate sleep from lifestyle and medical disorders.

ACKNOWLEDGMENT

Some aspects of the development of this manuscript were supported by the National Space Biomedical Research Institute through NASA cooperative agreement NCC 9-58. Dr. Takashi Abe's time and effort was supported by the Japan Society for the Promotion of Science Postdoctoral Fellowships for Research Abroad.

REFERENCES

Abe, T.,Komada, Y., Asaoka, S., Ozaki, A. and Inoue, Y. Questionnaire-based evidence of association between sleepiness while driving and motor vehicle crashes that are subjectively not caused by falling asleep. Sleep and Biological Rhythms, 2011a, 9: 134-43.

Abe, T., Komada, Y. and Inoue, Y. Short Sleep Duration, Snoring and Subjective Sleep Insufficiency Are Independent Factors Associated with both Falling Asleep and Feeling Sleepiness while Driving. Internal Medicine, 2012, 51: 3253-60.

Abe, T., Komada, Y., Nishida, Y., Hayashida, K. and Inoue, Y. Short sleep duration and long spells of driving are associated with the occurrence of Japanese drivers' rear-end collisions and single-car accidents. Journal of Sleep Research, 2010, 19: 310-6.

Abe, T., Nonomura, T., Komada, Y., Asaoka, S., Sasai, T., Ueno, A. and Inoue, Y. Detecting deteriorated vigilance using percentage of eyelid closure time during behavioral maintenance of wakefulness tests. International Journal of Psychophysiology, 2011b, 82: 269-74.

Ayas, N. T., White, D. P., Manson, J. E., Stampfer, M. J., Speizer, F. E., Malhotra, A. and Hu, F. B. A prospective study of sleep duration and coronary heart disease in women. Archives of Internal Medicine, 2003, 163: 205-9.

Balkin, T. J., Horrey, W. J., Graeber, R. C., Czeisler, C. A., Dinges, D. F. The challenges and opportunities of technological approaches to fatigue management. Accident Analysis and Prevention, 2011, 43: 565-72.

Banks, S. and Dinges, D. F. Behavioral and physiological consequences of sleep restriction. Journal of Clinical Sleep Medicine, 2007, 3: 519-28.

Banks, S, Dinges D. F. Chronic Sleep Deprivation. In: Kryger, M.H., Roth, T., Dement, W.C. (Eds.) Principles and Practice of Sleep Medicine (5th ed.), Elsevier, Philadelphia, PA, pp. 67-75, 2011.

Banks, S., Van Dongen, H. P., Maislin, G. and Dinges, D. F. Neurobehavioral dynamics following chronic sleep restriction: dose-response effects of one night for recovery. Sleep, 2010, 33: 1013-26.

Barger, L. K., Cade, B. E., Ayas, N. T., Cronin, J. W., Rosner, B., Speizer, F. E., Czeisler, C. A. and Harvard Work Hours Hlth Safety, G. Extended work shifts and the risk of motor vehicle crashes among interns. The New England Journal of Medicine, 2005, 352: 125-34.

Basner, M. and Dinges, D. F. Dubious Bargain: Trading Sleep for Leno and Letterman. Sleep, 2009, 32: 747-52.

Basner, M. and Dinges, D. F. Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. Sleep, 2011, 34: 581-91.

Basner, M., Fomberstein, K. M., Razavi, F. M., Banks, S., William, J. H., Rosa, R. R. and Dinges, D. F. American time use survey: sleep time and its relationship to waking activities. Sleep, 2007, 30: 1085-95.

Belenky, G., Wesensten, N. J., Thorne, D. R., Thomas, M. L., Sing, H. C., Redmond, D. P., Russo, M. B. and Balkin, T. J. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. Journal of Sleep Research, 2003, 12: 1-12.

Borbély, A. A. A two process model of sleep regulation. Human Neurobiology, 1982, 1: 195-204.

