The Interactive Effects of Extended Wakefulness and Low-dose Alcohol on Simulated Driving and Vigilance

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Objectives: Sleep deprivation and alcohol both impair driving performance. This study assessed the interactive effect of low-dose alcohol and extended wakefulness.

Design: Repeated-measures, crossover design evaluating psychomotor and driving function in a non–sleep-deprived state and after extended wakefulness with and without low-dose alcohol.

Setting: Teaching hospital sleep laboratory.

Participants: Nineteen volunteer professional drivers

Intervention & Measurements: Driving simulation (AusEdTM) and the Psychomotor Vigilance Task (PVT) were measured in a rested state (12-15 hours awake) and after extended wakefulness (18-21 hours awake) during two sessions. Alcohol was administered during one session, with performance measured at blood alcohol concentrations (BAC) of 0.00%, 0.03%, and 0.05% in a non–sleep-deprived state, and at 0.03% after extended wakefulness (at 01:00 and 03:00). During the second session, tests were performed at the same times without alcohol.

ROAD-SAFETY CAMPAIGNS IN AUSTRALIA AND THROUGHOUT THE WORLD AIMED AT REDUCING ALCOHOL-RELATED TRAFFIC DEATHS HAVE INCREASED public awareness of the risks of drinking and driving. Alcohol has serious deleterious effects on driving performance and perceptual judgement. A review of 200 scientific papers found that reactiontime, divided-attention, and psychomotor-function impairments are evident at blood alcohol concentrations (BAC) from 0.1% down to as low as 0.03%.¹ Alcohol concentrations above 0.05%, but below 0.08%, appreciably increase the risk of having a crash.^{1,2} Based on this evidence, the BAC level of 0.05% has been set as the legal limit for driving in Victoria and in all other states and territories of Australia.

Sleepiness also increases the risk of road crashes.³ It is estimated that 15% to 30% of traffic accidents are directly related to driver sleepiness, as determined by crash circumstances.⁴ Although there is a clear association between BAC and both simulated driving performance and road crashes,^{5,6} no laboratory-based objective

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Results: The combination of extended wakefulness and low-dose alcohol had significant deleterious effects on reaction time and lapses (PVT) and variation in lane position and speed (AusEd). Extended wakefulness (18-21 hours awake) combined with low-dose alcohol (0.03% BAC) resulted in more lapses (t = -2.75, P < 0.05) and greater variation in lane position (t = -3.94, P < 0.01) and speed (t = -2.79, P < 0.05) than did a BAC of 0.05% in a rested state.

Conclusion: The combination of legal low-dose alcohol and extended wakefulness results in impairment worse than that at an alcohol level known to increase accident risk. Avoiding alcohol when driving after extended wakefulness may reduce accident risk.

Keywords: Sleep deprivation, alcohol, driving, vigilance

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measure of sleepiness has been shown to relate to crash risk. Comparison of performance deterioration due to sleepiness with performance changes caused by alcohol (BAC of 0.05% or above) is one means of determining whether a particular level of sleepiness is likely to increase accident risk. Performance on a variety of tasks after 25 hours awake is similar to performance at a BAC of 0.08% to 0.10% in a non–sleep-deprived state.⁷⁻⁹ These studies also found impaired performance at relatively modest BACs below 0.05%.

Although there are conclusive data regarding the separate effects of alcohol and sleepiness on driving, in real-life situations it is common for these two conditions to occur simultaneously (alcohol-related accidents occur more commonly in the early hours of the morning).¹⁰ Data from roadside alcohol breath testing of drivers in Victoria, Australia, has revealed that the peak incidence of elevated alcohol levels occurs between 01:00 and 04:00. Nine percent of drivers tested on weekends during this time had a BAC between 0.010% and 0.049%, with 7.0% having a BAC of 0.050% or above.¹¹ In contrast, only 1.4% of drivers had a BAC between 0.010% and 0.049% between 07:00 and 14:00. Thus, there are many drivers in whom alcohol ingestion may interact with the effects of extended wakefulness.11 A roadside survey in Finland found that the rate of low alcohol readings (BAC < 0.05%) among drivers has doubled in the past 8 years and is three times more frequent at night.¹² The combination of alcohol and sleepiness appears to be synergistic, with the relative risk of death in crashes related to alcohol and fatigue combined being greater than the sum of the individual effects.13 A small number of experimental studies have assessed the combined effects of sleepiness and alcohol on simulated driving performance. Some studies have demonstrated a significant decline in driving performance when alcohol and sleep deprivation are combined, in comparison with either factor alone,¹⁴⁻¹⁷ whereas others have found no synergistic change in performance.18

Various methods of inducing sleepiness have been employed in these studies, including sleep restriction to 5 hours the previous night,^{14,16} circadian effects,^{15,19} and extended wakefulness.¹⁸ Varying alcohol levels have been used, including legal and illegal levels for driving. These studies raise the issue of when (due to circadian-rhythm effects or sleep deprivation) legal limits of alcohol may become a risk to the driver.^{14,17,20} However, a limitation of these studies is that the level of impairment observed is difficult to equate to a level known to increase crash risk.

