

Road Safety Research Report No. 62

Interactions Between Sleepiness and Moderate Alcohol Intake in Drivers

J.A. Horne, P.R. Barrett and L.A. Reyner
Sleep Research Centre
Loughborough University

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Department for Transport
Great Minster House
76 Marsham Street
London SW1P 4DR
Telephone 020 7944 8300
Web site www.dft.gov.uk

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1 EXECUTIVE SUMMARY

Both alcohol and sleepiness are known to be major contributors to road traffic accidents in the UK. There has been much debate on whether the current legal breath alcohol concentration (BrAC) limit for driving (35 µg alcohol per 100 ml breath) should be lower, as it is in several other countries in the European Union. The present limit may be satisfactory when a driver is fully alert, however the pressures of today's society mean that an increasing number of people may be sleep deprived. The consequences of a sleepy person driving after drinking a currently legally acceptable amount of alcohol have not been fully investigated. This report describes the result of a three-year study into the interaction of sleepiness and moderate alcohol intake. The main document summarises the findings — more detailed reports of which can be found in the appendices.

An initial literature review identified specific areas that needed to be investigated. Our research takes a 'lifelike' scenario, with only moderate sleep restriction (five hours in bed at night) and moderate alcohol consumption, producing BrACs of approximately half the UK legal driving limit. The drive, on a simulated dual carriageway, lasted for two hours and was very monotonous. The research programme was split into four main areas:

1. **young men** (most at risk group of drivers for sleep-related crashes) **driving in the afternoon** (when sleep-related crashes increase), under a 2×2 experimental design (**with and without alcohol at lunchtime**) and (**with and without prior sleep restricted to five hours**);
2. **an identical comparison with young women**;
3. a time-of-day comparison with **young men**, and **driving and alcohol consumption taking place in the early evening** (a time of day when we are naturally more alert); and
4. **a near-zero BrAC before starting the afternoon**, when **young men** have the same alcohol intake as in (1) but earlier.

During the afternoon circadian trough, the driving performance of both men and women is severely impaired when moderate sleep restriction and alcohol consumption are combined. Of particular concern is that men seem to be unable to perceive this greater impairment. Women generally appear to have a better perception of alcohol impairment, even without sleep loss. Moreover, unlike that of men, women's driving is less impaired by modest amounts of alcohol when they are alert, seemingly because they know their performance is affected and apply more compensatory effort. On the other hand, their impairment after alcohol, when combined with sleep loss, is well in excess of any compensatory effort.

Driving performance is generally better during the early evening hours, when we are naturally more alert, compared with the afternoon. Moderate alcohol intake does not impair driving performance during the early evening (unlike the afternoon). However, if this same alcohol dose is combined with sleepiness, then driving impairment does become apparent during the early evening, although to a lesser extent than that during the afternoon.

BrACs are a poor indicator of alcohol-related driving impairment, especially when combined with sleepiness. During the afternoon, even when BrACs have now fallen almost to zero at the start of a drive, sleepy drivers are still more impaired for the first hour of the drive if they have consumed this modest amount of alcohol at lunchtime. An unexpected rebound improvement in driving performance is seen in the second hour of the drive. In non-sleep-deprived, alert drivers, these same, near zero BrAC levels did not affect driving performance or significantly increase subjective sleepiness.

Our overall results indicate that, combined with modest sleepiness, alcohol intake producing BrACs well under the legal drink-drive limit impairs driving. This outcome supports recent and extensive findings from fatal and serious road crashes in France (Philip *et al.*, 2001). The combination also leads to an impairment (but to a lesser extent) in the early evening. All the driving impairments we report would, of course, be worse if the sleep loss was greater and/or BrACs were higher, but still under the legal limit. Greater public awareness is required in knowing the danger of driving after consuming any alcohol when sleepy. Currently, drivers seem generally unaware of this potentially dangerous interaction.

2 INTRODUCTION

2.1 Background

In the UK the legal limit for driving is a blood alcohol concentration (BAC) of 0.08% (80 mg of alcohol per 100 ml of blood; '80 mg%'). This BAC has an equivalent breath alcohol concentration (BrAC) of 35µg alcohol/100 ml breath. Throughout the European Union there are three principle alcohol limits in force for drivers: BACs of 0.08% (as in the UK), a lower limit of 0.05% (e.g. in Germany), and 0.005% (effectively zero) as in Sweden. In the USA, drink-driving limits vary between States, but many have a limit of 0.10% for drivers over 21 years old, and a limit of only 0.02% for those under 21. A zero limit does create a greater workload for police forces, more arrests, and would be unacceptable to the UK public (Dunbar *et al.*, 1987).

In recent years, public awareness on the dangers of drink driving has increased and, as a result, driving whilst over the legal limit has become socially unacceptable. More recently, public awareness has increased with regard to the risks of driving whilst tired. It is likely that in the UK, alcohol and sleepiness, as independent factors, cause similar numbers of road traffic accidents. However, sleepiness is more difficult to identify as a cause of a road crash. Drivers are unlikely to admit to having fallen asleep at the wheel and, unlike alcohol-related crashes, there is no definitive roadside measure of sleepiness. It is also possible that sleepiness is a contributing factor in many crashes where alcohol is involved, whether above or below the legal limit.

Little is known about the combined effects of alcohol and sleepiness on driving performance. Increasing pressures in today's society are claimed to be causing people to reduce the time they spend asleep; 26% of Americans believe that a successful career and adequate sleep cannot be combined (Dement, 1997). Combining reduced sleep time with a lunchtime alcoholic drink may have detrimental effects on a mid-afternoon drive, which is a time of the day when we naturally feel sleepier. A recent report looking at road crashes in France during 1994–98, found that fatigue, especially when combined with alcohol, presents a high risk of being involved in a road crash that results in death or serious injury, compared with alcohol or fatigue alone, even with BACs as low as 0.01% (Philip *et al.*, 2001).

It is important to establish to what extent driving performance is affected by combining moderate alcohol consumption (at a legally accepted level for driving) and moderate sleep loss. The legal limit for driving at present may be reasonable for rested non-sleepy drivers, however, when low doses of alcohol below the legal limit are combined with sleepiness, performance impairment may increase well above the acceptable level for safe driving.

2.2 Literature review – alcohol, sleepiness and performance, with reference to driving impairment

The initial literature review (Appendix 1), concentrates on the pharmacokinetic and pharmacodynamic properties of alcohol, as well as its effect on performance, with particular attention to simulated and real-car driving studies. The literature comparing alcohol-induced impairment with that of sleepiness was reviewed, followed by the limited number of studies that have investigated impairment caused by combining the two factors. Of the key points identified from the review, the following were considered to be of most importance and, as a result, the research programme was designed around these points:

- Monotonous tasks involving either passive concentration or reasonably difficult discrimination (divided attention) are most sensitive to alcohol.
- There appears to be a lack of perception of performance impairment following alcohol combined with sleep loss. There is a need for subjective ratings during the drive to monitor this.
- Men and women show marked differences in the pharmacokinetic properties of alcohol and, therefore, should be treated as separate experimental groups.
- The majority of studies on the effects of alcohol on performance have been carried out in the morning. Lunchtime onwards would appear to be a more realistic time to administer alcohol, and for simulating everyday life.
- Performance impairment on some tasks at low BACs may only be evident during the two troughs (early morning and mid-afternoon) in circadian sleepiness, and in contrast with the circadian peak (acrophase) in alertness during the early evening.
- BACs are not a good indicator of performance impairment. Residual sedation and decrements in performance have been found long after BACs have reached zero. This has not been investigated either with driving or with people who are already sleepy.

2.3 Research phases

Following the literature review, a research plan was formed and consisted of four main phases:

1. Combining moderate alcohol consumption and sleepiness in young men: the effect on driving performance in the afternoon.
2. Gender comparison – combining moderate alcohol consumption and sleepiness in young women: the effect on driving performance in the afternoon.
3. Time of day comparison – combining moderate alcohol consumption and sleepiness in young men: the effect on driving performance in the early evening.

4. Near-zero BrACs – combining moderate alcohol consumption and sleepiness in young men: the effect on driving performance in the afternoon when BrACs are approaching zero.

The findings from all four phases are now published in peer-reviewed international scientific journals. Copies of all four are enclosed in the appendices, where more complete results can be seen. We now present summary outlines of the methods used and for each phase of this research.

3 BRIEF METHODS

The methodology for each phase is very similar; the specific methods are described in the appropriate appendices.

Participants for all four phases underwent four separate conditions in a repeated-measures, balanced design, using the protocols:

- normal night sleep + no alcohol control;
- five-hour restricted night sleep (02:00h–07:00h) + no alcohol control;
- normal night sleep + alcohol; and
- five-hour restricted night sleep (02:00h–07:00h) + alcohol.

Alcohol, diluted with 300 ml orange juice, was consumed 30–45 minutes before the start of the drive (except in Phase 4 [near-zero BrACs]), when it was consumed an hour earlier (90–105 minutes before the start of the drive). Men were given 75 ml 37.5% proof vodka, and women 65 ml (producing similar target BrACs). The participants were ‘blind’ to the presence of alcohol. In the no-alcohol control condition, the rim of the glass was dipped in vodka.

Participants underwent a two-hour simulated drive on a monotonous dual-carriageway. The drive commenced at either 14:00h or 18:00h for the afternoon (Phases 1–3) and evening (Phase 4) sessions respectively. Driving performance (lane drifting), subjective sleepiness and the EEG were monitored throughout the drive.

4 PHASE 1: COMBINING MODERATE ALCOHOL CONSUMPTION AND SLEEPINESS IN YOUNG MEN: THE EFFECT ON DRIVING PERFORMANCE IN THE AFTERNOON

The results of Phase 1 have been published as a journal paper, which is reproduced as Appendix 2 of this report:

Horne, J.A., Reyner, L.A. and Barrett, P.R. (2003). Driving impairment due to sleepiness is exacerbated by low alcohol intake. *Occupational & Environmental Medicine*, **60**, pp. 689–692.

4.1 Summary

The objective was to assess whether low BrACs, around half the UK legal driving limit and undetectable by police roadside breathalysers, further impair driving that is already affected by sleepiness, particularly in young men, who are the most ‘at risk’ group of drivers.

Twelve healthy young men drove for two hours in the afternoon (14:00h–16:00h), in an instrumented car on a simulated dual-carriageway. In a 2×2 repeated measures, balanced design, they were given: alcohol versus control drink, and normal sleep versus prior sleep restriction. The measurements were driving impairment (lane drifting), subjective sleepiness, and EEG measures of sleepiness.

Whereas sleep restriction and alcohol each caused a significant deterioration in all indices, the combined effect further and significantly worsened lane drifting (which typifies sleep-related crashes). This combined effect was also reflected to a significant extent in the EEG, but not with subjective sleepiness. That is, alcohol did not significantly increase subjective sleepiness in combination with sleep loss when compared with sleep loss alone. Modest and apparently ‘safe’ levels of alcohol intake exacerbate driving impairment due to sleepiness. Sleepy drivers seemed not to have realized that alcohol had increased their sleepiness to an extent that was clearly reflected by a greater driving impairment and in the EEG.

4.2 Key points

- Owing to the natural circadian dip in the afternoon, drivers are more liable to be sleepy, especially after a night of disturbed sleep. Under these conditions alcohol may be particularly potent.

- Alcohol itself has soporific effects which accentuate underlying sleepiness, even with BrACs well within the legal limit.
- In young men, moderate sleep loss combined with low, legal BrACs well within the 'pass' region of roadside breathalysers, produces a marked worsening of driving impairment compared with either sleep loss or alcohol alone. This added effect is mirrored by an increase in 'sleepy' characteristics in the EEG. However, this added effect was not reflected by any increase in their perception of sleepiness.
- Young men who are moderately sleepy seem unable to perceive a further increase in sleepiness due to alcohol intake. Consequently, they may have a much greater driving impairment than they realise.

5 PHASE 2: GENDER COMPARISON – COMBINING MODERATE ALCOHOL CONSUMPTION AND SLEEPINESS IN YOUNG WOMEN: THE EFFECT ON DRIVING PERFORMANCE IN THE AFTERNOON

The results of Phase 2 have been published as a journal paper, which is reproduced as Appendix 3 of this report:

Barrett, P.R., Horne, J.A. and Reyner, L.A. (2004) Sleepiness combined with low alcohol intake in women drivers: greater impairment but better perception than men? *Sleep* 27, pp. 1057–1062 .

5.1 Summary

This study replicated that with men (Phase 1), but recruited young women participants. There are distinct physiological gender differences in the absorption, metabolism and central nervous system (CNS) effects of alcohol. It is possible that these also differentially affect driving performance and sleepiness in women. The alcohol dose was reduced from 75 ml (3 units), as in men, to 65 ml in the women in order to give similar BrACs.

Twelve healthy young women drove for two hours in the afternoon (14:00h–16:00h) in the instrumented car on a simulated dual-carriageway. In a 2×2 repeated measures, balanced design, they were given: alcohol versus control, and normal sleep versus prior sleep restriction. The measurements were driving impairment (lane drifting), subjective sleepiness, and EEG measures of sleepiness.

Sleep restriction significantly worsened driving performance and subjective sleepiness, as with men. Surprisingly, unlike men, women showed no apparent adverse effects of the alcohol alone on these indices; seemingly, they compensated. However, the alcohol's effects were profound when combined with sleep restriction. Nevertheless, the women were aware of this enhanced sleepiness, unlike men. After alcohol, the EEG showed increased beta activity, which was not seen in men, and indicated a differential pharmacokinetic effect of alcohol on the CNS and/or that the women were applying more compensatory effort. Debriefing questionnaires showed that the women were aware of the greater risks of driving when they noticed the effects of alcohol. Legally 'safe' BrACs markedly worsen sleepiness-impaired driving in women. However, women seem aware of their impaired driving and are able to judge the degree of risk entailed. Such an attitude may contribute to the

lower incidence of sleep- and/or alcohol-related road crashes in women compared with men.

5.2 Key points

- Low BrACs in otherwise **alert** women drivers do not appear to impair driving to the extent that it does in men, probably because women apply more compensatory effort.
- However, when combined with moderate sleepiness, this same BrAC level has a profound effect on women's ability to drive and on their subjective sleepiness, and to a greater extent than that seen in men.
- Women, however, seem more aware of this sleepiness and are able to judge the comparative driving risks involved.
- The much lower sleepiness and/or sleepiness-related crash rates in women may be due to their particular cognisance of these driving impairments.

6 PHASE 3: TIME OF DAY COMPARISON – COMBINING MODERATE ALCOHOL CONSUMPTION AND SLEEPINESS IN YOUNG MEN: THE EFFECT ON DRIVING PERFORMANCE IN THE EARLY EVENING

The results of Phase 3 have been published as a journal paper, which is reproduced as Appendix 4 of this report:

Barrett, P.R., Horne, J.A. & Reyner, L.A. (2005). Early evening low alcohol intake also worsens sleepiness-related driving impairment. *Human Psychopharmacology*, **20**, pp. 287–290.