Centers for Disease Control and Prevention. Drowsy driving-19 states and the district of Columbia.Morbidity and Mortality Weekly Report, 2013, 61:1033-7.

Connor, J., Norton, R., Ameratunga, S., Robinson, E., Civil, I., Dunn, R., Bailey, J. and Jackson, R. Driver sleepiness and risk of serious injury to car occupants: population based case control study. BMJ, 2002, 324: 1125.

Davis, S., Mirick, D. K. and Stevens, R. G. Night shift work, light at night, and risk of breast cancer. Journal of the National Cancer Institute, 2001, 93: 1557-62.

Dawson, D. and Reid, K. Fatigue, alcohol and performance impairment. Nature, 1997, 388: 235-35.

Dinges, D. F. An overview of sleepiness and accidents. Journal of Sleep Research, 1995, 4: 4-14.

Dinges, D.F., Mallis, M.M. Managing fatigue by drowsiness detection: Can technological promises be realized? In: Hartley, L. (Eds.) Managing Fatigue in Transportation, Elsevier Science Ltd., Kidlington, Oxford, UK, pp. 209-29, 1998.

Dinges, D.F., Maislin, G. Brewster, R.M., Krueger, G.P., Carroll, R.J. Pilot test of fatigue management technologies. Journal of the Transportation Research Board No. 1922, Transportation Research Board of the National Academies, Washington, DC, 175-82, 2005a.

Dinges, D. F., Mallis, M., Maislin, G., Powell, J. W. Evaluation of techniques for ocular measurement as an index of fatigue and the basis for alertness management. Final report, U.S. Department of Transportation, National Highway Traffic Safety Administration, 1-112, 1998.

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., Aptowicz, C. and Pack, A. I. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. Sleep, 1997, 20: 267-77.

Dinges, D. F. and Powell, J. W. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. Behavior Research Methods, Instruments, & Computers, 1985, 17: 652-5.

Dinges, D.F., Price, N.J., Maislin, G., Powell, J. W., Ecker, A. J., Mallis, M. M., Szuba, M. P. Prospective Laboratory Re-Validation of Ocular-Based Drowsiness Detection Technologies and Countermeasures. Subtask A in Report: Wierwille WW, et al.: HTSA Drowsy Driver Detection and Interface Project, DTNH 22-00-D-07007; Task Order No. 7; September, 2002.

Dinges, D. F., Rider, R. L., Dorrian, J., Mcglinchey, E. L., Rogers, N. L., Cizman, Z., Goldenstein, S. K., Vogler, C., Venkataraman, S. and

Metaxas, D. N. Optical computer recognition of facial expressions associated with stress induced by performance demands. Aviation, Space, and Environmental Medicine, 2005b, 76: B172-82.

Dinges, D. F., Venkataraman, S., Mcglinchey, E. L. and Metaxas, D. N. Monitoring of facial stress during space flight: Optical computer recognition combining discriminative and generative methods. Acta Astronautica, 2007, 60: 341-50.

Doran, S. M., Van Dongen, H. P. A. and Dinges, D. F. Sustained attention performance during sleep deprivation: Evidence of state instability. Archives Italiennes de Biologie, 2001, 139: 253-67.

Flatley, D., Reyner, L. A. and Horne, J. A. Sleep-related Crashes on Sections of Different Road Types in the UK (1995– 2001). Department for Transport, London, 2004.

George, C. F., Nickerson, P. W., Hanly, P. J., Millar, T. W. and Kryger, M. H. Sleep apnoea patients have more automobile accidents. Lancet, 1987, 2: 447.

Gnardellisa, C., Tzamaloukab, G., Papadakakib, M. and Chliaoutakis, J. E. L. An investigation of the effect of sleepiness, drowsy driving, and lifestyle on vehicle crashes. Transportation Research Part F: Traffic Psychology and Behaviour, 2008, 11: 270-81.