The current study assessed the effects of a legal BAC (0.03%) during extended wakefulness (also during the circadian nadir) on vigilance and simulated driving. Performance at a BAC of 0.03% during extended wakefulness was compared with performance at a BAC of 0.05% in a rested state. There are no published studies of this latter comparison, which is critical in that it may suggest that a combination of low blood alcohol levels and extended wakefulness could increase crash risk. In addition, this is the only study that has assessed the effect of extended wakefulness without prior sleep restriction in combination with low blood alcohol levels. It was hypothesized that driving performance and vigilance would be worse at 0.03% BAC after extended wakefulness, when compared with 0.05% BAC in a rested state.

METHODS

Subjects

Volunteer professional drivers were recruited from transport companies to participate in the study. Nineteen drivers (18 men) volunteered for the study. Drivers were required to have a current drivers license and be between the ages of 18 and 65 years. Drivers were excluded if they had (1) any medical contraindication to undertaking sleep deprivation or drinking alcohol, (2) a history of sleep apnea or any clinical features of sleep apnea (Multivariate Apnea Prediction score > 0.5,²¹ (3) narcolepsy or insomnia, or (4) visual acuity problems or (5) were on any medication or used illicit drugs that might affect performance. Drivers were excluded if they had chronic sleepiness (score greater than 10 on the Epworth Sleepiness Scale.^{22, 23} Drivers were offered a fixed payment of \$200 as reimbursement for time, paid at the end of the study. Written informed consent was gained from all drivers. The study was approved by the Human Research Ethics Committee at Austin Health, Melbourne.

Procedure

Medical examination and practice session

During the initial consultation, all drivers completed a medical examination, were screened for inclusion and exclusion criteria, and practiced the driving simulation and Psychomotor Vigilance Tasks (PVT). Drivers completed the Multivariate Apnea Prediction questionnaire and the Epworth Sleepiness Scale and were asked to keep a sleep diary and record caffeine and alcohol intake for the week before each session. On the night prior to study days, drivers were asked to have at least 7 hours of sleep and wake up at 07:00. They were also instructed to refrain from ingestion of caffeine or other stimulant medication from midday on the day of the study until after the study had ended.

Experimental Conditions

Drivers presented for two separate test conditions in the sleep laboratory in a randomized cross-over design, one week apart. Drivers attended the sleep laboratory from 19:00 until 04:00 the following morning. A calibrated Alcometer (model SD_400, Lion Laboratories, Glamorgan, UK) was used to confirm that no alcohol was consumed before the study. This instrument has an accuracy of plus or minus 10%. Drivers were given a standard meal (580 calories) before completing an initial driving simulation and PVT at 19:00.

During the alcohol condition, drivers consumed measured amounts of alcohol to reach a BAC of approximately 0.03% for session 1 (20:30) and over 0.05% in session 2 (22:00). For sessions 3 (01:00) and 4 (03:00), alcohol was administered to maintain a BAC of 0.03% (see Table 1). At each test time, drivers performed the PVT and simulated driving task. The order of the tasks was consistent across sessions. Standard measures of vodka were given orally in orange juice or soft drink to achieve the incremental increases in BAC. Blinding to the presence of alcohol was not attempted because other authors have shown that participants can determine whether or not they have received alcohol,⁹ but participants were blinded to the dose of alcohol and their BAC. Oral rinses (H₀O) were used after drinking to remove mouth alcohol. Approximately 15 minutes after each alcohol dose, breath alcohol level was measured. A BAC level within 0.005% of the desired level was accepted at each point. After the final test time, drivers stayed in the sleep laboratory until their BAC had returned to 0.00%.

During the no-alcohol condition, drivers performed simulated driving and the PVT at the same time points as described for the alcohol condition: 20:30, 22:00, 01:00, and 03:00. No alcohol was consumed by the drivers during this condition, and BAC was confirmed as being 0.00% by Alcometer. Drivers were taken home by taxi after both test sessions.