6.1 Summary

This phase provided a time-of-day comparison with the afternoon findings (Phase 1) in men. It examined whether low BrACs, at around half the UK legal driving limit, and in both alert and sleep-restricted drivers, impair driving performance during the early evening, when circadian influences facilitate greater alertness.

Eight healthy young men drove for two hours in the early evening (18:00h–20:00h) in the instrumented car on a simulated dual-carriageway. In a 2×2 repeated measures, balanced design, they were given: alcohol versus control drink, and normal sleep versus prior sleep restriction. The measurements were driving impairment (lane drifting), subjective sleepiness, and EEG measures of sleepiness.

Sleep restriction produced significant impairments to driving and subjective sleepiness, whereas alcohol on its own did not. However, alcohol combined with sleep restriction significantly worsened all indices when compared with sleep restriction alone. The combination also significantly worsened driving and subjective sleepiness when compared with alcohol alone. The extent of these findings was less than those found for afternoon driving with identical interventions. Although low BrACs may not affect driving in normally alert drivers in the early evening, the addition of moderate sleep restriction still produces a dangerous combination.

A reason why these drivers were able to detect that alcohol was increasing their sleepiness, whereas this was not apparent in Phase 1, is that afternoon sleepiness (as in Phase 1) was higher to begin with, unlike the sleepiness levels in the present study which were lower – that is, there was less of a ‘ceiling effect’ here.

Nevertheless, the findings from Phase 3 show that there is no ‘safe’ level of alcohol intake for otherwise sleepy drivers, at any time of the day.

6.2 Key points

- In the early evening, low alcohol intake in **alert** drivers did not significantly impair driving or cause any increase in subjective sleepiness or EEG.
- However, when combined with moderate sleepiness, low BrACs produced greater driving impairment than the sum of the effects produced by sleepiness and alcohol alone. This worsening was mirrored by increases in subjective sleepiness and EEG indices of sleepiness.
- The outcome from combining sleep restriction with alcohol intake in the early evening was less than the combined effect seen in the afternoon (Phase 1).
- However, even when people are usually most alert, during the circadian peak period, the consumption of a ‘legally safe’ level of alcohol by a partially sleep-deprived person intending to drive, still produces a dangerous combination.

7 PHASE 4: NEAR-ZERO BRACS – COMBINING MODERATE ALCOHOL CONSUMPTION AND SLEEPINESS IN YOUNG MEN: THE EFFECT ON DRIVING PERFORMANCE IN THE AFTERNOON WHEN BRACS ARE APPROACHING ZERO

The results of Phase 4 have been published as a journal paper, which is reproduced as Appendix 5 of this report:

Barrett, P.R., Horne, J.A. and Reyner, L.A. (2004). Alcohol continues to affect sleepiness related driving impairment, when breath alcohol levels have fallen to near-zero. *Human Psychopharmacology*, **19**, pp. 421–423.

7.1 Summary

Epidemiological findings by Philip *et al.* (2001) point to very low BrACs (less than 10 µg per 100 ml of breath) heightening the risk of sleep-related fatal road crashes. In Phase 1, driving impairment was still present at the end of the drive even when BrACs had reached zero. The objective of Phase 4 was to assess these findings further by advancing the near zero BrAC to the beginning of the drive.

Twelve healthy young men drove for two hours in the afternoon (14:00h–16:00h) in the simulator. In a 2 × 2 repeated measures, balanced design, they were given: alcohol versus control drink, and normal sleep versus prior sleep restriction. Following this an additional eight young men underwent just the two sleep-restricted conditions. Three units of alcohol were consumed 90 minutes before the start of the drive (i.e. an hour earlier than was the case in Phase 1), leading to near-zero BrACs on commencement of the drive. The measurements were driving impairment (lane drifting), subjective sleepiness, and EEG measures of sleepiness.

During the drive, near-zero BrACs had little effect on driving performance and sleepiness levels in non-sleep-restricted, alert drivers. However, if they were already sleepy (having been sleep restricted), near-zero BrACs produced interesting effects. First, and compared with nil alcohol, the alcohol condition increased sleepiness-related driving impairments for approximately the first hour of the drive. However, this was not mirrored by any increases in subjective sleepiness or in EEG changes indicative of sleepiness. An unexpected reversal (i.e. improvement) in driving impairment occurred in the second hour of the drive with the alcohol group. This was supported by a trend for improved subjective alertness. The worsened driving during the first hour, when alcohol was combined with sleep restriction, after BrACs had reached zero, together with the concurrent lack of any increase in perceived

sleepiness, further points to the dangerous combination of sleepiness even with modest alcohol intake, and supports the epidemiological findings of Philip *et al.* (2001).

7.2 Key points

- Following modest alcohol intake by **alert** young men at lunchtime, leading to near-zero BrACs during afternoon driving, there is no increase in driving impairment or sleepiness.
- However, if they have been sleep restricted, leading to increased afternoon sleepiness, then this near-zero BrAC will produce an initial driving impairment, which is not mirrored by any increase in subjective sleepiness. Thus, there again appears to be a lack of perception of the driving impairment.
- After this initial impairment under the combined alcohol and sleepiness condition, there is a rebound improvement in driving performance. This biphasic effect may be due to an alcohol rebound and/or an advance in the circadian late-afternoon rise in alertness.
- Consuming moderate quantities of alcohol when one is sleepy and planning to drive is hazardous to driving even if BrACs have fallen to zero.

8 CONCLUSIONS

In alert (non-sleep-restricted) drivers, but during the afternoon when there is a natural dip in alertness, BrACs less than half the UK legal driving limit are more detrimental to driving performance in men compared with women. However, women believe that their driving performance is affected by alcohol, and it seems that they apply more compensatory effort to counteract any effect that alcohol may be having.

In men, if sleep during the previous night is restricted by two to three hours to five hours, then afternoon driving impairment is similar to that with the alcohol alone. This is not the case with women, as they apply compensatory effort with the alcohol, but not during the sleep loss alone. Thus, their driving performance is worse with sleep loss alone compared with alcohol alone.

Combining moderate alcohol consumption with moderate sleepiness, however, produces altogether different results. Both men's and women's driving performance is severely impaired under these conditions, especially during the afternoon, with women showing a greater detriment in driving ability. However, despite being more affected, women appear to perceive this impairment better than do men. Men, during the afternoon, show a lack of any further increase in subjective sleepiness with alcohol, compared to when they are just sleepy. Despite increases in driving impairment and EEG measures of sleepiness, men seem unable to perceive their worsened driving impairment.

There are distinct gender differences in the perception of impairment after alcohol consumption. Women seem more conscious of the effect that alcohol has on their driving, and they appear to apply more compensatory effort to counteract this effect. When the women drivers are alert, their compensatory effort counteracts any driving impairment due to modest amounts of alcohol. However, if they are sleepy, the additional impairment with alcohol is greater than any potential compensatory effort.

Men account for 90% of drivers involved in sleep-related crashes on UK roads (Horne and Reyner, 1995), but the percentage of these drivers with 'legally safe' alcohol levels is unknown. Although men have greater exposure to driving (Li *et al.*, 1998) and are more likely to be on the roads at the time of day when sleep-related crashes occur (Horne and Reyner, 1995), it may be that women chose to avoid driving at these times or are more likely to stop driving when they feel incapable of doing so.

Men account for 85% of UK drivers over the legal limit when breathalysed (DfT, 2002). If women are better at perceiving alcohol's effects, then they may chose not to drive after consuming alcohol. In conversation with our female drivers, after they had completed their driving, and when they had consumed alcohol under the two

alcohol conditions (normal sleep and sleep restriction), the majority of them felt that they were over the legal drink-drive limit (despite their BrACs showing them to be approximately half that value). Men appear either to have a reduced ability to perceive this alcohol-related driving impairment or deny it, especially when sleepy.

In the non-sleep-deprived, alert driver, the time of day is also a contributory factor in the extent to which performance is affected by alcohol. In men, greater impairment with alcohol was seen during the afternoon compared with an early evening drive. This is to be expected as the former coincides with the afternoon circadian dip in alertness, whilst the latter is when the circadian rhythm approaches a time of greatest alertness. Despite having little effect in alert drivers during the early evening hours, alcohol does impair driving performance at this time if there is additional sleepiness from sleep restriction the night before.

BrACs are a poor indicator of driving impairment when drivers are already sleepy. Despite even lower BrACs, at virtually zero levels in the afternoon, our male drivers were still impaired (women were not studied in this respect), and again there was an apparent lack of perception of this decrement in performance in the men. An unexpected rebound improvement in driving performance was seen later in the drive. The initial decrement in driving is a matter for concern. A sleepy individual who waits, after drinking alcohol, for his or her BrAC to return to zero before driving is still placing themselves, unknowingly, at risk. This risk needs to be more widely known.

9 REFERENCES

- Dement, W.C. (1997). The perils of drowsy driving. *The New England Journal of Medicine*, **337**(11): 783–784.
- DfT. (2002). *Road accidents Great Britain: 2001*. Department for Transport.
- Dunbar, J.A., Penttila, A. and Pikkarainen, J. (1987). Drinking and driving: choosing the legal limits. *British Medical Journal*, **295**: 1458–1460.
- Horne J.A., Reyner L.A. (1995). Sleep related vehicle accidents. *British Medical Journal*, **310**: 556–567.
- Li G., Baker S.P., Langlois J.A. and Kelen, G.D. (1998). Are female drivers safer? An application of the decomposition method. *Epidemiology*, **9**: 379–384.
- Philip, P., Vervialle, F., Le Breton, P., Taillard, J. and Horne, J.A. (2001). Fatigue, alcohol and serious road crashes in France: factorial study of national data. *British Medical Journal*, **322**: 829–830.

Appendix 1

A review of alcohol, sleepiness and performance, with reference to driving impairment

P.R. Barrett, J.A. Horne and L.A. Reyner
Sleep Research Centre
Loughborough University
Report for DTLR

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INTRODUCTION

In the UK the legal limit for driving is a blood alcohol concentration (BAC) of 0.08% (g of alcohol per 100 ml of blood; 80mg%). This BAC has an equivalent breath alcohol concentration (BrAC) of 35 µg/100 ml. Throughout the European Union there are two principle limits in force, 0.08% (as in the UK) and, in three countries, a lower limit of 0.05%. In the USA, drink-driving limits vary between States, but many have a limit of 0.10% for drivers over 21 years old, and a limit of only 0.02% for those under 21. Ideally the BAC limit for driving would be 0.0%, however, this is just not practical. A zero limit would create a greater workload for police forces, increasing the number of arrests, and would be unacceptable to the general public (Dunbar *et al.*, 1987). In 1999 a campaign to reduce the UK legal limit to 0.05% was rejected by Parliament partially on the grounds that it would not be acceptable in rural areas, with such a lack of public transport.

Alcohol consumption is widely socially accepted in the UK. In recent years public awareness on the dangers of drink driving has increased and, as a result, driving whilst over the limit has become socially unacceptable. More recently, public awareness has increased on the risks of driving whilst tired. It is possible that in the UK alcohol and sleepiness cause a similar number of road traffic accidents. However, sleepiness is more difficult to identify as a cause of an accident. Drivers are unlikely to admit to having fallen asleep at the wheel and, unlike alcohol-related accidents, there is no definitive proof. It is also possible that sleepiness is a contributing factor in many accidents where alcohol is involved, whether above or below the legal limit.

Little is known about the combined effects of alcohol and sleepiness on driving performance. Increasing pressures in today's society are leading people to reduce the time they spend asleep; 26% of Americans believe that a successful career and adequate sleep cannot be combined (Dement, 1997). Combining reduced sleep time with a lunchtime alcoholic drink may have detrimental effects on a mid-afternoon drive when our bodies naturally feel sleepier than at other times of the day. A recent report looking at fatal or severe injury road crashes in France during 1994–1998 found that fatigue, especially when combined with alcohol, presented a high risk of being involved in a road accident resulting in death or serious injury, compared with alcohol or fatigue alone (Philip *et al.*, 2001).

It is important to establish to what extent driving performance is affected by combining alcohol and sleep deprivation. At present, the legal limit for driving may be a sensible limit for rested non-sleepy drivers, however, when low doses of alcohol below the legal limit are combined with sleepiness, performance impairment may increase well above the acceptable level for safe driving. In this review we aim to report on all the relevant studies carried out on acute alcohol consumption, alone and combined with sleepiness. This shall enable us to gain in-depth knowledge in the areas of research that require expansion.

ALCOHOL ABSORPTION, METABOLISM AND ELIMINATION

Absorption

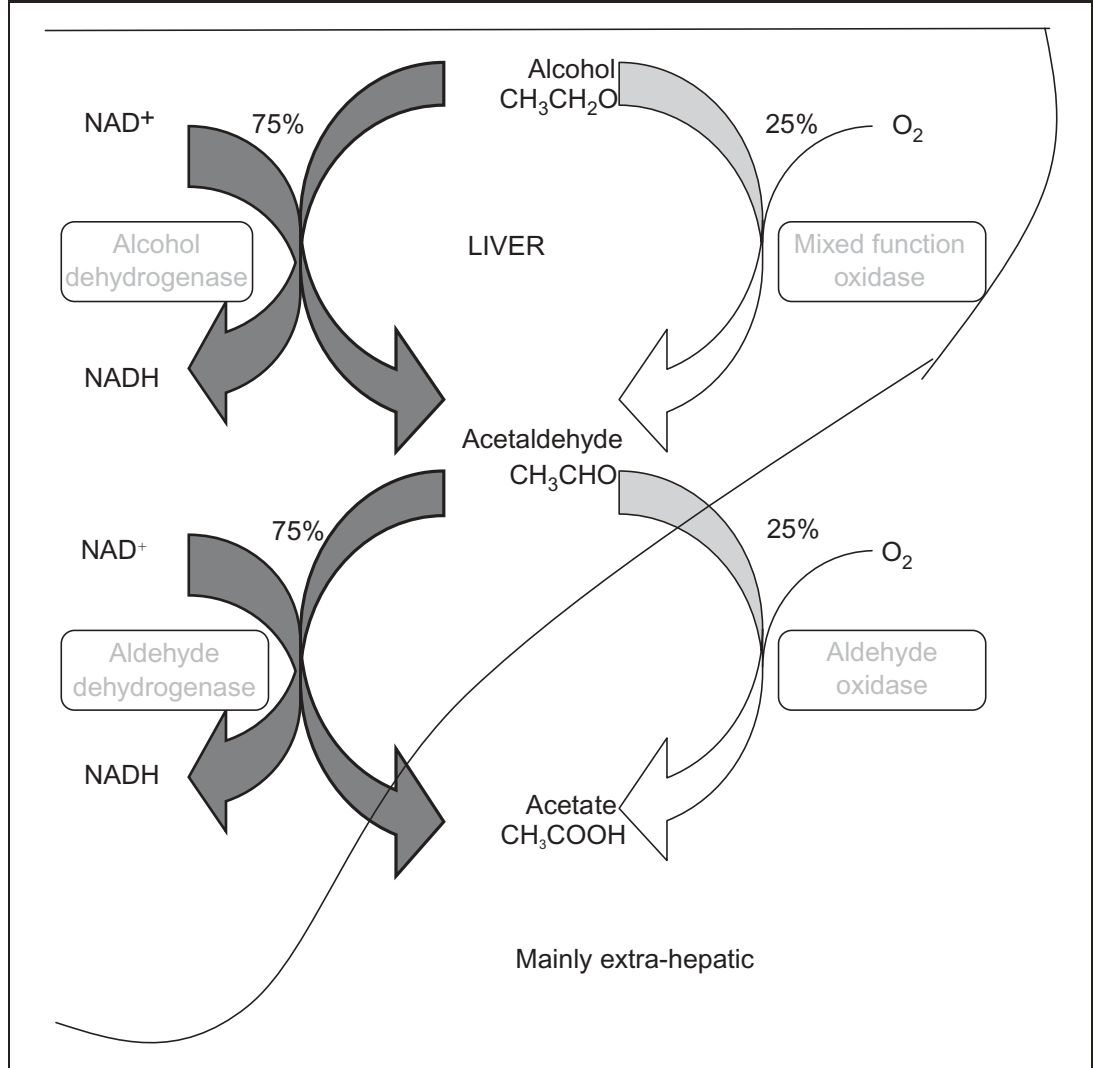
Although alcohol is absorbed mainly through the walls of the small intestine, it is one of the few substances that is also absorbed into the blood through the stomach wall. Alcohol is fairly lipid-soluble, and diffuses through the lipid membranes of the epithelial cells lining the stomach into the blood via the submucosal capillaries (Sherwood, 1995). However, the rate of absorption is slower via the gastric mucosa than the mucosa of the small intestine. Prior to leaving the stomach, some alcohol is metabolised by the enzyme gastric alcohol dehydrogenase (ADH). As women have lower levels of gastric ADH than men (Lieber, 2000), they have less alcohol metabolised prior to gastric absorption and gastric emptying.