Goel, N., Banks, S., Lin, L., Mignot, E. and Dinges, D. F. Catechol-O-methyltransferase Val158Met polymorphism associates with individual differences in sleep physiologic responses to chronic sleep loss. PLoS ONE, 2011a, 6: e29283.

Goel, N., Banks, S., Mignot, E. and Dinges, D. F. PER3 polymorphism predicts cumulative sleep homeostatic but not neurobehavioral changes to chronic partial sleep deprivation. PLoS ONE, 2009, 4: e5874.

Goel, N., Banks, S., Mignot, E. and Dinges, D. F. DQB1*0602 predicts interindividual differences in physiologic sleep, sleepiness, and fatigue. Neurology, 2010, 75: 1509-19.

Goel N, Van Dongen HPA, Dinges DF. Circadian Rhythm in Sleepiness, Alertness and Performance. In: Kryger MH, Roth T, Dement WC (Eds.) Principles and Practice of Sleep Medicine (5th ed.), Elsevier, Philadelphia, PA, pp. 445-55, 2011b.

Gottlieb, D. J., Punjabi, N. M., Newman, A. B., Resnick, H. E., Redline, S., Baldwin, C. M. and Nieto, F. J. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Archives of Internal Medicine, 2005, 165: 863-7.

Gottlieb,D. J., Redline, S., Nieto, F. J., Baldwin, C. M., Newman, A. B., Resnick, H. E. and Punjabi, N. M. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. Sleep, 2006, 29: 1009-14.

Horne, J. A. and Baulk, S. D. Awareness of sleepiness when driving. Psychophysiology, 2004, 41: 161-5.

Horne, J. A. and Reyner, L. A. Sleep related vehicle accidents. British Medical Journal, 1995, 310: 565-7.

Jewett, M. E., Dijk, D. J., Kronauer, R. E. and Dinges, D. F. Dose-response relationship between sleep duration and human psychomotor vigilance and subjective alertness. Sleep, 1999, 22: 171-9.

Kaneita, Y., Uchiyama, M., Yoshiike, N. and Ohida, T. Associations of usual sleep duration with serum lipid and lipoprotein levels. Sleep, 2008, 31: 645-52.

Klauer SG, driver inattention on near-crash/crash risk: An analysis using the 100-car naturalistic driving study data. National Highway Traffic Safety Administration, Report No. DOT HS 810 594, 226 pages, April 2006.

Kubo, T., Ozasa, K., Mikami, K., et al. Prospective cohort study of the risk of prostate cancer among rotating-shift workers: Findings from the Japan Collaborative Cohort Study. American Journal of Epidemiology, 2006, 164: 549-55.

Kuna, S. T., Maislin, G., Pack, F. M., Staley, B., Hachadoorian, R., Coccaro, E. F. and Pack, A. I. Heritability of performance deficit accumulation during acute sleep deprivation in twins. Sleep, 2012, 35: 1223-33.

Lim, J. L. and Dinges, D. F. Sleep deprivation and vigilant attention. Annals of the New York Academy of Sciences, 2008, 1129: 305-22.

Lim, J. L. and Dinges, D. F. A Meta-Analysis of the Impact of Short-Term Sleep Deprivation on Cognitive Variables. Psychological Bulletin, 2010, 136: 375-89.

Lindberg, E., Carter, N., Gislason, T. and Janson, C. Role of snoring and daytime sleepiness in occupational accidents. American Journal of Respiratory and Critical Care Medicine, 2001, 164: 2031-5.

Lloberes, P., Levy, G., Descals, C., Sampol, G., Roca, A., Sagales, T. and De La Calzada, M. D. Self-reported sleepiness while driving as a risk factor for traffic accidents in patients with obstructive sleep apnoea syndrome and in non-apnoeic snorers. Respiratory Medicine, 2000, 94: 971-6.

Lyznicki, J. M., Doege, T. C., Davis, R. M., Williams, M. A. and Am Med, A. Sleepiness, driving, and motor vehicle crashes. JAMA : the journal of the American Medical, 1998, 279: 1908-13.