Measures

Drivers completed a 10-minute PVT.²⁴ This task assesses reaction time to a visual stimulus, presented at varying intervals approximately 10 times per minute. Median reaction time and the number of lapses (reaction time > 500 ms) were recorded for the 10-minute PVT session. These measures are sensitive to circadian effects and sleep deprivation.²⁵

Following the PVT, drivers completed the AusEd[™] driving simulator.²⁰ This computer-based driving simulation program is sensitive to the effects of sleep deprivation and alcohol.^{14,27,28} Drivers undertook a 30-minute monotonous nighttime drive on a 2-lane highway, which included standard lane divisions and road edges marked with reflective posts. A 30-minute drive was chosen because previous studies have demonstrated sleepdeprivation effects within this time frame.^{22,23} The drive included a series of curved and straight sections, and subjects had to brake in response to coming up behind ten other vehicles. Drivers were asked to maintain their position in the middle of the left-hand lane on the road (in accordance with Australian driving code) and keep their speed within 60 to 80 kph on the speedometer. Variation in lane position (deviation from the subjects' median lane position averaged every 40 msec, excluding crashes),²⁹ variation in speed (outside the prescribed 60 to 80kph range), braking reaction

time, and mean number of crashes (off road, stoppage events, and truck collisions) were recorded. The road components and time of presentation of trucks was identical for each drive session. Variation in lane position and speed were chosen as the primary outcome variables because they have been shown to be sensitive to the effects of sleep loss and alcohol. Drivers then completed the Karolinska sleepiness Scale to measure state-related changes in subjective sleepiness.

Statistical Analysis

SPSS Version 12.1 (SPSS, Inc., Chicago, IL) was used for all statistical analyses. Repeated-measures analysis of variance was conducted to evaluate the effect of extended wakefulness on PVT and simulated driving performance in the no-alcohol and low-alcohol (0.03% BAC test times only) conditions (using Greenhouse-Geisser corrections where appropriate). Posthoc paired-sample t-tests were conducted where the omnibus F-test was significant. Following this, planned paired t-tests were used to assess differences in performance at different alcohol levels, adjusting for multiple comparison. The significance level was set at P < 0.05.

RESULTS

Three drivers were unable to complete all the alcohol sessions due to adverse reactions (nausea and vomiting) to the alcohol; therefore, data from 16 drivers were analysed. Mean age was 46.2 years (SD, 10.7 years). The mean Epworth Sleepiness Scale score of the drivers was 6.5. Drivers reported on their sleep diary that they slept an average of 6.7 hours (SD, 1.3 hours) on the night before the test session and 7.5 hours per night (SD, 1.3 hours) for the prior week. No drivers were excluded on the basis of their sleep diaries, and all drivers had a BAC of zero at the start of each test session. The mean BAC at each test time are shown in Table 1. The mean BAC at 03:00 was slightly below the target level.

Performance During Extended Wakefulness with and without Alcohol

There was significant deterioration in psychomotor and simulated driving performance following extended wakefulness and when drivers consumed low levels of alcohol. Median reaction time on the PVT deteriorated significantly following extended wakefulness in the alcohol condition ($F_{1.85, 25.94} = 14.66$, P < 0.001; partial $\eta^2 = 0.52$); however, this trend was not significant in the no-alcohol condition (P = 0.13; Figure 1A). Posthoc t-tests indicated that there was a significant difference between the 19:00 and 20:30 sessions ($t_{14} = -3.01$, P < 0.01) and the 20:30 and 01:00 sessions ($t_{15} = -2.80$, P < 0.05) in the alcohol condition. There were no significant differences between session times in the noalcohol condition. A comparison across conditions revealed that PVT reaction times were slower with a BAC of 0.03%, compared with without alcohol at 20:30 ($t_{15} = 4.07$, P < 0.001). Drivers were also slower at 03:00 after low-level alcohol consumption (t_{15} = 2.77, P < 0.05), when compared with performance in the noalcohol condition at the same time (Figure 1A).

Extended wakefulness also had a significant effect on the frequency of PVT lapses in combination with moderate BAC ($F_{1.44, 20.13} = 4.80$, P < 0.05 *partial* η^2 =0.26), but there was no significant *SLEEP, Vol. 30, No. 10, 2007*

 Table 1—Blood Alcohol Concentration for Each Session in the

 Alcohol Condition

Condition	Time	BAC, %
Non-sleep-deprived	19:00	0.000 (0.000)
	20:30	0.033 (0.006)
	22:00	0.053 (0.006)
Sleep-deprived	01:00	0.030 (0.005)
	03:00	0.026 (0.010)
Data are presented as mean centration.	(SD). BAC refers	to blood alcohol con

effect in the no-alcohol condition (P = 0.23; Figure 1B). Posthoc t-tests revealed that drivers had significantly more PVT lapses at 01:00, compared with 20:30, in the alcohol condition ($t_{15} = -2.4$, P < 0.05). There were no significant differences in the number of PVT lapses between the two conditions at any time point during the night.