Metabolism and elimination

Only around 2–10% of absorbed alcohol is eliminated unchanged via the kidneys and the lungs (Lieber and Abittan, 1999). The remaining alcohol is metabolised by the liver (with the exception of the small amount of alcohol metabolised whilst still in the stomach). There are three metabolic pathways that oxidise alcohol, converting it to acetaldehyde. They are the alcohol dehydrogenase (ADH) pathway, microsomal alcohol oxidizing system (MEOS), and the catalase pathway (Lieber and Abittan, 1999). The majority of alcohol (around 75%) is metabolised by the enzyme alcohol dehydrogenase.

Human liver ADH is a soluble cytoplasmic zinc metalloenzyme, of which there are five subclasses, made up from the association of eight different subunits. It oxidises alcohol to acetaldehyde, at the same time as reducing nicotinamide adenine dinucleotide (NAD⁺) to NADH (Figure 1; Rang *et al.*, 1995). Sigma-ADH, the recently discovered form of ADH which metabolises alcohol whilst still in the stomach, is not present in the liver. Acetaldehyde is highly reactive and toxic to the body, however it is normally rapidly metabolised to acetate; a non-toxic substance (Paton, 1994). The enzyme aldehyde dehydrogenase catalyses this second reaction, again reducing NAD⁺ to NADH. The final products of alcohol metabolism, after a chain of reactions, are carbon dioxide and water.

Figure 1: The main two pathways of ethanol metabolism in the liver, adapted from Rang *et al.* (1995)



Chronic alcohol consumption induces the MEOS, the other main alcohol metabolising pathway. The main cytochrome in this pathway has been found to be 4–10 times its normal level in liver biopsies from subjects who had recently ingested alcohol (Lieber and Abittan, 1999). The catalase pathway is only capable of oxidising alcohol in the presence of H_2O_2 , and therefore is limited by its small concentration in the body, playing only a very minor role in alcohol metabolism (Lieber and Abittan, 1999).

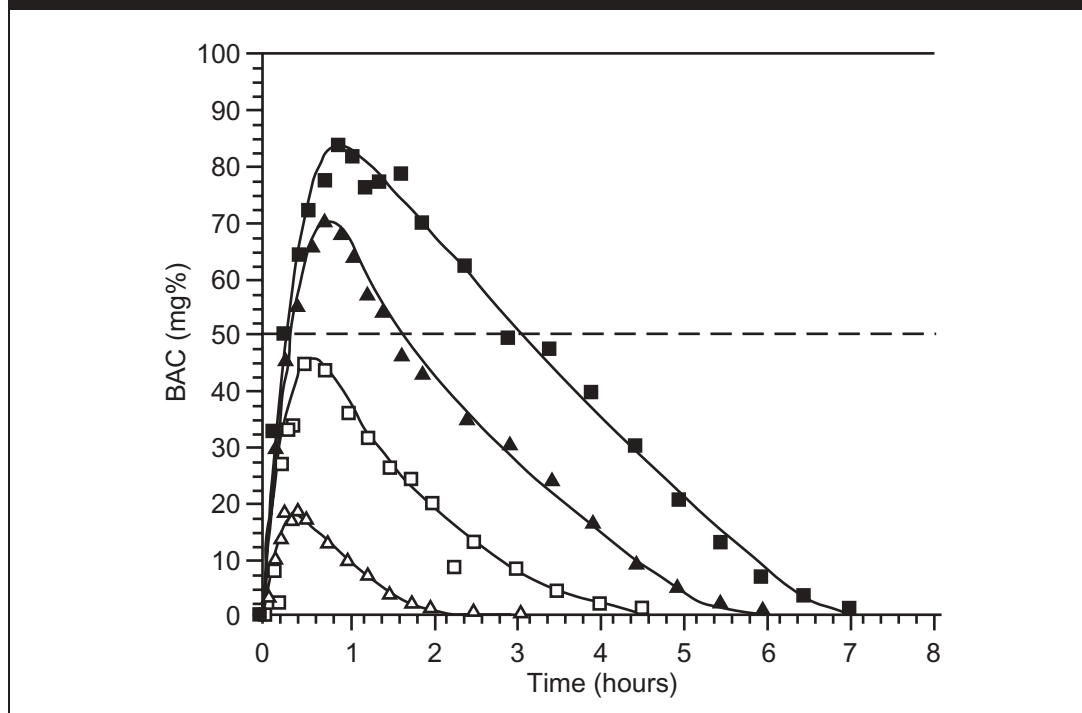
The overall rate at which alcohol is metabolised by the liver and eliminated from the body varies between individuals and between the drinking sessions of one individual. However, the average elimination rate is between 15–25 mg per 100 ml blood (0.015–0.025% BAC) every hour (Lion Laboratories Ltd, 2000). In heavy drinkers with liver damage, the metabolism of alcohol is accelerated (Paton, 1994).

BREATH AND BLOOD ALCOHOL CURVES

The presence of alcohol in the body can be measured either as a concentration in the blood or breath. The concentration in the blood is over 2,000 times as strong as that in the breath. The estimated blood:breath ratio varies between countries; in the UK a ratio of 2,300:1 is used, whereas 2,100:1 is used in the USA. The Lion Alcometer SD400 provides a BrAC reading in $\mu\text{g}/100\text{ ml}$. The legal limit for driving in the UK is $35\ \mu\text{g}/100\text{ ml}$, equivalent to 0.08% BAC.

After consumption of alcohol, the concentration of alcohol in the breath and blood increases (the absorption phase), reaches a peak, and then begins to decrease (the elimination phase). Only when the rate of absorption drops below the rate of elimination will the BAC begin to fall. Figure 2 shows the BAC curves of fasted male subjects after consuming set amounts of alcohol in a specific time span. The greater the concentration of alcohol ingested, the greater the peak BAC, and the longer the time to peak concentration (Wilkinson *et al.*, 1977).

Figure 2: Mean capillary alcohol concentrations of eight males after oral administration of 15 ml (Δ), 30 ml (\square), 45 ml (\blacktriangle), and 60 ml (\blacksquare) of 95% alcohol diluted to 150 ml with orange juice. Adapted from Wilkinson *et al.* (1977)



Both genetic and environmental factors can influence BrAC and BAC after the consumption of alcohol. Environmental factors (e.g. food consumption) often lead to intra-subject variation, and both environmental and genetic factors (e.g. gender and ethnic origin) can produce inter-subject variation (Li *et al.*, 2000).

Gender

For target BACs in both men and women, the recommended male:female ratio of alcohol volume consumption per kg of body weight is 1.1:1.0 (Friel *et al.*, 1999). There are several theories on the factors that influence between-sex variability. Alcohol distributes into body water, not fat, and, as women have more body fat, a dose of alcohol based on body weight will distribute into the smaller body water percentage of a woman, producing a higher BAC than in a man (Thomasson, 2000). These differences disappear after the age of 50, and men and women have very similar BACs if alcohol is administered intravenously. The gender difference occurs during the 1st-pass metabolism stage of alcohol (Lieber, 2000). As already stated, alcohol is mainly metabolised in the liver, however, some is metabolised by gastric ADH when still in the stomach. Women have lower levels of gastric ADH, therefore less is metabolised before it reaches the blood stream; leading to a higher BAC (Lieber, 2000). Nevertheless, one recent study not supporting this view (Lucey *et al.*, 1999), found no gender differences in the BACs of young adults (21–37 year olds). In the elderly (60–80 year olds), these authors only found a difference in alcohol metabolic curves when alcohol was administered orally after an eight hour fast.

Women have a faster alcohol elimination rate than men (Friel *et al.*, 1999). In one study, the alcohol elimination rate per unit lean body mass was found to be 33% greater in women than men (Thomasson, 2000). This faster elimination rate may be because women have a significantly greater liver mass/kg of body weight than men ($p < 0.0001$) (Li *et al.*, 2000), and therefore are able to metabolise the alcohol faster once it has reached the liver. The volume of alcohol consumed may also affect the gender differences in pharmacokinetic parameters. One study found no significant differences in these parameters between genders at either 0.33 mg/l or 0.48 mg/l target BrACs. However, a trend for slower absorption was found for women at the lower dose. The mean elimination rate in this study was significantly higher for women than men after the higher dose, but not after the lower dose of alcohol (Friel *et al.*, 1999). The authors also found that women had significantly higher (20%) BrAC decay rates than men.

Most studies involving alcohol administration give the alcohol per kg body weight. If the study involves both men and women (Friel *et al.*, 1995), then it is common to adjust the volume of alcohol using the Widmark equation, which accounts for the average male and female body water percentage. Differences in body water are, at present, the only biological sex differences that consistently relate to specific alcohol consumption effects and that can be easily measured. However, it is unknown whether its effect on peak blood alcohol levels is consistent across different levels of alcohol consumption (Graham *et al.*, 1998). At present, all other gender differences in alcohol absorption and metabolism cannot be reliably measured to enable adjustments in dosage effect.

Ethnic origin

Ethnic origin can also affect blood alcohol levels. Asians have either low or undetectable levels of sigma-alcohol dehydrogenase; a gastric specific ADH isozyme. Therefore they have a lower 1st-pass metabolism of alcohol, demonstrated by smaller differences in blood alcohol levels after oral and intravenous (IV) administration of alcohol (Lieber, 2000). African Americans have lower alcohol elimination rates than Caucasian Americans when given equivalent oral doses of alcohol, calculated on the basis of total body water (Li *et al.*, 2000). The authors of this study found that their Caucasian participants had significantly ($p < 0.0001$) greater liver mass per kg body weight than had the African Americans.

Age

Age has been shown to significantly outweigh gender as a factor that influences BACs (Lucey *et al.*, 1999). The authors found that elderly men (60–77 years) exhibited peak BACs 9–12% greater than young men (21–33 years) when given 0.3 g/kg body mass of alcohol, either orally or intravenously in a fasted or fed state. The elderly women (63–80 years) reached peak BACs 10–15% greater than the younger women (21–37 years) in all conditions except the oral administration after eight hours of fasting. The elderly women's BACs in this state were, on average, 47% greater than those of young women.

Individual differences

Even when the above factors are controlled for, there is still inter- and intra-subject variation. One study, which had a target BAC of 0.05%, with alcohol dosage calculated on lean body mass, repeated the same protocol five times on each subject. Between-subject time to peak varied from 10–25 minutes and mean peak BrACs ranged from 17–54 mg%. The individual subject variation of peak BrACs for each of the five subjects over five identical sessions were: 8–38 mg%, 8–35 mg%, 45–57 mg%, 39–51 mg% and 29–78 mg% (Li *et al.*, 2000).

Food intake

The consumption of food prior to consuming alcohol has been found to lower BACs. Gastric emptying is delayed after food ingestion, prolonging the retention of alcohol in the stomach, where absorption is considerably slower than in the duodenum (Gentry, 2000). The content of a meal is also important, with those having a high fat percentage inhibiting gastric motility and causing the greatest delay in gastric emptying (Sherwood, 1995). An earlier study, however, reported that meals high in carbohydrate reduced blood alcohol levels the most (Millar *et al.*, 1992). It is important in any study looking at the effects of alcohol that food consumption prior to alcohol ingestion is regulated, and is consistent for all participants. The prior ingestion of food increases the time taken to reach a peak BAC. Figure 3 shows the

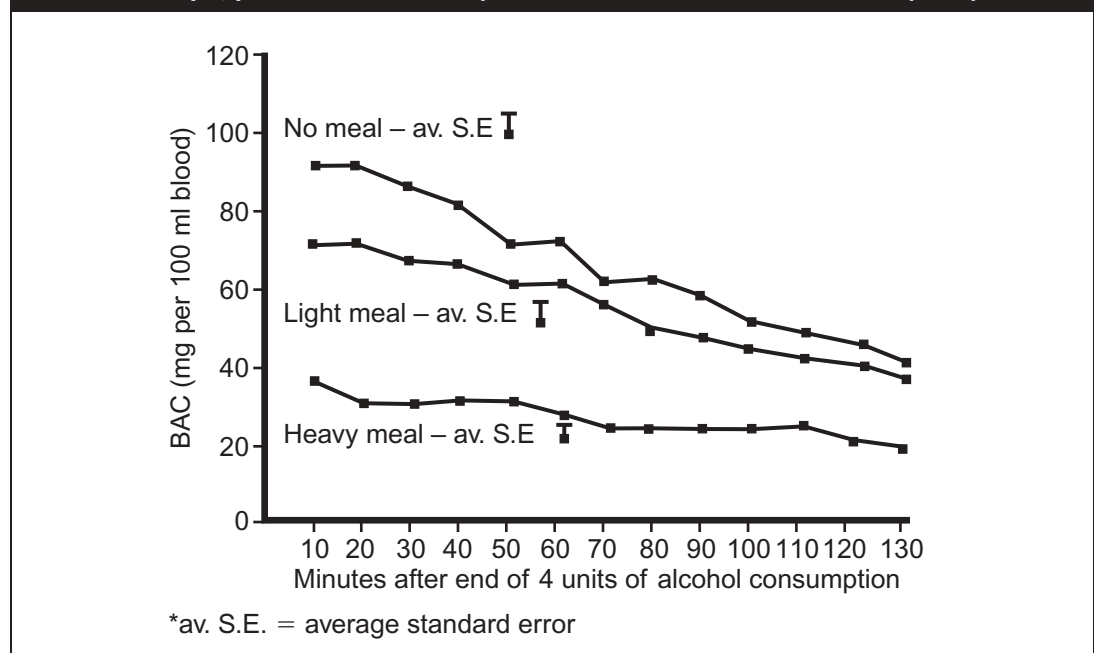
mean BAC curves of four women participants after fasting, a light meal and a heavy meal; there are clear reductions in BAC after food consumption (Horne and Gibbons, 1991).

