Research article

Caffeine withdrawal, sleepiness, and driving performance: What does the research really tell us?

Susan V. Heatherley

Department of Experimental Psychology, University of Bristol, 12a Priory Road, Bristol BS8 1TU, UK

As a psychostimulant, caffeine is thought to reduce road accidents by keeping drivers alert and wakeful. Studies have found that caffeine can improve performance on vigilance tasks and in driving simulators under normal sleeping conditions and after sleep restriction or deprivation. However, there is increasing evidence that these beneficial effects of caffeine are due to withdrawal reversal. Studies comparing the effects of caffeine versus placebo on driving performance have tested habitual caffeine consumers deprived of caffeine from the evening before the test day. The conclusion from this review is, therefore, that improvements in driving performance and alertness after caffeine are likely to represent withdrawal reversal rather than a net beneficial effect of caffeine. Further research using designs that control for caffeine withdrawal are necessary and, accordingly, advice given to the public on use of caffeine as an antidote to tiredness and impaired performance should be reviewed.

Keywords: Caffeine, Caffeine withdrawal, Driver sleepiness, Alertness, Sleep restriction, Driving performance

Introduction

Driver sleepiness is a major problem, for example, seemingly accounting for up to 20–25% of motorway accidents in the UK,[1] around 10% of serious road crashes in France,[2] and 1–3% of all US motor vehicle crashes.[3] Historically, it has been suggested that caffeine, found in tea, coffee, cola, energy drinks, chocolate, and some medication is useful for increasing wakefulness in drivers. Considering that falling asleep at the wheel may contribute to so many serious accidents on monotonous roads and motorways worldwide, caffeine's role in reducing these accidents could be significant. Indeed, the use of caffeine to overcome sleepiness is encouraged, with an abundance of caffeinated products (including self-heated cans, etc.) being sold in service stations and advice given to stop and 'take drinks containing caffeine'.[4] This is undemanding advice as more than 80% of the world's population consume caffeine daily.[5]

However, it may be that drivers do not find caffeine that useful. Maycock[6] reported that only 14% of male drivers listed drinking coffee as a 'measure found helpful' in counteracting driver sleepiness. More popular methods included opening the window (68%), stopping and taking a walk (57%), and listening to the radio or a passenger (30 and 25%, respectively). On the other hand, Reyner and Horne[7] found that cold air via an open window and loud music do not improve deteriorating driving performance, and it is possible that these are only popular options because they do not involve stopping.

While driver sleepiness is of paramount concern due to the seriousness of resulting accidents, the majority of accidents are caused by driver inattentiveness or distraction (e.g. looking at something out of the window, using a mobile phone or being distracted by another passenger).[8] Caffeine use may not directly affect such behavior, but it has been shown to decrease reaction time and improve performance in non-sleepy individuals, particularly in monotonous tasks that require prolonged vigilance. Therefore, caffeine's potential for improving driving performance may not be limited to sleepy drivers.

However, while many authors assume or argue that these psychostimulant effects of caffeine represent a net benefit to the user,[9,10] accumulating evidence supports a different conclusion. This is embodied by the withdrawal relief or withdrawal reversal hypothesis which states that the alerting and performance effects of caffeine observed in habitual caffeine consumers are due to withdrawal reversal.[11–13] That is, caffeine

Correspondence to: Susan V. Heatherley, Department of Experimental Psychology, University of Bristol, 12a Priory Road, Bristol BS8 1TU, UK. Email: Sue.Heatherley@hotmail.co.uk

DOI 10.1179/147683011X13019262348785

merely reverses the fatiguing effects of acute caffeine withdrawal and there is little or no net increase in alertness or enhancement of performance. There are two predictions of the withdrawal reversal hypothesis. First, habitual caffeine consumers who are deprived of caffeine overnight will be less alert and perform worse than non-consumers (who cannot be caffeine withdrawn). Second, following caffeine administration the consumers' alertness will increase and their performance will improve but only to the baseline (placebo) levels of the non-consumers and with no withdrawal symptoms to reverse the non-consumers' alertness and performance will not be enhanced by caffeine.