There were significant differences in speed variation on the driving simulator with extended wakefulness in both the alcohol ($F_{1.51, 21.10} = 6.33$, P < 0.05, *partial* $\eta^2 = 0.31$), and no-alcohol conditions ($F_{2.28, 31.94} = 3.63$, P < 0.05, *partial* $\eta^2 = 0.21$, Figure 1C). Drivers had significantly more speed variation at 01:00, compared with 20:30, in the alcohol condition ($t_{15} = -2.89$, P < 0.05) and in the no-alcohol condition ($t_{14} = -2.24$, P < 0.05). A comparison of the two conditions indicated that drivers showed greater speed variability in the alcohol condition (0.03% BAC), compared with when no alcohol was consumed, at 01:00 after 19 hours awake ($t_{14} = 2.29$, P < 0.05).

Extended wakefulness of 19 hours at 01:00 also increased variation in lane position on the driving simulator in the alcohol condition ($F_{1.93, 27.05} = 13.15$, P < 0.001, *partial* $\eta^2 = 0.48$; Figure 1D). Variation in lane position did not change significantly with extended wakefulness in the no-alcohol condition (P = 0.14). Drivers had significantly more variation in lane position at 01:00, compared with 20:30, in the alcohol condition ($t_{15} = -4.14$, P < 0.01). Posthoc testing revealed significantly greater variation in lane position at 01:00 after alcohol (0.03% BAC), compared with the no-alcohol condition ($t_{15} = -2.85$, P < 0.05). Interestingly, although performance was worse with alcohol (0.03% BAC) at 03:00 than without, no significant difference between the two conditions was found in this sample (P = 0.21).

There was a significant change in Karolinska Sleepiness Scale scores in both the alcohol ($F_{1.84, 59.0} = 18.6$, P < 0.01, *partial* $\eta^2 = 0.55$) and no-alcohol conditions ($F_{1.50, 61.0} = 23.6$, P < 0.01, *partial* $\eta^2 = 0.63$).

The Combined Effect of Extended Wakefulness and Low-dose Alcohol on Performance Compared with Different Alcohol Levels in a Rested State

Performance during extended wakefulness (01:00) with lowdose alcohol (0.03%) was compared with performance at different BAC (0.00%, 0.03% and 0.05%) in a rested state using paired samples t-tests. Median reaction time on the PVT at 01:00 with a BAC of 0.03% was similar to PVT reaction time in a rested state (22:00) at a BAC above 0.05%, which is above the legal limit in Australia (Figure 2A). Drivers had significantly more lapses