This food effect becomes more evident the higher the alcohol dose, when comparing fasted to non-fasted conditions. Millar *et al.* (1992) compared target BACs of 0, 20, 40 and 80 mg/100 ml in the two fed states. They found that, proportionately, the BAC reduction was greatest for the lower alcohol dose, with reductions of 53.4%, 38.2% and 24.0%, for target concentrations 20, 40 and 80 mg/100 ml respectively, after a standard pasta-based meal (435 kcal, 31.5 g carbohydrate, 22.5 g fat and 22.2 g protein).

Nature of the alcohol consumed

The concentration of the alcohol consumed affects the rate of absorption and thus the BAC. Absorption is most rapid (on an empty stomach) if the concentration in the drink ranges between 20–30% proof (e.g. neat sherry or one part whisky to one part water; Paton, 1994). Stronger solutions of alcohol (e.g. spirits) can irritate the stomach wall, slowing the opening of the pyloric valve, and causing a slower rate of absorption. Beers, with a lower alcohol concentration (3–8%) are more slowly absorbed due to their larger volume, through which alcohol must diffuse before reaching the stomach wall. The presence of carbon dioxide in soda water and drinks such as champagne increases the rate of absorption, although the cause is not fully understood (Lion Laboratories Ltd, 2000).

Figure 3: Mean BAC after consumption of four units of alcohol (38% proof vodka) after no meal, a light meal (cheese roll) and a heavy meal (steak pie, chips, peas and ice cream). Taken from Horne and Gibbons (1991)



Conclusions

It is essential that we treat data collected from men and women as two separate groups due to their differences in alcohol absorption, metabolism and elimination. Although many studies provide alcohol dose per kg body weight, using the recommended 1.1:1.0, male:female dose ratio, we recommend that the forthcoming study does not adopt this method. In a 'real-life' situation people do not consume alcohol in respect of their body weight, but consume (in the case of spirits) unit quantities. Body weight is rarely considered, perhaps with the exception of larger males thinking that they can consume more before reaching the legal limit. The ethnic origin of participants should also be considered. Differences in absorption and metabolism rates between ethnic groups may have a similar impact to gender on results. If we target a specific ethnic group then we are discriminating against a percentage of the population, and our data set will not be a true representation of the overall population. This is something that needs to be considered.

Although age appears to influence BACs (with the elderly producing higher BACs), we suggest that the forthcoming study targets young drivers (especially males). This group of drivers are most at risk from involvement in alcohol-related accidents. They are more likely to combine alcohol and sleep deprivation due to their lifestyle than the elderly, which is the primary interest of this study. It is essential that we control stomach content, therefore participants will be asked to refrain from eating after 10:00 h prior to an afternoon drive. They will be provided with food upon arrival at the laboratory. The recommendation of one cheese roll (as stated in the original proposal) is not really enough food for a subject (as they will not consume anything else until after 16:00 h). Therefore, we suggest a pilot study comparing the consumption of various foods (including one versus two cheese rolls) on BAC over a period of time. Despite controlling for all the factors mentioned here, there is still likely to be a large inter- and intra-subject variation on BAC during alcohol administration conditions.

EFFECT OF ALCOHOL ON THE BRAIN

Alcohol is a central nervous system (CNS) depressant. Until fairly recently it was thought that alcohol acted in a non-specific way, penetrating cell membranes and altering their fluidity (Carvey, 1998), and the function of embedded proteins in some way (Charness *et al.*, 1989). Alcohol's solvent properties probably do alter lipid membranes, providing access to receptor sites on membrane proteins. However, alcohol is now known to act on specific receptors and to facilitate enzyme action, interacting with both excitatory and inhibitory systems (Nutt and Peters, 1994).

Effect of alcohol on inhibitory systems

In the brain the main inhibitory neurotransmitter is GABA (γ -aminobutyric acid). There are two types of GABA receptor, GABA_A and GABA_B, the former being the main inhibitory receptor. The GABA_A receptor is ionotropic, and five protein subunits form around a central ion channel, which is anion selective, with specificity for chloride ions (Cl⁻). The GABA inhibitory system is tonically active. GABA acts on the GABA_A receptor producing an influx of Cl⁻, producing hyperpolarisation of the cell and increased inhibition (Nutt and Peters, 1994). Alcohol potentiates GABA's inhibitory effect, producing the sedation, amnesia, anxiolysis and ataxia (incoordination) symptoms of intoxication (Nutt, 1999). GABA_A receptors are sensitive to alcohol in specific brain regions and are involved in both the acute actions of alcohol, tolerance and dependence (Grobin *et al.*, 1998; Grobin *et al.*, 2000).

Both barbiturates and benzodiazepines act at allosteric sites of the GABA_A receptor. Their administration produces similar symptoms to alcohol intoxication, suggesting that alcohol acts in a similar way (Charness *et al.*, 1989). In the past there has been conflicting evidence as to whether alcohol did act on the GABA_A receptor; this is due to there being at least 16 different genes coding for GABA_A receptor subunits. One specific subunit, the γ -2 subunit, is required for alcohol to have an effect (Pritchett *et al.*, 1989). Even after this discovery, data were still conflicting. In 1991, two variants of the γ -2 subunit were found. Alternate splicing of one gene produced both proteins. The long form, essential for alcohol's action, contains an eight amino acid insertion, one of which is serine. The phosphorylation of this one amino acid is required for alcohol to potentiate GABA's inhibitory effects (Wafford and Whiting, 1992). The numerous subunits of GABA_A receptors and the specificity required for alcohol to have an effect may provide some explanation to the broad range of individual differences seen in the sedative and performance effects of alcohol consumption. The action of alcohol on GABA_A receptors occurs at low BACs (< 0.10%), so is relevant to the levels of intoxication we are reviewing. At higher BACs (> 0.25%), alcohol causes a prolonged opening of the chloride channel independently of GABA, by acting directly on the receptor (Nutt, 1999). If BAC

reaches a high enough level, excessive Cl^- influx leads to paralysis of the brainstem neurones responsible for respiration, and asphyxiation can occur.

Effect of alcohol on excitatory systems

Glutamate is the main excitatory neurotransmitter in the CNS. It acts directly on three types of receptor; the AMPA (α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate), kainate and NMDA (N-methyl-D-aspartate) receptors. Alcohol predominantly acts on the NMDA receptor, which is ionotropic like the GABA_A receptor. It is cation specific, allowing calcium ions (Ca^{2+}) into the cell (Collingridge and Bliss, 1995). Before the NMDA receptor can open, a glycine molecule must bind to it and a magnesium ion blocking the channel must be expelled by partial depolarisation of the neurone, initiated by glutamate acting on AMPA receptors (Ganong, 1995). Ca^{2+} influx can lead to long-term changes in neuronal and synaptic function (long-term potentiation; LTP), (Collingridge and Bliss, 1995).

Alcohol is an NMDA receptor antagonist. It blocks the action of glutamate, stopping Ca^{2+} from entering the neurone. At BACs $> 0.10\%$, amnesia and sedation can occur (Lovinger *et al.*, 1989). In chronic alcohol administration, the brain compensates for the continuous lack of Ca^{2+} influx (inactivation) via NMDA receptors by increasing the number of NMDA receptors on the surfaces of neurones. However, when alcohol levels fall, the excess Ca^{2+} influx causes a hyperexcitable state, which can produce withdrawal symptoms (Nutt and Peters, 1994). High levels of Ca^{2+} cause cell death and the development of dementia, in some long-term alcoholics.

Other neurotransmitter changes

GABA and glutamate are not the only neurotransmitters to have their function altered by alcohol consumption. The increased release of dopamine and noradrenaline produces the enlivening effects of alcohol. An increase in dopamine (Bacopoulos *et al.*, 1979), serotonin and endogenous opioids (endorphins and enkephalins) produce pleasure and euphoric effects (Nutt, 1999). Addiction to alcohol is thought to arise primarily from the increase in dopamine and endogenous opioid release (Cotman and McGaugh, 1980) — dopamine, noradrenaline and adrenaline are also involved in the development of alcohol tolerance (Shafik *et al.*, 1991).

Alcohol's effect on the brain and the relationship with sleep-wake mechanisms

There are many neurotransmitters involved with the sleep-wake mechanisms, although their precise actions are not known in humans. Human sleep investigation

rarely involves invasive methods, and hypothesising mechanisms from non-human studies is unreliable as mechanisms differ between species. A few studies have shown similarities with the involvement of neurotransmitters in alcohol's sedative effect. GABA has been found to induce non-rapid eye movement (REM) sleep in both humans and rats (Lancel, 1999). The sedatory effect of alcohol and the involvement of the GABAergic system agree with this finding. The activation of noradrenergic neurones have been found to promote wakefulness, and serotonergic neurones promote slow-wave sleep (Bradley, 1989). Sleep-wake mechanisms are related to specific areas of the brain. The activity of neurotransmitters to induce sleep or wakefulness may be restricted to these areas. Similarly, alcohol may only affect GABAergic or glutamic neurones in specific brain regions.

SEDATING EFFECTS OF ALCOHOL

Although alcohol is classified as a depressant, it is thought that it can have both sedative and stimulatory actions, known as a biphasic effect of alcohol. Most multiple sleep latency test (MSLT) studies have been carried out on the descending limb of the BAC curve, and show sedatory effects. However, one study investigated sleep latency on the ascending limb and peak of the BAC curve (Papineau *et al.*, 1998). The authors found that sleep latency increased during the first 75 minutes after alcohol consumption, translating to greater 'stimulation'. However, subjectively using the Biphasic Alcohol Effects Scale (BAES), the stimulatory effects of alcohol on the ascending limb of the BAC curve were not experienced subjectively as stimulation, but merely as reduced sedation. Although only relatively mild, the stimulation seen in this initial post-alcohol consumption phase is equivalent to increased sleep latency occurring after consuming low dose stimulants.

There are a lot of inconsistencies with regard to the biphasic effect of alcohol. If it is true that the stimulatory effects only occur on the ascending limb of the BAC curve, then it provides little time to test, and may explain why studies have produced differing results. A recent study provided another explanation for the inconsistent results (Holdstock and de Wit, 1998). The authors studied the effects of three doses of alcohol, using various questionnaires and psychomotor performance, in assessing the ascending and descending limbs of the BAC curve. Only the highest dose of alcohol (0.8 g/kg; approximately peak BAC 0.075%) produced signs of stimulation on the ascending limb of the curve. However, only about half of the participants reported these biphasic effects, with the other half reporting only sedative effects caused by the alcohol ingestion. They concluded that there are significant, robust individual differences in the qualitative nature of participants' subjective responses to alcohol.

The time of day that alcohol is consumed can alter its sedating properties. There have been two studies comparing afternoon and evening performance after alcohol consumption. Horne and Gibbons (1991) investigated vigilance tasks with the consumption of alcohol at 13:00h and 18:30h. They found that after two or four units of vodka, performance was worse during the afternoon than the evening. They concluded that alcohol was twice as potent if consumed in the afternoon compared with consumption in the evening. Supporting this theory, another study investigated MSLT, divided attention and auditory vigilance after the consumption of 0.5 g/kg body weight alcohol (peak BAC 0.04%) at 09:00h and 17:00h (Roehrs *et al.*, 1992). The authors found an overall time of drinking (day versus evening) by alcohol interaction on sleep latency. During the day, when basal levels of sleepiness are high, alcohol significantly reduced sleep latency, whereas in the evening, when basal levels of sleepiness are low, alcohol failed to significantly affect sleep latency. Alcohol affected divided attention performance during daytime and evening testing. However, the absolute level of performance was better during the evening than the

daytime. Auditory vigilance performance was affected five hours after alcohol consumption, when BACs were approaching zero, although to a lesser extent during the evening compared to daytime.

The majority of alcohol consumed in our society is drunk during the evening hours. Between 23:00h and 08:00h there are profound reductions in MSLT latencies, therefore alcohol consumption often occurs when alertness is already compromised. Individuals who, on normal MSLT scores, would be classed as alert have been found to have significantly reduced alertness in the early hours of the morning after the consumption of a moderate amount of alcohol (mean peak BAC 0.069%; Walsh *et al.*, 1991). This study, however, looked at MSLT scores between 23:00h and 05:00h, when participants had already been awake since around 08:00h the day before. A factor of sustained wakefulness is therefore involved, so results cannot be compared with placebo MSLT tests and the effects of alcohol in daytime hours.

BACs are not necessarily a good indicator of impairment. The consumption of alcohol has been found to cause residual sedation and impairment long after the BAC has reached zero (Roehrs *et al.*, 1994b). The consumption of 0.5 and 0.9 g/kg body weight of alcohol (administered at 10:30h and 07:30h respectively, and producing peak BACs of around 0.04% and 0.06% respectively), produced reduced sleep latencies after BACs had reached zero (at approximately 15:30h for both doses). This residual sedation appears to be of short duration and the higher alcohol dose did not increase the intensity of the sedation. Subjectively, participants were unaware of the residual sedation and impairment on a divided attention task. These residual effects, well after the BAC has reached zero, indicate that alcohol, or its metabolites, still continue to act on the CNS.

Alcohol also causes varying degrees of sedation in individuals (Zwyghuizen-Doorenbos *et al.*, 1990). The authors of this study divided 24 participants into two groups depending on their sleep latency during an initial screening day. Those with sleep latencies ≤ 6 minutes were allocated to the 'sleepy' group, whereas those with sleep latencies ≥ 16 minutes were allocated to the 'alert' group. The effect of 0.75 g 100% alcohol/kg body weight on sleep latency, divided attention and subjective measures on these two groups was observed. Peak BACs of approximately 0.06% were achieved (30 minutes after completion of consumption), reaching zero six hours later. On MSLT, alert participants were immediately and markedly affected by the sedating effects of alcohol compared to the placebo, while sleepy participants showed only delayed moderate sedative effects. However, after consuming alcohol the alert participants were never as sedated as the sleepy participants, even after the placebo. This difference is not accounted for by BACs, as mean BACs and their rate of decline were the same for both groups. Despite objective differences in sleepiness, the participants in both groups subjectively reported similar levels in sleepiness and impairment. This lack of subjective difference between the two participant groups may be due to participants providing subjective ratings with reference to their individual basal sleepiness level.