While the withdrawal reversal hypothesis is gaining increasing support, there are still some authors who maintain the view that caffeine has net benefits. Smith *et al.*[14] found effects of caffeine on non-consumers in comparison with overnight-withdrawn participants and Childs and de Wit[15] have also found caffeine effects in what they refer to as light non-dependent caffeine users. On the other hand, Rogers *et al.*[12] did not find effects of caffeine in their low consumers. Haskell *et al.*[16] compared caffeine consumers and non-consumers and found no baseline differences in the performance of the two groups with both groups demonstrating increased self-reported alertness and improvements on various cognitive tasks following caffeine treatment. However, in this study Haskell may have underestimated the amount of caffeine consumed by their 'non consumers' as their systemic level of caffeine after abstaining for at least 12 hours was 0.36 μg/ml, not too dissimilar to the 'consumers' (0.50 μg/ml). In contrast, in a recent study by Rogers *et al.*[17] salivary caffeine concentration was found to be 0.02 and 0.39 μg/ml for low consumers and high consumers, respectively.

Evidence of a lack of an immediate effect of caffeine was demonstrated by Heatherley *et al.*,[18] who found positive effects of caffeine (increase in energetic mood, improved simple reaction time performance and increased accuracy on a focus of attention task), but only 8 hours after an initial dose and not after 4 or 6 hours of caffeine abstinence. The half-life of caffeine varies between 3 and 6 hours,[19] and thus it appears that caffeine may only be beneficial when systemic levels of caffeine in the body have fallen substantially, between 6 and 8 hours after consumption.[18] Therefore, overnight caffeine withdrawal (adopted in most studies) would be a sufficiently long interval to demonstrate 'positive' effects of caffeine versus placebo.

It is generally believed that caffeine can cause sleep delay or disruption and, therefore, it has been argued that it may have an overall benefit at times of low alertness, for example when restricted or deprived of sleep. This suggests that caffeine may indeed be useful in counteracting driver sleepiness.

Studies have demonstrated that high doses of caffeine taken before bedtime will delay sleep onset in many individuals and consequently most people control their daily consumption to avoid caffeine at this time.[10] Research into the effects of caffeine on sleep-deprived or -restricted individuals tends to demonstrate an increase in alertness and decrease in drowsiness following caffeine administration in comparison with placebo. However, these studies are also confounded by caffeine withdrawal as participants have been deprived of caffeine and therefore may be experiencing fatigue due to caffeine withdrawal as well as sleep deprivation.

Rogers *et al.*[20] conducted a sleep restriction experiment studying the mood and cognitive performance effects of caffeine. A battery of cognitive tasks were given before and after caffeine or placebo administration following sleep restriction of 5 hours (an average reduction of 3 hours sleep for the participants). Crucially, though, in this particular study the participants were moderate caffeine consumers either overnight withdrawn, or long-term withdrawn. The latter group unknowingly consumed decaffeinated drinks for 3 weeks prior to sleep reduction and the caffeine versus placebo challenge. This method of testing the effects of caffeine on 'former caffeine consumers' avoids the argument that non-consumers may behave in a different way to consumers because they are a self-selected group.

The results confirmed the predictions of the withdrawal reversal hypothesis: the overnight-withdrawn participants performed worse at baseline in comparison with the long-term-withdrawn particiants, and caffeine affected performance in the former, but not the latter group.[20] That is, caffeine did not benefit performance in the long-term-withdrawn participants, even in a state of low alertness induced by sleep restriction. Although this is not a driving study, an effect of caffeine was found in the overnight-withdrawn participants for simple and choice reaction time tasks. These tasks require continuous vigilance and are rather monotonous. Therefore, they may bear some similarity to driving tasks where continuous vigilance in monotonous circumstances is often required of the driver.

If participants are caffeine consumers, acutely abstinent from caffeinated products, then benefits attributed to caffeine could be due to the amelioration of withdrawal symptoms. If this is the case, then the only benefit caffeine may have on driving performance would be in regular consumers deprived of caffeine and this benefit would, at most, bring the driver up to a normal level of functioning.

The remainder of this paper aims to examine caffeine's effect on driving performance. With or without sleep restriction/deprivation, are the improvements (if any) in driving performance after caffeine attributable to withdrawal reversal, or are there net benefits of consuming this popular drug when driving? In addition, is there evidence that caffeine can improve mental performance in sleepy individuals that may in turn help drowsy drivers? I will examine a number of the most popular simulator driving studies, including those that have influenced the advice given to drivers. I have chosen studies where information has been given on caffeine abstinence prior to the study as without this knowledge we cannot assume whether the participants were withdrawn or not.

Driving studies

Probably the most well-known caffeine and driving studies are those by James Horne and Louise Reyner at Loughborough University.