Mallis, M. M., Mejdal, S., Nguyen, T. T. and Dinges, D. F. Summary of the key features of seven biomathematical models of human fatigue and performance. Aviation, Space, and Environmental Medicine, 2004, 75: A4-14.

Marshall, N. S., Glozier, N. and Grunstein, R. R. Is sleep duration related to obesity? A critical review of the epidemiological evidence. Sleep Medicine Reviews, 2008, 12: 289-98.

Masa, J. F., Rubio, M. and Findley, L. J. Habitually sleepy drivers have a high frequency of automobile crashes associated with respiratory disorders during sleep. American Journal of Respiratory and Critical Care Medicine, 2000, 162: 1407-12.

Maycock, G. Driver Sleepiness as a Factor in Car and HGV Accidents. Transport Research Laboratory, Crowthorne, 1995.

McCartt, A. T., Ribner, S. A., Pack, A. I. and Hammer, M. C. The scope and nature of the drowsy driving problem in New York State. Accident; Analysis and Prevention, 1996, 28: 511-17.

McCauley, P., Kalachev, L. V., Smith, A. D., Belenky, G., Dinges, D. F. and Van Dongen, H. P. A new mathematical model for the homeostatic effects of sleep loss on neurobehavioral performance. Journal of Theoretical Biology, 2009, 256: 227-39.

Mitler, M. M., Carskadon, M. A., Czeisler, C. A., Dement, W. C., Dinges, D. F. and Graeber, R. C. Catastrophes, Sleep and Public-Policy – Consensus report. Sleep, 1988, 11: 100-09.

Mollicone, D. J., Van Dongen, H. P. A., Rogers, N. L., Banks, S. and Dinges, D. F. Time of Day Effects on Neurobehavioral Performance During Chronic Sleep Restriction. Aviation Space and Environmental Medicine, 2010, 81: 735-44.

Mulgrew, A. T., Nasvadi, G., Butt, A., Cheema, R., Fox, N., Fleetham, J. A., Ryan, C. F., Cooper, P. and Ayas, N. T. Risk and severity of motor vehicle crashes in patients with obstructive sleep apnoea/hypopnoea. Thorax, 2008, 63: 536-41.

Nabi, H., Gueguen, A., Chiron, M., Lafont, S., Zins, M. and Lagarde, E. Awareness of driving while sleepy and road traffic accidents: prospective study in GAZEL cohort. BMJ, 2006, 333: 75.

National Survey of Distracted and Drowsy Driving Attitudes and Behaviors: 2002. Volume 1. Findings Report. Submitted to the National Highway Traffic Safety Administration by The Gallup Organization. http://www.nhtsa.dot.gov/people/injury/drowsy_driving1/survey-distractive03/index.htm

Pack, A. I., Pack, A. M., Rodgman, E., Cucchiara, A., Dinges, D. F. and Schwab, C. W. Characteristics of crashes attributed to the driver having fallen asleep. Accident; Analysis and Prevention, 1995, 27: 769-75.

Papadakaki, M., Kontogiannis, T., Tzamalouka, G., Darviri, C. and Chliaoutakis, J. Exploring the effects of lifestyle, sleep factors and driving behaviors on sleep-related road risk: a study of Greek drivers. Accident; Analysis and Prevention, 2008, 40: 2029-36.

Philip, P., Vervialle, F., Le Breton, P., Taillard, J. and Horne, J. A. Fatigue, alcohol, and serious road crashes in France: factorial study of national data. BMJ, 2001, 322: 829-30.

Pizza, F., Contardi, S., Antognini, A. B., Zagoraiou, M., Borrotti, M., Mostacci, B., Mondini, S. and Cirignotta, F. Sleep quality and motor vehicle crashes in adolescents. Journal of Clinical Sleep Medicine, 2010, 6: 41-5.