EFFECTS OF ALCOHOL ON PERFORMANCE

The consumption of even moderate amounts of alcohol, producing BACs of around 0.03% (well below the legal limit for driving in the UK) can impair performance on specific tasks (Hingson *et al.*, 1999). One study at a stable BAC of 0.05% (administered by IV infusion, BAC unknown to participants) asked participants whether they felt capable of driving a car safely if required to do so in the event of an emergency. All 12 participants in the study stated that they felt their psychomotor performance was affected at this BAC and that they felt incapable of driving even in an emergency (Grant *et al.*, 2000). A review paper written in 1986 on driving-related skills impairment took 399 publications and summarised the effects of low BACs on specific tasks (Moskowitz and Robinson, 1986). We have used the basis of their review to look at papers prior to 1986, and have added other papers, prior to 1986, that were not included in that review, which we consider to be important. There are eight categories of performance task related to driving that we will cover: information processing, vigilance performance, reaction time, tracking, visual functions, divided attention, psychomotor skills and perception.

Information processing

This category can include studies of divided attention, vigilance and perception. Moskowitz and Robinson (1986) reviewed 24 studies involving information processing (after removing those that involved the above three tasks). They concluded that information processing skills are impaired at relatively low BACs, with 75% of those studies reviewed reporting impairment at or below 0.08%. One study prior to 1986, that used a visual backward masking task measuring the rate at which visual information is processed, showed that impairment is present at BACs as low as 0.015% (Moskowitz *et al.*, 1985). This study compared the task with a divided attention test and concluded that information processing is less sensitive to alcohol than the later task.

Vigilance performance

Vigilance tasks require sustained concentrated attention. Participants in studies involving vigilance testing are required to detect and respond to specific changes in stimulus situation that occur rarely and unpredictably (Koelega, 1995). It is often stated that vigilance tasks are rather insensitive to the effects of alcohol. Moskowitz and Robinson (1986) stated that it was one of the least sensitive variables, with no study showing impairment below 0.05%. However, a more recent review of 38 studies on the effect of alcohol compared to a placebo on vigilance tasks concluded that some types of vigilance task, particularly those using non-verbal, spatial information processing, can be highly sensitive to low doses of alcohol (Koelega, 1995). This type of vigilance task is similar to the type of vigilance required whilst driving a vehicle. Around half (70% for studies with a sample size of more than 15)

of all the studies included in the review found a decrease in overall performance and an increase in reaction time to stimuli.

One example of a non-verbal, spatial vigilance task is where participants have to identify when a repetitive visual signal changes slightly. In one study participants were presented with two dots on a screen every second for 30 minutes. Most of the dots were 60 mm apart, and were classed as non-signals. Participants responded to each non-signal by pressing a button. Occasionally (on average 1 every 60 seconds, range 20–100 seconds) the distance between the dots would change to 48 mm. Participants then responded by pressing a different button (Erwin *et al.*, 1978). Testing commenced at 16:30h and participants were tested under four alcohol conditions with BACs of 0.0%, $0.036 \pm 0.002\%$, $0.070 \pm 0.002\%$ and $0.102 \pm 0.003\%$ at the start of testing. The authors found that both alcohol dose and time after drinking had significant effects. The number of correct responses was significantly reduced after the highest alcohol dose compared with all other doses, and response latencies were prolonged. At the low and medium doses, men were less affected by the alcohol than were the women. However, dosage was calculated on body weight only, and not percentage body water.

Interestingly, the authors of the above study also observed the eyelids of participants, monitoring blinks and eyelid closures (≥ 1 second duration). They found that the percentage time the eyelids were closed throughout the 30-minute trial increased from 2.45% in the placebo condition through 6.34% (low dose), 11.95% (medium dose), to 17.15% after the high dose. This was highly significant, indicating that increasing alcohol dose increases drowsiness. This drowsiness (indicated by eyelid closures) was responsible for 26.4% of all missed responses.

Horne and Gibbons (1991) compared the effects of specific alcohol doses (0, 2 and 4 units) on the Wilkinson Auditory Vigilance Task at two times of day (14:00h and 19:00h). Participants were required to listen to monotone auditory signals, generated at 30 per minute for one hour. Seventy-five per cent of the signals were background signals of 0.5 second duration. The remaining 25% were randomly interspersed and of slightly shorter duration (0.45 second). These were the target signals. Participants responded to each signal by pressing the relevant button. The authors found that reaction time increased with alcohol dose. There was a significant interaction of alcohol dose and time of day, with the impairing effect of alcohol being greatest in the afternoon compared with the evening. Some participants appeared to trade-off poorer accuracy for faster speed and others, vice versa. However, overall performance impairment was greatest in the afternoon with the highest dose of alcohol, and performance impairment was present when BACs were under half the UK legal limit (0.04%). The BAC curves for each dose of alcohol were similar for both afternoon and evening, showing no time of day effect. Therefore BAC readings are a poor indicator to actual performance impairment on vigilance tasks (Horne and Gibbons, 1991).

Reaction time

There are two types of reaction time studies, simple and complex. Moskowitz and Robinson (1986) stated that complex reaction time tasks showed greater impairment at lower BACs than simple ones. They stated that it is fairly unreliable as a measure of alcohol's impairment, with impairment occurring inconsistently at various BACs, although it typically occurs at higher BACs than in other performance areas.

Simple reaction time

Simple reaction time is a form of vigilance task. An example of a simple reaction task is the standard Psychomotor Vigilance Task (PVT; Dinges and Powell, 1985). One study using the PVT found that with increasing BACs, reaction time significantly increased. Impairment was found at the lowest BAC tested, 0.057% (Powell *et al.*, 1999). A much earlier study investigating low doses of alcohol found differences between men and women with regard to reaction time (Taberner, 1980). In the control group (no alcohol consumed; N = 260), the women had an approximately normal frequency distribution of reaction times, with a median of 300 ms, whilst men had a markedly skewed distribution, with a median of 280 ms. In general, men were faster to respond. Two alcohol doses of 0.15 ml/kg and 0.76 ml/kg body weight were given in this study. However, the authors only measured BACs for two-thirds of the participants in the higher dose group; the mean of which seems extremely high (168% and 181.6% for men and women respectively). Despite this, the authors concluded that, at the low dose of alcohol, reaction time was significantly increased in men 60 minutes post-dose and 90 minutes post-dose in women. At the higher dose, men showed a far longer increase in reaction time at all post-drink test times, whereas women only showed a significant impairment at 90 minutes post-dose.

Choice reaction time (complex)

Choice reaction time (CRT) has been found to significantly increase with increasing BAC (Grant *et al.*, 2000). A VDU-based CRT task, where participants had to respond when one of five circles on the monitor changed colour by pressing the spatially associated key on a keyboard, found that BACs of 0.05% and 0.08% (not 0.02%; kept constant by IV infusion throughout testing), produced significantly increased reaction times. However, a similar study testing participants at BACs of around 0.057% and 0.097% on CRT, only found impairment at the higher dose (Liguori *et al.*, 1999). The increase in total reaction time at 0.097% was due to the impairment of the recognition reaction time (information processing) rather than the motor reaction time. Impairment at the lower BAC may not have been found as performance testing was carried out when BACs were descending, unlike the former study where BACs were kept constant throughout.

Tracking

Moskowitz and Robinson (1986) reviewed 28 studies on the effects of alcohol on tracking tasks, providing 60 BAC assessments. Over half the studies showed impairment at BACs of 0.05%, although many of them were in multi-task situations providing an element of divided attention to the task. The authors stated that the context in which the tracking was examined appeared to be more important than the differences among the types of task.

A recent study that administered 10–15 g alcohol at 30-minute intervals, until participants BACs reached 0.10%, whilst testing them every 30 minutes on a computer-based unpredictable tracking task, found that for each 0.01% increase in BAC, performance decreased by 1.16%. At a mean BAC of 0.10%, mean relative performance on the tracking task had decreased by 11.6% (Dawson and Reid, 1997).

Another form of tracking task is the pursuit rotor task. Performance on this task has been shown to be impaired more in participants who have a swifter rise in BAC (despite similar consumption speed and stomach content to other participants), when targeting a BAC of around 0.06% (Fillmore and Vogel-Sprott, 1998). This suggests that the rate of the rise of BAC rather than actual BAC may be a better indicator of impairment.

Visual functions

Visual functions are those that are likely to be tested by optometry rather than more complex information processing. Retinal functions, such as glare recovery, visual acuity, flicker fusion and peripheral vision, are least likely to be impaired by alcohol. Studies which did report impairment at low BACs tended to be related to oculomotor control (Moskowitz and Robinson, 1986). A recent study backed up the lack of impairment on Critical Flicker Fusion (CFF). No impairment of CFF performance was seen at BACs of 0.057% and 0.097% (Liguori *et al.*, 1999).

Divided attention tasks

Divided attention tasks require participants to carry out two or more tasks simultaneously. Moskowitz and Robinson (1986) reviewed 15 studies of divided attention. The majority of these studies found impairment at low BACs, with 60% of studies reporting it below 0.05%. Impairment began at a BAC below 0.02% in some studies. Comparison of a divided attention task (consisting of a compensatory tracking task and a visual search task) with an information processing task, at target BACs ranging from 0% to 0.06%, found the more complex divided attention task to be more sensitive to alcohol's effects (Moskowitz *et al.*, 1985). Impairment was found at all BACs tested, including the lowest target BAC of 0.015%.

A more recent study, investigating performance impairment at constant BACs (0%, 0.02%, 0.05% and 0.08%), maintained by IV alcohol infusion, studied a primary tracking task combined with a secondary visual reaction time task (Grant *et al.*, 2000). Both secondary reaction time performance and tracking performance deteriorated significantly with increasing BAC. On the secondary reaction time task there was a significant difference between baseline (0.00%) and all BACs, reaction time at 0.02% was also significantly faster than at the two higher BACs. Performance on the tracking task was significantly worse at 0.05% and 0.08% compared with the baseline performance, and a significant difference was found between 0.02% and 0.08%. Divided attention tasks are readily affected by alcohol consumption, and appear to be the most sensitive task to its effects.

Perception

This category of performance impairment limits itself to subjective cognitive perceptual tasks, including auditory functions, field dependence and visual illusions. Those studies, which can be classed as divided attention or information processing tasks, are not included in this category. Out of the 21 studies reviewed, Moskowitz and Robinson (1986) concluded that these tasks were not particularly sensitive to BACs below 0.08%.

Psychomotor skills

Studies involving psychomotor skills that could not be categorised elsewhere were included in this group (Moskowitz and Robinson, 1986). There were 29 studies, which examined 68 BAC levels. The majority of impairments occurred above a BAC of 0.07%, although nine were impaired at or below 0.05%. Those tasks involving skilled motor performance and co-ordination were more likely to be impaired at lower BACs.

Summary of performance impairment

Throughout the studies investigating the effects of alcohol on performance tasks there are a lot of inconsistencies. Specific types of tasks vary within the studies, as does alcohol dosing, producing varied impairment levels. The tasks most sensitive to alcohol are those that are monotonous and involve passive concentration, and those involving reasonably difficult visual discrimination (divided attention). Impairment has been seen in vigilance and divided attention tasks at BACs as low as 0.015%. Driving is a type of divided attention task and motorway driving can be very monotonous. Therefore one can predict that driving is likely to be sensitive to alcohol at low doses. Despite reaction time being important whilst driving, it is an unreliable measure of alcohol impairment. In some studies alcohol has been found to improve reaction time, but at the expense of correct responses. Missed responses rather than an increase in response time is more common after alcohol consumption. Impairment of simple psychomotor tasks may only occur at high BACs. Alcohol

doses which do not affect certain mood states or impair simple psychomotor tasks may well impair complex psychomotor tasks such as driving (Liguori *et al.*, 1999). Many studies have investigated skills related to and utilised in driving, in an attempt to evaluate alcohol's effects. However, unless all the skills of driving are combined, an accurate picture of driving impairment cannot be given. Therefore, actual or simulated driving will give a more realistic evaluation of driver impairment after alcohol consumption.

EFFECT OF ALCOHOL ON SIMULATED AND ACTUAL DRIVING

Prior to 1986, Moskowitz and Robinson reviewed 22 studies involving on-road and simulated driving studies. They found a wide variability in the results. The authors concluded that these differences were due to driving requiring a wide and diverse range of behavioural and performance tasks.

Simulation studies

A study carried out in 1991 on 24 young women (20–25 years) investigated the effect of four units (40% proof) of vodka (maximum mean BAC 10 minutes after alcohol consumption 0.072%) on simulated driving performance early in the afternoon compared to early evening (Horne and Baumber, 1991). Participants had to drive for 40 minutes on a two-lane motorway maintaining a self-selected safe distance behind a variable speed lorry. After alcohol consumption, participants were less able to maintain a safe distance behind the lorry; this was more evident in the afternoon than the evening. Three participants collided with the back of the lorry at least once; all of which occurred in the early afternoon. Alcohol or time of day did not significantly affect lateral position. The authors concluded that, although participants were within the UK legal limit for driving, some were so adversely affected by alcohol that they could be considered dangerous. The potential for motorway accidents following moderate alcohol intake is much greater in the afternoon than early evening. The UK legal limit may well be too high for safe driving during the early afternoon for women.

A recent study investigating differences between younger men (mean age 36 years) and older men (mean age 69 years) on the effect of alcohol on simulated driving performance used a closed-loop simulator consisting of an eight mile course that took approximately 20 minutes to complete (Quillian *et al.*, 1999). The course included stop lights, junctions, unexpected obstacles and diversions, with speed limits and other road signs. Driving started after BACs had reached their peak (target BAC 0.08%). In both age groups alcohol produced more inappropriate braking, fewer appropriate full stops and more time spent negotiating turns across oncoming traffic. Although not statistically significant, this dose also produced more variability of speed, bump collisions and wrong turns. There were no differences in the effect of alcohol on age, but under the placebo condition, older men performed worse on the simulator. The older drivers drove slower, had more speed variability, spent more time negotiating turns across traffic, had more inappropriate braking, made fewer appropriate full stops and had more crashes.

Reaction time whilst driving in a simulated environment has also been studied. Total reaction time (braking latency) and accelerator pedal release response time, to

avoid hitting a barrier appearing in front of the car, increased with increasing alcohol dose (Liguori *et al.*, 1999). Reaction distance (distance travelled before braking) increased from 50 feet to 53 feet and 60 feet at BACs of 0.057% and 0.097% respectively.