The authors have repeatedly tested the effect of caffeine in alleviating driver sleepiness. They have done this in various combinations of treatment such as testing the efficacy of: 200 mg of caffeine with restricted and completely sleep-deprived drivers;[21] an energy drink (containing caffeine, taurine, and glucuronolactone) with sleep-restricted drivers;[22] a 'functional energy drink' on sleep-restricted drivers.[23]

The methods were similar for each study. Participants were usually graduates and experienced and regular drivers. They were given a 2-hour practice drive, presumably to familiarize them with the driving simulator. Sleep restriction was achieved by the participants wearing wrist actimeters and delaying their bedtime the night before the test days which, where more than one treatment or condition was administered, were held a week apart.

In addition, participants were generally described as being 'moderate consumers of caffeinated coffee (2–4 cups a day)' and were asked not to consume any caffeinated drinks after 6 pm the previous evening. Presumably, this was first so that participants were not given a drug with which they were not familiar, and second so that any caffeine they consumed prior to the experiment did not add to the test dose of caffeine. Ideally, the authors would have carried out a more detailed investigation of their participants' daily caffeine consumption as there can be a great variation in the amount of caffeine consumed depending on the type of caffeinated beverage preferred. For example, Heatherley *et al.*[24] found that, on average, instant coffee contained 54 mg of caffeine whereas ground coffee contained 108 mg. Therefore, Horne and Reyner's participants would have been consuming between 108 and 420 mg of caffeine per day. It is unlikely that the latter amount would be considered a moderate consumption of caffeine as it is estimated that most adults in Western countries consume between 200 and 300 mg/day.[25]

Furthermore, Horne and Reyner claim that there is no evidence that at these levels of caffeine consumption (2–4 cups of caffeinated coffee) the placebo-treated participants would experience withdrawal effects. They typically cite James.[26] However, elsewhere James provides 'substantial if not conclusive evidence' that Horne and Reyner's participants would experience withdrawal effects given the design.[27] This is supported, for example, by a comparison between 'low' and 'moderate' caffeine users, that found withdrawal effects in the moderate consumers but not the low users who consumed 205 and 47 mg per day, respectively.[28] As we cannot determine an exact amount of daily caffeine from the information provided by Horne and Reyner, we can only assume that each participant consumes at least 108 mg per day. It has been suggested that consumption of as little as 100 mg caffeine per day is sufficient to cause dependence.[5]

It is, therefore, highly plausible that findings in Horne and Reyner's studies can be explained by withdrawal reversal. Indeed, even if only a proportion of participants consumed sufficient caffeine to make them dependent, a significant effect of caffeine in the group as a whole could occur in absence of any net benefit.

In many caffeine studies, a saliva sample is taken prior to the assessment to test for systemic levels of caffeine. On analysis, it can confirm compliance with caffeine restriction instructions and participants can be removed from the analysis if caffeine levels appear unexpectedly high. Horne and Reyner could improve their design by including these analyzes as non-compliance with abstinence instructions would cause net beneficial or withdrawal reversal effects of caffeine in dependent participants to be underestimated.

Effects of caffeine on sleep-restricted or -deprived participants

Insufficient sleep appears to be a significant cause of road traffic accidents. Although, as described above, the psychostimulant effects of caffeine appear to be accounted for at least largely by withdrawal reversal, it has been argued that caffeine may be particularly useful at times of low alertness, for example, when sleep deprived.[10]

Reyner and Horne[21] studied the effectiveness of 200 mg of caffeine on eight sleep-restricted and eight totally sleep-deprived drivers early in the morning. Participants were given the caffeine before commencing a 2-hour drive 30 minutes later. After receiving only 5 hours sleep the participants who received caffeine experienced fewer driving incidents than those who received placebo. The number of their incidents remained consistent and low until the final half-hour of the drive. In contrast, the placebo group's incidents increased in a linear trend throughout the drive. The interaction for time and caffeine was nearly significant. This pattern is consistent with other caffeine studies where performance declines over time due to increasing withdrawal symptoms such as fatigue and headache.[20] There was a main effect of caffeine on sleepiness, as indicated by their responses on the Karolinska Sleepiness Scale[29] (completed every 200 seconds); however, *post hoc* analysis only revealed a difference in the second 30-minute period and there was no interaction between caffeine and time. There was a significant difference in EEG data between the two groups, with the caffeine group showing less sleepiness, but only for the 30–60-minute driving period. Caffeine could not compensate for the more severe effects of sleep deprivation. Although it reduced the number of incidents compared with the placebo group during the first 30 minutes of the drive, both groups demonstrated such markedly poor performance overall that the study was abandoned after 1 hour. It appears that caffeine does not have the ability to prevent severe sleepiness and should, therefore, not be used as a substitute for sleep.