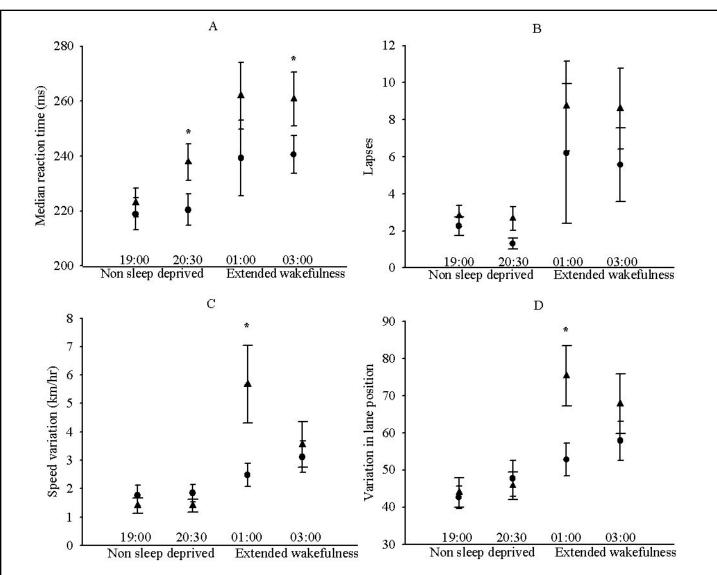


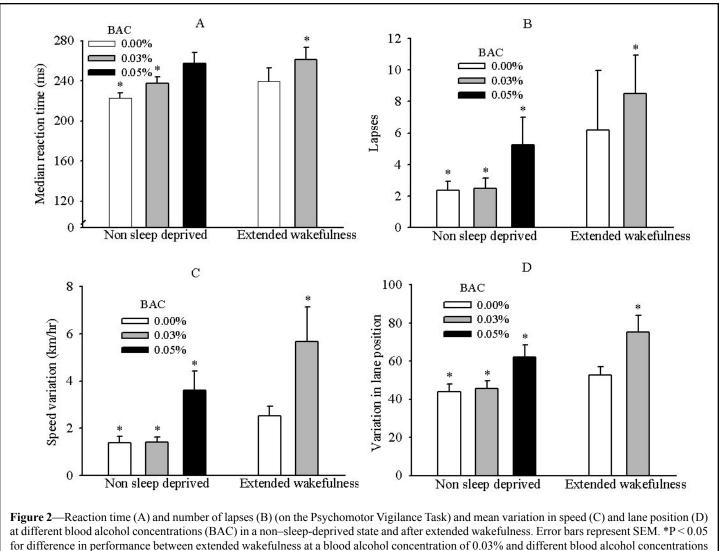
Figure 1—Reaction time (A) and number of lapses (B) (on the Psychomotor Vigilance Test [PVT]) and mean variation in speed (C) and lane position (D) at 0.03% blood alcohol concentration (BAC) (\blacktriangle) and 0.00% BAC (\bullet) in a non–sleep-deprived state and after extended wakefulness. There was a significant increase in reaction time, number of lapses, and variation in lane position with extended wakefulness in the alcohol condition only (F_{1.85, 25.94} = 14.66, P < 0.001; F_{1.44, 20.13} = 4.80, P < 0.05; and F_{1.93, 27.05} = 13.15, P < 0.001, respectively). Variation in speed increased with extended wakefulness in both the alcohol (F_{1.51, 21.10} = 6.33, P < 0.05), and no-alcohol conditions (F_{2.28, 31.94} = 3.63, P < 0.05). Error bars represent SEM. *P< 0.05.

on the PVT at 01:00 with a BAC of 0.03% than in a rested state (22:00) with a BAC of 0.05% ($t_{15} = -2.75$, P < 0.05; Figure 2B). Variation in lane position was greater with low levels of alcohol (0.03% BAC) at 01:00, compared with low levels of alcohol at 20:30 ($t_{14} = -4.07$, P < 0.001; Figure 2D). It was also significantly higher at 01:00 with a BAC of 0.03% than at a BAC of 0.05% in a rested state (22:00; $t_{14} = -3.94$, P < 0.001). Speed variability also increased significantly with low alcohol levels (0.03% BAC) in a sleep-deprived state compared with the same alcohol level (0.03% BAC $t_{14} = -2.78$, P <0.05) and 0.05% BAC ($t_{14} = -2.79$, P < 0.05) in a rested state (Figure 2C).

DISCUSSION

In this study, we examined the driving and psychomotor decrements associated with extended wakefulness and low levels of alcohol that are legal for driving. The study was designed to replicate a common real-life scenario, such as driving home from a party or late-night dinner. We found that low levels of alcohol (BAC of 0.03%) resulted in greater deterioration in driving and psychomotor performance after extended wakefulness (18-21 hours awake) than did the same BAC in a non-sleep-deprived state. The combination of extended wakefulness and low levels of blood alcohol (0.03%), which are legal for driving, resulted in driving and psychomotor performance impairment that was worse than or equivalent to that observed at illegal alcohol levels (BAC of 0.05%) in a rested state. The findings suggest that extended wakefulness in combination with low, legal alcohol levels may impair driving performance to a degree that would increase crash risk to a similar or greater degree than the risk associated with illegal BACs.

Testing in the rested state for this study was performed in the early evening after 11 to 14 hours awake. No deleterious effect on performance is expected from sleep loss or circadian rhythm factors at this time.^{7,30} The addition of alcohol slowed reaction time at this time of the evening, even at a low level (0.03% BAC), but



in a non-sleep-deprived state.