Real-car studies

There are very few real-car studies, due to the legal restrictions of driving whilst intoxicated. They either exist as closed-course studies on private land or, in rare cases, the police agree to close roads for the duration of the research. Investigation of a range of BACs (0.0%–0.122%) on driving performance over a 25 km closed stretch of road (taking approximately 20 minutes) showed a clear dose dependent impairment of performance (Louwerens *et al.*, 1987). Participants were asked to keep a constant speed of 90 km/h, with a constant lateral position between the right hand lane boundaries. Women were more sensitive to the effects of alcohol than men, and significant impairment occurred at BACs of 0.06% and above. Speed control was not significantly affected by alcohol, and a participant's self-assessment of performance was poorly correlated with the standard deviation of lateral position and BAC.

Studies comparing real car and simulator driving performance

Only one study has been carried out comparing the effect of alcohol dose on driving performance in a real car and in a driving simulator (Gawron and Ranney, 1988), with the lowest BAC tested being 0.07%. The authors matched the experimental procedures as closely as possible using the same alcohol dosing technique, target BACs, drive duration (two hours), background scene, and gender and age matched participants. In the closed-course (real car) study, increasing BACs increased the frequency of lane position errors and accidents. The variability of speed and lateral position also increased. At a BAC of 0.12%, drivers failed to reduce speed whilst negotiating bends. In the simulator study at BACs of 0.12%, tracking behaviour in the approach to and negotiation of curves was more variable. There was also an increase in speed violations and the number of obstacles struck.

The differences between the two driving tasks included the amount of attentional demand, type of acceleration cues, fidelity of auditory cues, and the salience of the experimenters' presence. These differences led to varying effects; the most noticeable of which was time. Whilst driving the simulator, participants increased their speed over time, whereas in the real car, participants decreased speed over time (Gawron and Ranney, 1988).

Summary

Simulation and actual driving studies have found that alcohol alone can increase the frequency of lane crossing, increase variability of lateral position, increase speed and speed variability, increase the frequency of accidents and increase variability in following distance. Not all studies found the same performance impairment measures, and again, as with general performance tasks, there are a lot of inconsistencies.

EXPECTANCY

Expectancy can affect the actions of alcohol on performance in two ways. Firstly, the expectancy of impairment at the time when alcohol is consumed and, secondly, the individual's perception of how they are generally affected by alcohol. The first of these is demonstrated by a study undertaken in 1978 investigating the effects of alcohol on divided attention (Vuchinich and Sobell, 1978). Forty men were divided into four condition groups: told that they were given alcohol (with tonic water) and actually given alcohol (TA/GA); told that they were given alcohol, but only given tonic water (TA/GT); told that they were given only tonic water, but were given alcohol (TT/GA); and told that they were given tonic, and were given tonic (TT/GT). When given alcohol, BACs of around 0.06% were reached. Drinks were prepared in front of the participants using 'dummy' bottles of vodka and tonic. The authors found that the participants' reports on what they consumed were determined largely by what they had been told and saw, rather than what beverage they actually consumed. Those participants who were told they were consuming alcohol (regardless of whether they were or not) made more errors than those told they were consuming just tonic.

Individuals' perceptions of how they are affected by alcohol has been shown to correlate with performance impairment (Fillmore and Vogel-Sprott, 1998). The authors asked participants to rate the expected effect of alcohol on performance at a pursuit rotor task, by asking them how 'two beers drank in one hour' would affect their performance. Performance tests were undertaken on the ascending limb of BAC, with a mean BAC of 0.047% pre-trial and 0.067% post-trial. Those expecting more impairment displayed greater impairment after alcohol consumption. All participants thought that they had consumed alcohol in the placebo condition and, again, those with higher expectations of impairment tended to perform more poorly in this condition. Expectancy did predict individual differences in impairment under alcohol with psychomotor performance tasks (Fillmore and Vogel-Sprott, 1998).

PERCEPTION OF RISK AND RISK-TAKING BEHAVIOUR IN RELATION TO DRIVING

Despite the risks involved with driving whilst intoxicated, some people still drink and drive. They not only risk losing their licence if caught doing so, but also risk their health, well-being and life, not to mention that of others. Young drivers are over-represented in traffic accidents and fatalities, and although they may be less likely to drive after drinking than older drivers, their risk of crashing if doing so is greater. Young drivers (especially males) are thought to perceive driving situations as less risky, and accident risk as less likely, compared with older drivers (Leigh, 1999).

People may (objectively) take risks not because they feel like it, but because they do not perceive the risk correctly. Alcohol may interfere with peoples' ability to attend to peripheral cues and to foresee the consequences of their behaviour. Attentional or information processing may be adversely affected by alcohol, altering the calculation of risk (Leigh, 1999). Perceptions about the risks of drinking are associated with drinking habits. Those that drink heavily perceive a less likely chance of unpleasant consequences than lighter drinkers.

The heavy consumption of beer, more than heavy wine or spirit consumption, has been found to be strongly predictive of risk perception (Greenfield and Rogers, 1999). When predicting the reported frequency of drunk driving, the authors found a significant interaction between heavy beer consumption and perceived risk. They concluded that individuals underestimate beer's intoxicating effects, compared with other alcoholic drinks. This helps to explain its over-representation in drink-driving violation reports.

Those groups most at risk of impaired driving are high volume drinkers, frequent heavy drinkers and individuals with alcohol dependence. One in seven of the high-risk drinkers (3.8% of all current drinkers) in the US fall into all three categories (Dawson, 1999). This small population of people accounted for 36.4% of reported impaired driving incidents. The authors also reported that 64% of individuals with alcohol dependence in the past year reported tolerance symptoms, compared with only 11% of high-volume drinkers and 7% of frequent heavy drinkers. Those with tolerance were only about half as likely to report impaired driving as those without tolerance. The study concluded that resources should be funnelled into a combination of strategies to reduce impaired driving, targeting both hazardous alcohol consumption among all drinkers and providing treatment for individuals with alcohol dependence.

Risk-taking behaviour

The effect of light alcohol consumption on risk perception and the decision to drive has been investigated at BACs of 0.0%, 0.015% and 0.03% (Frick *et al.*, 2000). At a BAC of 0.015% participants performed better than the two other conditions on perception of risks and hazards. When provided with negative feedback on their performance, participants' perceived handicap of driving was worse than after positive feedback. The authors also found that neither alcohol consumption, feedback nor sex had any influence on participants' decision to drive in a series of different social situations.

Risk-taking behaviour for monetary reward is affected by individual differences in basal sleepiness and differences in response to alcohol (Greenwald *et al.*, 1999). Relative to alert participants, sleepy participants were more vulnerable to alcohol's decision-impairing effects, reducing their ability to discriminate when it was optimal to take risks for monetary reward.

To our knowledge, there have been no studies on the combined effect of alcohol and actual sleep deprivation on drivers' perceptions of their ability to drive.

COMPARING ALCOHOL IMPAIRMENT WITH SUSTAINED WAKEFULNESS

General performance tasks

Several studies have been carried out in recent years comparing impaired performance induced by alcohol consumption with that produced by prolonged wakefulness/sleep deprivation. The first of these compared 28-hour continuous wakefulness (08:00h–12:00h next day), with BACs up to 0.10%, using a computer-based unpredictable, 10-minute tracking task (Dawson and Reid, 1997). The authors found that at 17 hours wakefulness (at 03:00h) performance decreased to that produced by a BAC of 0.05%. After 24 hours of sustained wakefulness (at 08:00h), performance was equivalent to that of a BAC of around 0.10%.

Two years later, the same laboratory produced another report, developing their initial research further (Lamond and Dawson, 1999). Whereas the initial study only looked at one hand-eye co-ordination task, the second expanded this to look at four types of performance task; a simple sensory comparison task, unpredictable tracking task (again), vigilance task and grammatical reasoning. Again, performance on BACs up to 0.10% and sustained wakefulness for 28 hours was studied. Increasing BACs produced increasing performance impairment on all but the simple sensory comparison task. As hours of wakefulness increased, performance levels decreased on all but the simple sensory comparison and the grammatical reasoning tasks. Specific psychomotor tasks vary in sensitivity to fatigue, the more complex tasks were more sensitive than the simpler tasks in this study. The overall findings suggest that after only 20 hours of sustained wakefulness (03:00h – a reasonable period for someone to stay awake for) performance impairment was equivalent to a BAC of 0.10%.

Another laboratory has also followed up the 1997 report by Dawson and Reid (Williamson and Feyer, 2000). Using a similar protocol, with BACs of 0%, 0.025%, 0.05%, 0.075% and 0.10% and 28 hours of sustained wakefulness, the authors looked at performance on the following tests: Mackworth clock, simple reaction time, tracking, dual task (combining the previous two tasks), symbol digit test, spatial memory search, memory and search test, and grammatical reasoning. The results of this study were similar to those produced above, indicating that, on average, a BAC of 0.05% was equivalent to being awake for about 18 hours (around midnight). Beyond this, an impairment equivalent to a BAC of 0.10% is seen. The public regards 16–17 hours of wakefulness as fairly normal, so it is likely that many people drive at a level of impairment equivalent to or above the legal alcohol limit in this country.

The most recent study comparing the effects of alcohol and fatigue on performance (Williamson *et al.*, 2001), again followed a similar protocol to the above studies. The aim of the study was to develop a battery of tests that would be useful for detecting fatigue in the evaluation of work-rest schedules, using alcohol as a comparison. The authors studied performance on eight computerised psychomotor and cognitive tests: simple reaction time, unstable tracking, dual task (combining the previous two tasks), Mackworth clock vigilance test, symbol digit coding, visual search task, sequential spatial memory and logical reasoning. Participants also filled in questionnaires and subjective fatigue rating scales. Alcohol impaired performance on all tests, however, fatigue affected performance on some tasks more readily than others. Monotonous tasks involving passive concentration, e.g. the Mackworth clock vigilance test, and those tasks involving reasonably difficult visual discrimination (simple reaction time and dual task) were affected most by sleep loss. The more complex tasks (logical reasoning and visual search) showed little or no effect of 28 hours of sustained wakefulness. One should remember, though, that the longer the duration of a task, especially if it is also dull, the more sensitive it is to sleep loss.

The above study (Williamson *et al.*, 2001) concluded that the simple reaction test, unstable tracking, the dual task and the Mackworth clock test are the best evaluation tools for studying levels of fatigue. Although comparing fatigue to alcohol and providing graphs of this nature, the report does not provide any stated sustained wakefulness periods that are equivalent to a specific BAC. However, the study did make a valid point with regard to developing tests for use in industry. They used long-haul truck drivers as their participants and found that, compared to controls, the drivers performed differently on certain tasks. The investigators concluded that, if developing a set of performance tests for a specific group of people, it is essential that the tasks are evaluated within that population.

Comparison of the effect of sleep deprivation and alcohol doses on sleep latency using the MSLT has also been carried out (Roth *et al.*, 1999). Alcohol doses peaking at BACs of 0.09%, 0.04% and 0.02% were given in conjunction with MSLTs carried out for a seven hour period post-dose. Sleep-restricted participants were allowed 6 hours, 4 hours or 0 hours time in bed. The authors found that one night of total sleep deprivation produced a greater reduction in the MSLT than did 0.09% BAC, which produced a mean sleep latency equivalent to only 2–4 hours of sleep loss.

A study comparing the reaction time of healthy alcohol impaired participants and patients with sleep-disordered breathing (SDB) found that all measures of reaction time in the SDB group were worse than those produced at a BAC of 0.057% (Powell *et al.*, 1999). For three out of seven measurements, the standard deviation of reaction time, maximum reaction time and the mean of the 10 fastest reaction times were all worse in the SDB group than for a BAC of 0.08%. When driving whilst sleepy as a result of SDB, it may be the equivalent of driving whilst above the legal alcohol limit.

Simulated driving studies

There have only been two studies comparing the effects of alcohol with prolonged wakefulness or sleep deprivation on a simulated driving task; both of them being recent. The first, published in 1999, compared the effects of partial sleep deprivation (four hours in bed), full sleep deprivation (remaining awake all night) and target BACs of 0.08–0.10% on performance in a driving simulator over three consecutive 40-minute periods (Fairclough and Graham, 1999). The authors found that full sleep deprivation impaired both safety-critical and non-safety-critical changes. Participants exhibited the highest frequency of lane crossing and highest mean time headway separation to a lead vehicle. The partially sleep-deprived group exhibited normal lateral control (safety-critical), but showed the same reduced steering input level (non-safety-critical) as the fully sleep-deprived group. The only evidence of any impairment in the part sleep-deprived group was an increase in near-lane-crossings, suggesting they were making steering adjustments only when absolutely necessary. Both partially and fully sleep-deprived participants showed increased variability in speed.

Alcohol consumption differed in comparison to sleep deprivation in that performance impairment was limited to safety-critical changes rather than non-safety-critical changes. Participants exhibited more frequent lane crossing compared to the control and partially sleep-deprived group, and travelled closer to a lead vehicle compared to the fully sleep-deprived group. The effect of time on task was also significantly different between the alcohol and fully sleep-deprived group. Impairment after sleep deprivation increased with time on task, however, after alcohol consumption, impairment of lateral control was stable throughout the drive, despite a descending BAC.

The second study by Arnedt *et al.* (2001), comparing alcohol and prolonged wakefulness on simulated driving, was undertaken as a comparison to the study by Dawson and Reid (1997). A 30-minute simulated drive was performed at BACs of 0.00%, 0.05% and 0.08%, and compared with 30-minute drives performed after 16, 18.5, 21 and 23.5 hours of prolonged wakefulness (at 24:00h, 02:30h, 05:00h, 07:30h respectively). There was a dose-dependent relationship between alcohol consumption and performance degradation, with clear decrements in driving performance evident at a BAC of 0.05%. Both tracking errors and off-road incidents occurred at this BAC.

These authors compared performance impairment at the BACs and equivalent prolonged wakefulness periods, as undertaken by Dawson and Reid (1997). The former found that changes in mean tracking, tracking variability and speed variability were similarly impaired at the equivalent BACs and duration of wakefulness. However, alcohol appears to produce a more rapid deterioration in performance than the equivalent wakefulness periods stated by Dawson and Reid (1997). After alcohol consumption, participants drove significantly faster than those

who were sleep deprived, which may indicate a loss of inhibition and increased confidence after alcohol. Alternatively, those being sleep deprived may be more aware of impairment and consequently compensate their driving behaviour (Arnedt *et al.*, 2001).

Summary

The interest in the comparison of alcohol consumption and prolonged wakefulness or sleep deprivation is fairly recent. Since 1997 several studies have found that impairment seen at a BAC of 0.05% is equivalent to around 17 hours of wakefulness on several general performance tasks. This is a very common time period for people to be awake for — a 6am rise from bed can often be followed with an 11pm bedtime. Of the non-driving tasks, simple reaction time, unstable tracking, dual tasks and the Mackworth clock test have been found to be the best evaluation tools for fatigue, although if any of these tasks are to be developed as performance tests, evaluation must be population specific (Williamson *et al.*, 2001). One of the two simulated driving studies (Arnedt *et al.*, 2001) looked again at prolonged wakefulness, however, we are interested in sleep restriction as was studied by Fairclough and Graham (1999). Unfortunately, their study only investigated BACs equivalent to or greater than the legal drink-drive limit and we are interested in low BACs.