The data could show a net benefit of caffeine; however, the results are also consistent with withdrawal reversal. The lack of some significant effects are probably due to the low number of participants. Considering the possible variation, among the participants, in consumption habits, response to caffeine and response to sleep deprivation more participants would be beneficial.

In a subsequent study, Horne and Reyner[22] tested the effects of an energy drink containing 160 mg of caffeine versus a control drink (same drink without caffeine, glucuronolactone, and taurine) on 11 participants restricted to 5 hours sleep the previous night. Testing took place in the afternoon at a time when vehicle accidents peak. At baseline, both groups of participants had a similar number of driving incidents (car wheel crossing a lane marking) and similar reaction times (to an additional task while driving). As anticipated, the energy drink improved driving performance, decreasing the number of incidents in comparison to the placebo group. However, performance after the energy drink deteriorated with time on the task (the number of incidents rose in a linear fashion over the 2-hour driving period). Although the number of incidents remained lower than the control group throughout, by 90 minutes into the task there was no significant difference between the two groups. These results are similar to the previous study in that following an initial improvement that could be an indication of withdrawal reversal, the participants performance deteriorates. The placebo group's performance does not demonstrate a typical pattern, withdrawal or otherwise, as although the number of incidents increase over the first hour of the task (indicative of increasing withdrawal), they then demonstrate an improvement in performance. The reaction time data show very little real difference between the two groups.

Some of the results from this study are somewhat perplexing. It may be that using a drink with other active ingredients and including a distracting reaction time task has over complicated the study.

Reyner and Horne[23] then carried out a similar study testing the efficacy of the energy drink Red Bull™ that contains 80 mg of caffeine. They used a control drink for the placebo that tasted the same but contained no caffeine, taurine, or glucuronolactone. Participants were tested after 5 hours of sleep restriction. Participant sleepiness was recorded using the Karolinska Sleepiness Scale and EEG. Unsurprizingly, the group who received Red Bull™ felt less sleepy and had less driving incidents. The difference between the two groups only persisted for an hour and a half, after which the Red Bull™ group reported equally high levels of sleepiness to the control group. It appears that while the Red Bull™ drink brought about an improvement in performance in comparison with the placebo group, it failed to have a long-term effect on sleepiness. Due to the lower amount of caffeine in this drink (80 mg), the authors suggest the results could be due to an effect of the other ingredients in the drink. However, 80 mg of caffeine is well within the range of doses previously found to affect alertness and task performance.[30] There were no significant findings from the EEG data.

These various results could indicate a net benefit of caffeine for simulated driving performance impaired by sleep restriction and deprivation. However, they are equally consistent with withdrawal reversal because, as noted previously, the participants in these studies were caffeine consumers who were deprived of caffeine from the evening before the test day.

Effects of caffeine on driving following normal sleep

Apart from a lack of sleep, long working hours and circadian factors can contribute significantly to fatigue and sleepiness,[31] and consequently driving accidents. Furthermore, as previously mentioned a lack of attention can also contribute to road accidents. It is, therefore, important that driving experiments are also conducted on participants without sleep restriction.

Brice and Smith[31] conducted such a test with 24 participants carrying out a 1-hour simulated drive before and after caffeine (3 mg/kg), or placebo. They also chose to compare driving performance with performance on a similarly timed cognitive battery of tasks. Thus, participants carried out four different test sessions. The participants who received caffeine demonstrated less steering variability on the driving task while an increase in steering variability was found following placebo. There was also an increase in alertness following caffeine ingestion. The results of the cognitive tasks are unclear. While the participants who received caffeine in comparison with placebo were more accurate on a repeated digits detection task, the task was only 3 minutes long and the authors have not included the results of the rest of the hour-long battery that may have proved more insightful.

Although, Brice and Smith argue that their results are not due to caffeine withdrawal, participants in this study were regular consumers of coffee and were asked to abstain from caffeinated products before each session. The authors do not state the duration of caffeine abstinence, nor are they specific about the time testing took place. Therefore, we can only estimate how long the participants were caffeine abstinent for although we can possibly assume that most participants would have abstained overnight. Furthermore, declining performance following placebo administration, seen in their results, is indicative of increasing caffeine withdrawal.