there was little effect on simulated driving performance. The drivers recruited in the current study were regular drinkers and would have some tolerance to the effects of alcohol, whereas people who do not drink regularly may have had more-pronounced effects on performance.³¹ During extended wakefulness (no-alcohol condition), a deleterious effect was expected on performance as a result of extended hours of wakefulness (18-21 hours) and operating during the circadian nadir period between 01:00 and 04:00.²³ When low levels of alcohol were added (0.03% BAC), there was a significant deterioration in drivers' ability to maintain the correct speed and lane position at 01:00 after 18 hours awake, when compared with the no-alcohol condition. This suggests that even low levels of alcohol can impair a driver's performance when sleepiness is also present, as a result of extended wakefulness and operating during the circadian nadir. The lack of significant differences between performance at a BAC of 0.00% and 0.03% for lapses and reaction time on the PVT at 01:00 may have been due to large intraindividual differences in performance and inadequate power to detect small changes in performance. The timing of each session was planned to closely replicate common real-world driving situations. The combination of alcohol and extended wakefulness appears to impair performance to a greater extent than would be expected from the single additive effect of the two factors.

Arnedt et al¹⁸ found that the addition of alcohol at 0.08% to 20 hours of wakefulness resulted in a performance decrement that was greater than the individual effects of each component. This interaction was studied at a relatively high alcohol level, which in itself is expected to cause major performance impairment and is an illegal level for driving in Australia.

Several previous studies have examined the effect of low alcohol levels and sleep restriction on performance using different sleep-restriction paradigms, but they have not compared the degree of performance impairment to that at an alcohol level of 0.05%. In a study of young men, the addition of alcohol (0.038% BAC) following a restricted night's sleep resulted in at least an additive negative effect on driving performance.¹⁶ In a further study by the same group on women, there was a marked increase in the number of lane crossings during the driving simulation due to sleepiness when low alcohol levels were combined with sleep restriction. compared with either intervention alone.¹⁷ Inducing sleepiness in these studies relied on the effects of sleep restriction on the night prior to testing, and the tests were performed during the midafternoon circadian dip. One study assessed the combined effect of sleepiness and low alcohol levels in young drivers by studying them at 01:00 in addition to restricting them to 5 hours sleep on the night prior to testing.¹⁴ Drivers were given alcohol

prior to testing (0.037% BAC). The addition of alcohol at this level resulted in deterioration in driving performance, increased crashes on the simulator, and increased alpha activity on the electroencephalogram. This study did not compare performance to a control session (no sleep restriction or alcohol). These studies have used various sleepiness-inducing paradigms, but this is the first study to examine the effect of extended wakefulness and low-dose alcohol without prior sleep restriction.

This study assessed the implications of driving at various times during the circadian cycle and following extended wakefulness at alcohol levels that are commonly found in road-side testing. A common real-life scenario, which our protocol mimicked, is for people to drive home at night after consuming a moderate amount of alcohol, against a background of a normal sleep on the previous night. Some drivers may intentionally wait until they believe their BAC has dropped enough to be safe to drive; however, in doing so, they may be prolonging wakefulness or potentially increasing the circadian impact on their driving.³² The combination of extended wakefulness and low alcohol levels is therefore more ecologically valid (9% of drivers driving between 01:00 and 04:00 on weekends have been show to have a BAC between 0.010% and 0.049%). Previous studies have used slightly higher alcohol levels than the current study, which were close to the legal limit for driving in Australia. None of the previous studies has attempted to compare the combined effect of sleepiness and low alcohol levels to a standard that indicates an increased accident risk (performance at a BAC of 0.05%).

Interestingly, although performance on all measures was poorer at 03:00, after 20 hours awake, when alcohol was consumed, only reaction time differed significantly between the two conditions. For the driving variables, there was actually some improvement at the 03:00 session compared with the 01:00 session in the alcohol condition, when performance was significantly worse compared with extended wakefulness alone. This is surprising given that a more pronounced negative circadian rhythm and sleep loss effect is expected at that time.^{33,34} The mean alcohol level was slightly lower at 03:00, compared to at 01:00 (0.026% vs 0.03%), so there may have been less of an alcohol effect at 03:00. Sustained steadystate alcohol levels have a constant effect on tasks such as reaction time.³⁵ Hence, no improvement or deterioration in performance is expected as a result of maintaining BAC at a sustained high level, apart from the direct effect of the BAC at that time. Low doses of alcohol have a less-depressant effect as the BAC rises and a more depressant effect during the elimination phase.³⁶ This can result in some variability of the effect of alcohol on performance despite drivers having a similar BAC. Therefore, when the drivers were dropping from 0.05% BAC to 0.03% BAC between 23:00 and 01:00, there may have been a more-depressant effect from alcohol, which could have been less evident at 03:00. Due to the design of the study, it was difficult to control for these potential effects at each time point. Although measuring performance at different BACs and times during separate sessions would avoid the differential effects of rising and falling alcohol levels on performance, in reality both situations occur. Finally, it is also possible that drivers were more motivated at 03:00 when they knew it was their final session, and this may have enhanced their performance at that time. Motivation may counteract the effects of sleep deprivation to some degree during performance of a monotonous task.