COMBINING ALCOHOL AND SLEEPINESS

General performance tasks

There have been relatively few studies that have combined alcohol and sleepiness, investigating their interaction on general performance impairment. Combining these two factors can have no interaction (impairment is the sum of individual effects), be synergistic (greater than the sum of the individual effects), or be antagonistic (less than one or both individual effects, (Peeke *et al.*, 1980). The first study combining these factors investigated their effect on a five-choice reaction task (Wilkinson and Colquhoun, 1968). Participants were classified with BACs above and below 0.032%. With BACs below 0.032%, 30 hours of sleep deprivation reduced the adverse effect of alcohol on performance speed, whereas those with BACs above 0.032% showed the opposite effect. It would be interesting to know the time of day and the time after the alcohol consumption that the testing took place, however, these are not stated in the paper.

A later study produced results agreeing with those of Wilkinson and Colquhoun (Peeke *et al.*, 1980), although the level at which the antagonism occurred was not the same. The authors found that combining alcohol and sleep deprivation improved reaction time and increased alertness compared to the reduced levels produced by alcohol or sleep deprivation alone, although increased alertness only occurred after a BAC of approximately 0.06%, not 0.03%.

A study on the effects on sleep latency, of combining increased daytime sleepiness (due to sleep restriction) with alcohol consumption, found that as the basal level of sleepiness increased, alcohol dose had a reduced effect on sleep latency (Zwyghuizen-Doorenbos *et al.*, 1988). A moderate amount of alcohol (peak BAC 0.03%) in a sleepy person produced a mean sleep latency similar to that seen in a rested person who had consumed an excessive amount (peak BAC 0.07%) of alcohol. The main conclusions were, firstly, that a modest reduction in sleep time, (five hours in bed) when combined with modest amounts of alcohol, increased the risk of an alcohol-related accident. Secondly, reduction of sleep latency after alcohol consumption continues after the alcohol is no longer detectable. Therefore, measurement of BAC alone may cause an underestimation of the degree of alcohol-related impairment.

To complement the above study, this research group subsequently found that increasing time in bed (sleep extension) reversed the effects of alcohol (peak BAC 0.06%) on sleep latency (Roehrs *et al.*, 1989). Increasing time in bed from 8 to 10 hours for five consecutive nights produced MSLT scores (following this BAC) that were the same as the placebo. The study also found that performance of a divided attention task after sleep extension and alcohol was similar to that of a placebo prior to the sleep extension.

In alert, fully rested participants one study found that BACs between 0.05% and 0.08% did not produce sleepiness to the degree it did after five or eight hours of time in bed (Lumley *et al.*, 1987). The authors found that alcohol consumption was not sensitive to sleep restriction (five hours in bed for two nights) compared to normal sleep (eight hours). They concluded that this may have been due to the sleep restriction not being persistent enough.

Driving studies

There have only been three studies combining alcohol and prolonged wakefulness or sleep deprivation on actual driving (real or simulated) performance. The first of these papers was in 1974 and required participants to drive a real car round 10 laps of a short, simple pylon-defined serpentine course (Huntley and Centybear, 1974). Each participant was tested at two BAC targets (0.0% and 0.10%), two sleep conditions (normal sleep and 29 hours of prolonged wakefulness) and at two driving speeds (10 and 15 mph). The authors found that alcohol caused a significant increase in coarse-steer, fine-steer, accelerator responses and speed-change rate (a reduction in accuracy of speed maintenance). They also found an alcohol-by-participant interaction for coarse steering, where alcohol consumption caused a rate increase for 10 participants, but a rate decrease for the remaining two. The authors attributed these effects to personality differences, with increases in steering reversal rates associated with alcohol; further increasing with the greater the extraversion.

There was an interaction between sleep deprivation and alcohol on coarse steering. Following normal sleep, alcohol caused an increase in coarse-steering rates, but not after sleep deprivation. This indicates that the BAC alone may provide little information on its impairing effects when combined with other factors (e.g. sleep deprivation; Huntley and Centybear, 1974).

The two, more recent studies both used driving simulators to evaluate driving performance after alcohol and sleep deprivation. The first compared four hours and eight hours of time in bed, combined with target BACs of either 0.0% or 0.05%, on 30 minutes of driving at 10:00h (BAC of 0.05%) and 14:00h (BAC 0.013%; Roehrs *et al.*, 1994). In the morning testing session an increase in left deviations (from the centre of the lane), right deviations and absolute deviations were seen after four hours in bed with alcohol, compared with both placebo beverage conditions. Left and right deviations also increased in this condition compared with eight hours in bed with alcohol. In the afternoon testing session when BACs were approaching zero, similar significant effects of condition were found, and participants also performed better on all measures during the eight hours in bed placebo condition, compared with any other condition. This is an important finding as very few studies have found performance effects at BACs as low as 0.013%. The authors concluded that it may be that performance impairments at low BACs can only be produced at the two circadian rhythm sleepiness peaks. These results illustrate the increased risks associated with lunchtime drinking, and may be a good indicator of the risks

associated with low BACs during the main sleepiness peak during the early hours of the morning (03:00h–06:00h; Roehrs *et al.*, 1994).

The most recent study combining alcohol and sleepiness was published in 2000 (Arnedt *et al.*, 2000). Participants drove a car simulator for 30 minutes under four different conditions, combining target BACs of either 0.0% or 0.08% with either 16 hours or 20 hours of wakefulness (24:00h and 04:00h respectively). During the alcohol conditions, participants also underwent a second 30-minute drive after a 30-minute break, allowing the authors to compare performance on the ascending and descending limbs of the BAC curve. Prolonged wakefulness and alcohol each produced significant impairment on a number of simulated driving performance measures. When combining the two factors, although driving performance was worse than would be expected from the additive combination of these conditions, it was not statistically significant.

A BAC of 0.08% and 20 hours of prolonged wakefulness individually produce very similar impairment of driving performance, backing up the original comparison findings of Dawson and Reid (1997) and similar papers since then. Both conditions produced more variable speed and lane position, with a tendency to drive towards the centre of the road, and drive off the road more frequently. Although BACs were lower during the driving session on the descending limb of the BAC curve, driving performance was consistently worse than on the ascending limb, which is contradictory to the majority of studies. This may be due to the participants driving whilst further into the circadian peak for sleepiness when on the descending BAC drive. The authors only found a modest association between perceived and actual driving impairment after prolonged wakefulness and alcohol consumption, which is of some concern as participants seemed unaware of their reduced ability to drive safely (Arnedt *et al.*, 2000).

Summary

Surprisingly there are relatively few studies combining alcohol and sleep deprivation, especially at low BACs. Both synergistic and antagonistic effects have been seen on general performance after combining the two, however, the conversion from antagonistic to synergistic responses has been seen at different BACs.

Combining alcohol and sleepiness can have particularly detrimental effects on sedation. For example, laboratory studies have found that sleep restriction combined with a low BAC result in a similar sleep latency to that of a rested person having a BAC near the UK legal limit for driving. Perhaps the most impressive evidence of this nature comes from the recent findings from Philip *et al.* (2001), based on 67,671 road crashes, over a five-year period from 1994, that involved death or serious injury. In France, police record actual breathalyser values, down to 10 mg%. Whereas Philip *et al.* found that BACs as low as this level can increase the likelihood of death in a road crash by a factor of 4.2, when such BACs were combined with sleepiness this likelihood increased to 6.8.

CONCLUSION – KEY POINTS

- Men and women show marked differences in absorption, metabolism and elimination of alcohol. They should be treated as separate experimental groups in any study involving alcohol consumption.
- The ethnic origin of participants must be considered. Similar to sex differences, different ethnic groups demonstrate differences in alcohol absorption, metabolism and elimination. As with different sexes, ethnic groups must be treated as separate experimental groups in any study involving alcohol consumption.
- Most studies on alcohol and performance give participants an alcohol dose per kg body weight, with different values for men and women due to body water content. However, if studying ‘real-life’ consumption, a set measure of alcohol given in units simulating pub measures, regardless of body weight, is more realistic.
- Although age appears to significantly influence BACs (with the elderly producing higher BACs), young drivers (especially males) are most at risk of involvement in alcohol-related accidents. They are also more likely to combine alcohol and sleep deprivation than the elderly, due to their lifestyle.
- Stomach content must be controlled for in alcohol consumption studies. Participants should be asked to refrain from eating for three hours prior to arriving for testing, and to consume just a light meal before then. Caffeine containing drinks should not be consumed on the day of testing, and in the three hours prior to arrival only water should be consumed. Food should be provided for participants on arrival at the laboratory. A suggestion for a standard control meal is two cheese rolls.
- The majority of studies on the effect of alcohol on performance have been carried out in the morning. Lunchtime onwards would appear to be a more realistic time to administer alcohol, simulating everyday life. A lunchtime drink with afternoon drive (during the circadian dip) and evening drink after work with a drive home are common scenarios.
- Performance impairment on some tasks at low BACs may only be evident during the two peaks of circadian sleepiness. This illustrates the increased risk associated with lunchtime drinking, and may be a good indicator of the risk associated with low BACs during the main circadian peak of sleepiness, during the early hours of the morning (03:00h–06:00h).
- Comparison of performance in the ascending and descending limbs of the BAC curve, comparing any improvement in performance (stimulatory effect) that may be seen in the former with sedatory effects in the later, needs to be investigated further. However, due to the low doses of alcohol being used, the time to peak

BAC is relatively short, so comparison could be difficult. Biphasic effects of alcohol are rarely seen at such a low dose, and individuals differ in whether they actually experience these effects or not.

- BACs are not a good indicator of performance impairment. Residual sedation and decrements in performance have been found long after BACs have reached zero. No studies have investigated this on either actual or simulated driving. By administering alcohol 1–2 hours earlier, participants will commence the drive as BACs approach zero, thus investigating whether residual sedation has any effect on driving performance.
- It is essential that participants are screened carefully. Those with high levels of basal sleepiness are likely to be affected more severely than alert participants by alcohol's sedative effects. Those participants with an Epworth Sleepiness Scale above 10 should be excluded from the study to rule out any possible underlying sleep disorders. Those that fit the criteria could be classified into two groups (sleepy and alert). We can then investigate whether actual driving performance after alcohol consumption is impaired to a greater extent in those participants with greater levels of basal sleepiness.
- Expectancy can affect participants' performance after alcohol consumption. Participants should remain blind to the presence of alcohol (providing cues of alcohol presence in the placebo condition). However, if trying to simulate 'real life' where people know when they have consumed alcohol, consideration should be given as to whether participants should be told of the content of their drink.
- Despite reaction time being important whilst driving, it is an unreliable measure of alcohol impairment. In some cases after alcohol consumption, reaction time actually improves at the expense of correct responses. As with sleepiness, a response is more likely to be missed completely rather than slowed after alcohol consumption.
- Both monotonous tasks involving passive concentration and those involving reasonably difficult visual discrimination (divided attention) are most sensitive to alcohol consumption. Unfortunately driving falls into both these categories. Impairment has been seen at BACs as low as 0.015% on some divided attention tasks.
- Various studies have compared performance after alcohol consumption and during sustained wakefulness. Impairment seen at a BAC of 0.05% has generally been found to be equivalent to around 17 hours of wakefulness, a common time period to be awake.
- Driving after alcohol consumption alone has been found to increase the frequency of lane crossing, variability of lateral position, speed, speed variability and frequency of accidents, and participants have been unable to maintain a safe

distance behind a lead vehicle. Not all studies have found significant differences in these factors.

- The combined effect of alcohol and sleep deprivation on driving performance has been sparsely studied. As with alcohol alone, lane deviation and speed variability has been seen. In the most recent study, however, although performance was worse than the individual conditions, it was not significantly so.
- A recent field study by Philip *et al.* (2001) points to a worrying interaction of sleepiness with low BAC. Combining the two factors, a driver creates a high-risk factor of involvement in a road-traffic accident resulting in death or serious injury.
- There have been very few studies looking at the interaction of alcohol and fatigue on driving performance. Only one simulated driving study has looked at the effects of alcohol on driving for a two-hour period. All other studies made participants drive for a much shorter time. The longest driving period used for studying combined alcohol and sleep deprivation is 30 minutes. It is important that participants drive for at least two hours, as is common in motorway driving. The effect of monotony will not be seen so clearly if driving only lasts for 30 minutes.
- Participants seem unaware of their performance impairment following alcohol and sleep deprivation, which is of some concern. There is a need for subjective ratings during the drive to monitor this. As well as a subjective sleepiness rating, participants should be asked after the drive how impaired they felt their driving performance was.

REFERENCES

- Arnedt, J.T., Wilde, G.J.S., Munt, P.W. and MacClean, A.W. (2000). Simulated driving performance following prolonged wakefulness and alcohol consumption: separate and combined contributions to impairment. *Journal of Sleep Research* **9**: 233–241.
- Arnedt, J.T., Wilde, G.J.S., Munt, P.W. and MacLean, A.W. (2001). How do prolonged wakefulness and alcohol compare in the decrements they produce on a simulated driving tasks? *Accident Analysis and Prevention* **33**: 337–344.
- Bacopoulos, N.G., Bize, I., Levine, J. and Van Orden III, L.S. (1979). Modification of ethanol intoxication by dopamine agonists and antagonists. *Psychopharmacology* **60**: 195–201.
- Bradley, P.B. (1989). Anaesthetics, hypnotics and sedatives. *Introduction to Neuropharmacology*, Butterworth and Co. Ltd.
- Carvey, P.M. (1998). Drugs of abuse and addiction. *Drug action in the central nervous system*. Oxford, Oxford University Press: 317–371.
- Charness, M.E., Simon, R.P. and Greenberg, D.A. (1989). Ethanol and the nervous system. *The New England Journal of Medicine* **321**(7): 442–454.
- Collingridge, G.L. and Bliss, T.V.P. (1995). Memories of NMDA receptors and LTP. *Trends in Neuroscience* **18**(2): 54–56.
- Cotman, C.W. and McGaugh, J.L. (1980). Alcoholism. *Behavioural Neuroscience. An Introduction*, Academic Press Inc.: 760–767.
- Dawson, D.A. (1999). Alternative definitions of high risk for impaired driving: the overlap of high volume, frequent heavy drinking and alcohol dependence. *Drugs and Alcohol Dependence* **54**(3): 219–228.
- Dawson, D. and Reid, K. (1997). Fatigue, alcohol and performance impairment. *Nature* **388**: 235.
- Dement, W.C. (1997). The perils of drowsy driving. *The New England Journal of Medicine* **337**(11): 783–784.
- Dinges, D.F. and Powell, J.W. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments and Computers* **17**(6): 652–655.
- Dunbar, J.A., Penttila, A. and Pikkarainen, J. (1987). Drinking and driving: choosing the legal limits. *British Medical Journal* **295**: 1458–1460.
- Erwin, C.W., Wiener, E.L., Linnoila, M.I. and Truscott, T.R. (1978). Alcohol-induced drowsiness and vigilance performance. *Journal of Studies on Alcohol* **39**(3): 505–516.