Powell, N. B., Schechtman, K. B., Riley, R. W., Guilleminault, C., Chiang, R. P. and Weaver, E. M. Sleepy driver near-misses may predict accident risks. Sleep, 2007, 30: 331-42.

Pukkala, E., Martinsen, J. I., Lynge, E., Gunnarsdottir, H. K., Sparen, P., Tryggvadottir, L., Weiderpass, E. and Kjaerheim, K. Occupation and cancer - follow-up of 15 million people in five Nordic countries. Acta Oncologica, 2009, 48: 646-790.

Reyner, L. A. and Horne, J. A. Falling asleep whilst driving: are drivers aware of prior sleepiness? International Journal of Legal Medicine, 1998, 111:

120-3.

Roehrs, T., Burduvali, E., Bonahoom, A., Drake, C. and Roth, T. Ethanol and sleep loss: A "Dose" comparison of impairing effects. Sleep, 2003, 26: 981-85.

Roehrs T, Carskadon MA, Dement WC, Roth T. Daytime sleepiness and alertness. In: Kryger MH, Roth T, Dement WC (Eds.) Principles and Practice of Sleep Medicine (5th ed.), Elsevier, Philadelphia, PA, pp. 49-53, 2011.

Sagaspe, P., Taillard, J., Bayon, V., Lagarde, E., Moore, N., Boussuge, J., Chaumet, G., Bioulac, B. and Philip, P. Sleepiness, near-misses and driving accidents among a representative population of French drivers. Journal of Sleep Research, 2010, 19: 578-84.

Sagberg, F. Road accidents caused by drivers falling asleep. Accident; Analysis and Prevention, 1999, 31: 639-49.

Schernhammer, E. S., Laden, F., Speizer, F. E., Willett, W. C., Hunter, D. J., Kawachi, I. and Colditz, G. A. Rotating night shifts and risk of breast cancer in women participating in the nurses' health study. Journal of the National Cancer Institute, 2001, 93: 1563-68.

Stutts, J. C., Wilkins, J. W., Scott Osberg, J. and Vaughn, B. V. Driver risk factors for sleep-related crashes. Accident; Analysis and Prevention, 2003, 35: 321-31.

Van Dongen, H. P., Maislin, G., Mullington, J. M. and Dinges, D. F. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep, 2003, 26: 117-26.

Van Dongen, H. P., Mott, C. G., Huang, J. K., Mollicone, D. J., Mckenzie, F. D. and Dinges, D. F. Optimization of biomathematical model predictions for cognitive performance impairment in individuals: accounting for unknown traits and uncertain states in homeostatic and circadian processes. Sleep, 2007, 30: 1129-43.

Van Dongen, H. P. A., Baynard, M. D., Maislin, G. and Dinges, D. F. Systematic interindividual differences in neurobehavioral impairment from sleep loss: Evidence of trait-like differential vulnerability. Sleep, 2004, 27: 423-33.

Viola, A. U., Archer, S. N., James, L. M., Groeger, J. A., Lo, J. C. Y., Skene, D. J., Von Schantz, M. and Dijk, D. J. PER3 polymorphism predicts sleep structure and waking performance. Current Biology, 2007, 17: 613-18.

Williamson, A. M. and Feyer, A. M. Moderate sleep deprivation produces impairments in cognitive and motor performance equivalent to legally prescribed levels of alcohol intoxication. Occupational and Environmental Medicine, 2000, 57: 649-55.

Williamson, A. M., Feyer, A. M., Mattick, R. P., Friswell, R. and Finlay-Brown, S. Developing measures of fatigue using an alcohol comparison to validate the effects of fatigue on performance. Accident; Analysis and Prevention, 2001, 33: 313-26.

Wolff, B., Volzke, H., Schwahn, C., Robinson, D., Kessler, C. and John, U. Relation of self-reported sleep duration with carotid intima-media thickness in a general population sample. Atherosclerosis, 2008, 196: 727-32.

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