Although previous authors have demonstrated that the addition of low alcohol levels to the effects of sleep loss has a compounding negative effect on performance, it has not been demonstrated whether this degree of performance impairment is likely to result in increased crash risk.^{14,16,17} This study addressed the hypothesis that performance would be worse following extended wakefulness combined with a low BAC, when compared with a high BAC (>0.05%) when not sleepy. It was also expected that drivers' performance would deteriorate during this time of the night due to circadian effects. The level of 0.05% was chosen because it is associated with at least a two-fold increase in crash risk and 0.05% BAC has been selected as the level at which it is illegal to drive in Australia.² Drivers showed significantly more lapses on the PVT and variability in speed and lane position at 01:00 with a BAC of 0.03%, when compared with an BAC of 0.05% in a non-sleep-deprived state. This suggests that the combination of extended wakefulness and low alcohol levels results in a degree of performance impairment that may increase crash risk. This combination is legally permitted and common in real life.¹¹

Sleepiness, especially when combined with alcohol, presents a particularly high risk of off-road crashes resulting in death or serious injury. The relative risk of death in a crash related to fatigue has previously been estimated to be 1.65, and, for alcohol-related crashes, the relative risk is 4.2 fold. ¹³ For alcohol and fatigue combined, the relative risk of death is 6.8 fold.¹⁵ This combined risk is largely unrecognized in Australia. This study has demonstrated a marked interactive effect of low (legal) alcohol levels and extended wakefulness in an experimental setting. The combination of extended wakefulness and low alcohol levels is common among weekend drivers.¹¹ Circadian effects would also play a role in performance impairments during extended wakefulness. Although it is difficult to relate simulated driving performance to actual driving, this study provides insight into the effects of sleepiness and alcohol on different skills essential to driving, such as reaction time, steering control, and speed variability. In applying these result to the general population, it needs to be considered that professional drivers may have a different response to sleep loss and alcohol and that women may have a response that is different from that of men.¹⁷ This study, together with other laboratory studies, suggests that careful analysis of road-crash data is warranted to assess whether low levels of alcohol in combination with sleepiness results in an unacceptable increase in crash risk. Although there is public awareness of the individual risks of sleepiness and alcohol on driving, knowledge about the potential synergistic impact of these 2 factors is limited. Restricting alcohol intake during extended wakefulness may result in reduced road accidents and thus warrants further assessment.

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REFERENCES

- 1. Dunbar JA, Penttila A, Pikkarainen J. Drinking and driving: choosing the legal limits. BMJ Clin Res Ed 1987;295:1458-60.
- 2. Hurst PM, Harte D, Frith WJ. The Grand Rapids dip revisited. Accid Anal Prev 1994;26:647-54.
- 3. Connor J, Whitlock G, Norton R, Jackson R. The role of driver sleepiness in car crashes: a systematic review of epidemiological studies. Accid Anal Prev 2001;33:31-41.