- Fairclough, S.H. and Graham, R. (1999). Impairment of driving performance caused by sleep deprivation or alcohol: a comparative study. *Human Factors* **41**(1): 118–128.
- Fillmore, M.T. and Vogel-Sprott, M. (1998). Behavioural impairment under alcohol: cognitive and pharmacokinetic factors. *Alcoholism: Clinical and Experimental Research* **22**(7): 1476–1482.
- Frick, U., Rehm, J. Knoll, A., Reifinger, M. and Hasford, J. (2000). Perception of traffic accident risk and decision to drive under light alcohol consumption – a double-blind experimental study. *Journal of Substance Abuse* **11**(3): 241–251.
- Friel, P.N., Baer, J.S. and Logan, B.K. (1995). Variability of ethanol absorption and breath concentrations during a large-scale alcohol administration study. *Alcoholism: Clinical and Experimental Research* **19**(4): 1055–1060.
- Friel, P.N., Logan, B.K., O'Malley, D. and Baer, J.S. (1999). Development of dosing guidelines for reaching selected target breath alcohol concentrations. *Journal of Studies on Alcohol* **60**(4): 555–565.
- Ganong, W.F. (1995). Synaptic and junctional transmission. *Review of Medical Physiology*. J. Dolan and C. Langan (eds). Connecticut, Appleton and Lange: 75–104.
- Gawron, V.J. and Ranney, T.A. (1988). The effects of alcohol dosing on driving performance on a closed course and in a driving simulator. *Ergonomics* **31**(9): 1219–1244.
- Gentry, R.T. (2000). Effect of food on the pharmacokinetics of alcohol absorption. *Alcoholism: Clinical and Experimental Research* **24**(4): 403–404.
- Graham, K., Wilsnack, R., Dawson, D. and Vogeltanz, N. (1998). Should alcohol consumption measures be adjusted for gender differences? *Addiction* **93**(8): 1137–1147.
- Grant, S.A., Millar, K. and Kenny, G.N. (2000). Blood alcohol concentration and psychomotor effects. *British Journal of Anaesthesia* **85**(3): 401–406.
- Greenfield, T.K. and Rogers J.D. (1999). Alcoholic beverage choice, risk perception and self-reported drunk driving: effects of measurement on risk analysis. *Addiction* **94**(11): 1735–1743.
- Greenwald, M.K., Roehrs, T.A., Turner, L., Furcron, E. and Roth, T. (1999). Living on the edge: effects of ethanol, caffeine, and basal sleepiness on risk-taking behaviour. *Sleep* **22**: S88.
- Grobin, A.C., Matthews, D.B., Devaud, L.L. and Morrow, A.L. (1998). The role of GABA (A) receptors in the acute and chronic effects of ethanol. *Psychopharmacology (Berl)* **139**(1–2): 2–19.

- Grobin, A.C., Papadeas, S.T. and Morrow, A.L. (2000). Regional variations in the effects of chronic ethanol administration on GABA(A) receptor expression: potential mechanisms. *Neurochemistry International* **37**(5–6): 453–461.
- Hingson, R.W., Heeren, T. and Winter, M.R. (1999). Preventing impaired driving. *Alcohol Research and Health* **23**(1): 31–39.
- Holdstock, L. and de Wit, H. (1998). Individual differences in the biphasic effects of ethanol. *Alcoholism: Clinical and Experimental Research* **22**(9): 1903–1911.
- Horne, J.A. and Baumber, C.J. (1991). Time-of-day effects of alcohol intake on simulated driving performance in women. *Ergonomics* **34**(11): 1377–1383.
- Horne, J.A. and Gibbons, H. (1991). Effects on vigilance performance and sleepiness of alcohol given in the early afternoon ('post lunch') vs. early evening. *Ergonomics* **34**(1): 67–77.
- Huntley, M.S. and Centybear, T.M. (1974). Alcohol, sleep deprivation, and driving speed effects upon control use during driving. *Human Factors* **16**: 19–28.
- Koelega, H.S. (1995). Alcohol and vigilance performance: a review. *Psychopharmacology* **118**: 233–249.
- Lamond, N. and Dawson, D. (1999). Quantifying the performance impairment associated with fatigue. *Journal of Sleep Research* **8**: 255–262.
- Lancel, M. (1999). Role of GABA(A) receptors in the regulation of sleep: initial sleep responses to peripherally administered modulators and agonists. *Sleep* **22**(1): 33–42.
- Leigh, B.C. (1999). Peril, chance, adventure: concepts of risk, alcohol use and risky behaviour in young adults. *Addiction* **94**(3): 371–383.
- Li, T.K., Beard, J.D. Orr, W.E., Kwo, P.Y., Ramchandani, V.A. and Thomasson, H.R. (2000). Variation in ethanol pharmacokinetics and perceived gender and ethnic differences in alcohol elimination. *Alcoholism: Clinical and Experimental Research* **24**(4): 415–416.
- Lieber, C.S. (2000). Ethnic and gender differences in ethanol metabolism. *Alcoholism: Clinical and Experimental Research* **24**(4): 417–418.
- Lieber, C.S. and Abittan, C.S. (1999). Pharmacology and metabolism of alcohol, including its metabolic effects and interactions with other drugs. *Clinics in Dermatology* **17**(4): 365–379.
- Liguori, A., D'Agostino, R.B.J., Dworkin, S.I., Edwards, D. and Robinson, J.H. (1999). Alcohol effects on mood, equilibrium, and simulated driving. *Alcoholism: Clinical and Experimental Research* **23**(5): 815–821.
- Lion Laboratories Ltd (2000). *Alcohol in the Human Body*. Cardiff: Lion Labs.
- Louwerens, J.W., Gloerich, A.B.M., Vries, D., Brookhuis, K.A. and O'Hanlon, J.F. (1987). *The relationship between drivers' blood alcohol concentration (BAC) and*

actual driving performance during high speed travel. Alcohol, Drugs and Traffic Safety – T86. Amsterdam, Excerpta Medica.

Lovinger, D.M., White, G. and Weight, F.F. (1989). Ethanol inhibits NMDA-activated ion current in hippocampal neurons. *Science* **243**: 1721–1724.

Lucey, M.R., Hill, E.M., Young, J.P., Demo-Dananberg, L. and Beresford, T.P. (1999). The influences of age and gender on blood ethanol concentrations in healthy humans. *Journal of Studies on Alcohol* **60**(1): 103–110.

Lumley, M., Roehrs, T., Asker, D., Zorick, F. and Roth, T. (1987). Ethanol and caffeine effects on daytime sleepiness/alertness. *Sleep* **10**(4): 306–312.

Millar, K., Hammersley, R.H. and Finnigan, F. (1992). Reduction of alcohol-induced performance impairment by prior ingestion of food. *British Journal of Psychology* **83**: 261–278.

Moskowitz, H., Burns, M.M. and Williams, A.F. (1985). Skills performance at low blood alcohol levels. *Journal of Studies on Alcohol* **46**(6): 482–485.

Moskowitz, H. and Robinson, C. (1986). *Driving-related skills impairment at low blood alcohol levels*. Alcohol, Drugs and Traffic Safety – T86. Amsterdam, Excerpta Medica.

Nutt, D. (1999). Alcohol and the brain. *British Journal of Psychiatry* **175**: 114–119.

Nutt, D.J. and Peters, T.J. (1994). Alcohol: the drug. *British Medical Bulletin* **50**(1): 5–17.

Papineau, K.L., Roehrs, T.A., Petrucelli, N., Rosenthal, L.D. and Roth, T. (1998). Electrophysiological assessment (The Multiple Sleep Latency Test) of the biphasic effects of ethanol in humans. *Alcoholism: Clinical and Experimental Research* **22**(1): 231–235.

Paton, A. (1994). Alcohol in the body. *ABC of Alcohol*, BMJ Publishing Group: 11–12.

Peeke, S.C., Callaway, E., Jones, R.T., Stone, G.C. and Doyle, J. (1980). Combined effects of alcohol and sleep deprivation in normal young adults. *Psychopharmacology* **67**: 279–287.

Philip, P., Vervialle, F., Le Breton, P., Taillard, J. and Horne, J. (2001). Fatigue, alcohol and serious road crashes in France: factorial study of national data. *British Medical Journal* **322**: 829.

Powell, N.B., Riley, R.W., Schechtman, K.B., Blumen, M.B., Dinges, D.F. and Guilleminault, C. (1999). A comparative model: reaction time performance in sleep-disordered breathing versus alcohol-impaired controls. *Laryngoscope* **109**(10): 1648–1654.

- Pritchett, D.B., Sontheimer, H., Shivers, B.D., Ymer, S., Kettermann, H., Schofield, P.R. and Seeburg, P.H. (1989). Importance of a novel GABA(A) receptor subunit for benzodiazepine pharmacology. *Nature* **338**: 582–585.
- Quillian, W.C., Cox, D.J., Kovatchev, B.P. and Phillips, C. (1999). The effects of age and alcohol intoxication on simulated driving performance, awareness and self-restraint. *Age and Ageing* **28**: 59–66.
- Rang, H.P., Dale, M.M. and Ritter, J.M. (1995). Drug Dependence and Drug Abuse. *Pharmacology*. B. Simmons and S. Beasley (eds). New York, Churchill Livingstone: 645–664.
- Roehrs, T., Beare, D., Zorick, F. and Roth, T. (1994a). Sleepiness and ethanol effects on simulated driving. *Alcoholism: Clinical and Experimental Research* **18**(1): 154–158.
- Roehrs, T., Claiborne, D., Knox, M. and Roth, T. (1994b). Residual sedating effects of ethanol. *Alcoholism: Clinical and Experimental Research* **18**(4): 831–834.
- Roehrs, T., Zwyghuizen-Doorenbos, A., Knox, M., Moskowitz, H. and Roth, T. (1992). Sedating effects of ethanol and time of drinking. *Alcoholism: Clinical and Experimental Research* **16**(3): 553–557.
- Roehrs, T., Zwyghuizen-Doorenbos, A., Timms, V., Zorick, F. and Roth, T. (1989). Sleep extension, enhances alertness and the sedating effects of ethanol. *Pharmacol Biochem Behav* **34**(2): 321–324.
- Roth, T., Roehrs, T., Bonahoom, A., Burduvali E. and Rosenthal, L. (1999). Comparative ‘dose’ effects of ethanol and sleep loss. *Sleep* **22**: S87–S88.
- Shafik, E.N., Aiken, S.P. and McArdle, J.J. (1991). Regional catecholamine levels in brains of normal and ethanol-tolerant long-sleep and short-sleep mice. *Brain research* **563**: 44–48.
- Sherwood, L. (1995). Digestive System. *Fundamentals of physiology – a human perspective*. New York, West Publishing Company: 418–461.
- Taberner, P.V. (1980). Sex differences in the effects of low doses of ethanol on human reaction time. *Psychopharmacology (Berl)* **70**(3): 283–286.
- Thomasson, H. (2000). Alcohol elimination: faster in women? *Alcoholism: Clinical and Experimental Research* **24**(4): 419–420.
- Vuchinich, R.E. and Sobell, M.B. (1978). Empirical separation of physiologic and expected effects of alcohol on complex perceptual motor performance. *Psychopharmacology* **60**: 81–85.
- Wafford, K.A. and Whiting, P.J. (1992). Ethanol potentiation of GABA(A) receptors requires phosphorylation of the alternatively spliced variant of the $\gamma 2$ subunit. *Federation of European Biochemical Societies* **313**(2): 113–117.

- Walsh, J.K., Humm, T., Muehlbach, M.J., Sugerman, J.L. and Schweitzer, P.K. (1991). Sedative effects of ethanol at night. *Journal of Studies on Alcohol* **52**(6): 597–600.
- Wilkinson, H.L. and Colquhoun, W.P. (1968). Interaction of alcohol with incentive and sleep deprivation. *Journal of Experimental Psychology* **76**: 623–629.
- Wilkinson, P.K., Sedman, A.J., Sakmar, E., Kay, D.R. and Wagner, J.G. (1977). Pharmacokinetics of ethanol after oral administration in the fasting state. *Journal of Pharmacokinetics and Biopharmaceutics* **5**(3): 207–224.
- Williamson, A.M. and Feyer, A.M. (2000). Moderate sleep deprivation produces impairments in cognitive and motor performance equivalent to legally prescribed levels of alcohol intoxication. *Occupational and Environmental Medicine* **57**(10): 649–655.
- Williamson, A.M., Feyer, A.-M., Mattick, R.P., Friswell, R. and Finlay-Brown, S. (2001). Developing measures of fatigue using an alcohol comparison to validate the effects of fatigue on performance. *Accident Analysis and Prevention* **33**: 313–326.
- Zwyghuizen-Doorenbos, A., Roehrs, T., Lamphere, J., Zorick, F. and Roth, T. (1988). Increased daytime sleepiness enhances ethanol's sedative effects. *Neuropsychopharmacology* **1**(4): 279–286.
- Zwyghuizen-Doorenbos, A., Roehrs, T., Timms, V. and Roth, T. (1990). Individual differences in the sedating effects of ethanol. *Alcoholism: Clinical and Experimental Research* **14**(3): 400–404.

Appendix 2

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The relevant article may be found via oem.bmjournals.com/

Driving impairment due to sleepiness is exacerbated by low alcohol intake

J.A. Horne*, L.A. Reyner, and P.R. Barrett
*corresponding author

Sleep Research Centre
Loughborough University

Appendix 3

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Sleepiness combined with low alcohol intake in women drivers: greater impairment but better perception than men?

Pauline R. Barrett,
James A. Horne*,
and Louise A. Reyner,
*corresponding author

Sleep Research Centre
Loughborough University

Appendix 4

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The relevant article may be found via
www3.interscience.wiley.com/cgi-bin/jtoc/4216/
or the generic www.interscience.wiley.com

Early evening low alcohol intake also worsens sleepiness-related driving impairment

Pauline R. Barrett,
James A Horne*
and Louise A Reyner
*corresponding author

Sleep Research Centre
Loughborough University

Appendix 5

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<http://www3.interscience.wiley.com/cgi-bin/jtoc/4216/>
or the generic www.interscience.wiley.com

Alcohol continues to affect sleepiness related driving impairment, when breath alcohol levels have fallen to near-zero

P.R. Barrett,
J.A. Horne*
and L.A. Reyner
*corresponding author

Sleep Research Centre
Loughborough University

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