- Akerstedt T. Consensus statement: fatigue and accidents in transport operations. J Sleep Res 2000;9:395.
- Liguori A, D'Agostino RB, Jr., Dworkin SI, Edwards D, Robinson JH. Alcohol effects on mood, equilibrium, and simulated driving. Alcohol Clin Exp Res 1999;23:815-21.
- 6. Glucksman E. Alcohol and accidents. Br Med Bull 1994;50:76-84.
- 7. Dawson D, Reid K. Fatigue, alcohol and performance impairment. Nature 1997;388:235.
- Williamson AM, Feyer AM, Mattick RP, Friswell R, Finlay-Brown S. Developing measures of fatigue using an alcohol comparison to validate the effects of fatigue on performance. Accid Anal Prev 2001;33:313-26.
- 9. Lamond N, Dawson D. Quantifying the performance impairment associated with fatigue. J Sleep Res 1999;8:255-62.
- Swann P. Drugs, Alcohol and Fatigue in Heavy Vehicle Safety. Vicroads; 2002. Available from: http://www.ntc.gov.au/filemedia/publications/ drugsalcoholfatigueinhvsafetydrp.pdf. Accessed: December, 2006.
- Swann P. Australia's Major Interlock Program. Proceedings of the 6th Annual Ignition Interlock Symposium; September 5, 2005; Annecy, France.
- Penttila A, Portman M, Kuoppasalmi K, Lunetta P, Nevala P. Roadside surveys in uusimaa finland. increase of the rate of motor vehicle drivers with low blood alcohol content in traffic. Proceedings of International Conference on Alcohol, Drugs & Traffic Safety; 2004; Glasgow, UK.
- Philip P, Vervialle F, Le Breton P, Taillard J, Horne JA. Fatigue, alcohol, and serious road crashes in France: factorial study of national data. BMJ 2001;322:829-30.
- Banks S, Catcheside P, Lack L, Grunstein RR, McEvoy RD. Low levels of alcohol impair driving simulator performance and reduce perception of crash risk in partially sleep deprived subjects. Sleep 2004;27:1063-7.
- Horne JA, Baumber CJ. Time-of-day effects of alcohol intake on simulated driving performance in women. Ergonomics 1991;34:1377-83.
- Horne JA, Reyner LA, Barrett PR. Driving impairment due to sleepiness is exacerbated by low alcohol intake. Occup Environ Med 2003;60:689-92.
- Barrett PR, Horne JA, Reyner LA. Sleepiness combined with low alcohol intake in women drivers: greater impairment but better perception than men? Sleep 2004;27:1057-62.
- Arnedt JT, Wilde GJ, Munt PW, MacLean AW. Simulated driving performance following prolonged wakefulness and alcohol consumption: separate and combined contributions to impairment. J Sleep Res 2000;9:233-41.
- Barrett PR, Horne JA, Reyner LA. Early evening low alcohol intake also worsens sleepiness-related driving impairment. Hum Psychopharmacol 2005;20:287-90.
- Barrett PR, Horne JA, Reyner LA. Alcohol continues to affect sleepiness related driving impairment, when breath alcohol levels have fallen to near-zero. Hum Psychopharmacol 2004;19:421-3.
- 21. Maislin G, Pack AI, Kribbs NB, et al. A survey screen for prediction of apnea. Sleep 1995;18:158-66.
- 22. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540-5.
- 23. Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest 1993;103:30-6.
- 24. Dinges DF, Powell JW. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. Meth Instrum Comp 1985;17:652-5.
- 25. Dinges DF, Orne MT, Whitehouse WG, Orne EC. Temporal placement of a nap for alertness: contributions of circadian phase and prior wakefulness. Sleep 1987;10:313-29.
- Desai A, Wilsmore B, Bartlett D, et al. The utility of the AudEd driving simulator in the clinical assessment of driver fatigue. Behaviour Research Methods 2006;In Press.

- 27. Howard M, Gora J, Swann P, Pierce R. Alpha and theta activity and slow eye closure are related to driving performance in professional drivers. Sleep 2002;25:A148.
- 28. Howard M, Gora J, Swann P, Pierce R. Evidence of poor perception of sleepiness in professional drivers. Sleep 2002;25:A146.
- Ramaekers JG, O'Hanlon JF. Acrivastine, terfenadine and diphenhydramine effects on driivng performance as a function of dose and time after dosing. Eur J Clin Pharmacol 1994;47:261-266:261-266.
- Van Dongen HP, Maislin G, Mullington JM, Dinges DF. 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.
- 31. Hiltunen AJ. Acute alcohol tolerance in social drinkers: changes in subjective effects dependent on the alcohol dose and prior alcohol experience. Alcohol 1997;14:373-8.
- Wilson RJ, Fang M, Cooper PJ, Beirness DJ. Sleepiness among night-time drivers: relationship to blood alcohol concentration and other factors. Traffic Inj Prev 2006;7:15-22.
- Corsi-Cabrera M, Arce C, Ramos J, Lorenzo I, Guevara MA. Time course of reaction time and EEG while performing a vigilance task during total sleep deprivation. Sleep 1996;19:563-569.
- 34. Cajochen C, Brunner DP, Krauchi K, Graw P, Wirz-Justice A. Power density in theta/alpha frequencies of the waking EEG progressively increases during sustained wakefulness. Sleep 1995;18:890-4.
- Hiltunen AJ, Saxon L, Skagerberg S, Borg S. Acute tolerance during intravenous infusion of alcohol: comparison of performance during ascending and steady state concentrations--a pilot study. Alcohol 2000;22:69-74.
- Roehrs T, Roth T. Sleep, sleepiness, and alcohol use. Alcohol Res Health 2001;25:101-9.
- Horne JA, Wilkinson S. Chronic sleep reduction: daytime vigilance performance and EEG measures of sleepiness, with particular reference to "practice" effects. Psychophysiology 1985;22:69-78.