Heatherley *et al.*[32] also conducted a simulated driving study without sleep deprivation. However, the driving test took place in the afternoon when participants would potentially feel sleepy and sleep-related driving accidents frequently occur.[1] Participants were tested either overnight withdrawn from caffeine, or long-term withdrawn, having unknowingly had their normal tea and coffee replaced by decaffeinated versions for 2 weeks prior to testing. Participants were then tested before and after 1.2 mg/kg body weight of caffeine, or placebo on measures of speed deviation (they were given speed markings to follow) and steering variability. The pre-treatment results supported the withdrawal hypothesis: the overnight-withdrawn participants demonstrated far more tracking errors (steering variability measure) than the long-term-withdrawn participants (see Fig. 1). Unfortunately, there were no significant effects of caffeine versus placebo for either group, perhaps because this aspect of the study was somewhat underpowered.

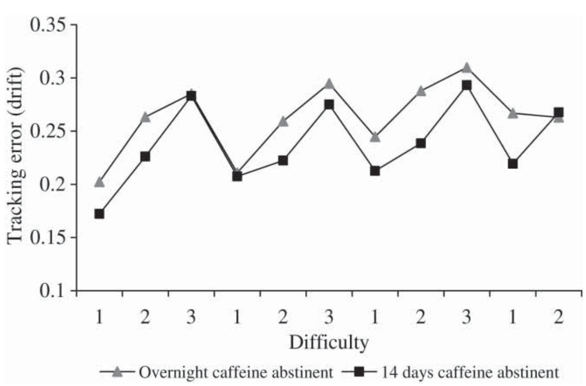

Figure 1 Tracking error in overnight and 14 day caffeine abstinent drivers during a 30-minute drive of a lap containing three levels of difficulty one being the easiest.

Summary and conclusion

Undisputably, the most influential studies discussed demonstrate improvements in driving performance following caffeine administration in comparison with placebo. However, the participants in these studies were habitual caffeine consumers deprived of caffeine overnight. Consequently, the improvements illustrated could be due to the reversal of withdrawal-induced decrements, or an overall benefit of caffeine. While some of the findings are equivocal, the data generally show a pattern consistent with withdrawal reversal as supported by numerous studies.

EEG and subjective sleepiness measures both show the effects of sleep deprivation, but again these measures could be confounded by caffeine withdrawal that gives similar EEG readings and produces the same symptoms, respectively. Furthermore, while driving performance and sleepiness in sleep deprived participants is improved following caffeine administration this is not long lasting and, therefore, would not be beneficial to people driving for long periods. Nervertheless, it is important that caffeine consumers maintain sufficient caffeine intake to avoid withdrawal effects.

Apart from the fatiguing effects of caffeine withdrawal, caffeine has acute negative effects such as increased anxiety and jitteriness[33] and increased hand tremor.[18,20] These symptoms may be particularly prominent with high doses of caffeine. Unfortunately, drivers may be inclined to consume large doses of caffeine, wrongly assuming each dose will have an additive positive effect on alertness and attention.

Rogers *et al.*[17] argue that a chronic tolerance develops to caffeine-induced anxiety with frequent caffeine consumption. It is unknown whether drivers who consume very little caffeine, or none at all, choose to consume it at times of low alertness when driving. However, if they did, they would be more likely to experience raised anxiety.

On the other hand, it is well documented that caffeine (regardless of level of habitual consumption) has the effect of raising blood pressure caused by vasoconstriction due to caffeine's action of antagonism of adenosene. In experiments where realistic doses of caffeine have been administered, systolic blood pressure has been raised by 5–15 mm Hg and diastolic by as much as 5–10 mmHg.[5] Furthermore, these increases are additive to increases in blood pressure caused by smoking and stress. Therefore, caffeine may be not be a healthy long-term antidote to sleepiness for individuals who drive for a living.

Individual responses to caffeine are varied and may be dependent on a number of factors including daily consumption habits. While it is pharmacologically likely that caffeine interferes with sleep, for some individuals this may not be the case. For example, Sanchez-Ortuno *et al.*[34] found no relationship between total sleep time and daily caffeine intake up to 7 cups of coffee per day. This is consistent with other cross-sectional surveys that have yielded equivocal results.[5] On the other hand, laboratory studies have supported the notion that caffeine intereferes with sleep.[35] However, as tolerance to the anxiogenic properties of caffeine occurs in consumers,[17] so may a tolerance develop into sleep interference. It may be that caffeine disrupts sleep in individuals with a habitually low level of consumption in higher doses. Even if caffeine has the capacity to delay the onset of sleep, we are unable to decisively measure whether it also has the capacity to keep a drowsy driver awake enough to drive safely.

If the advice given is to 'stop and have a caffeinated drink' we must consider the beverages in which caffeine may be consumed. On the one hand caffeine consumed in beverages such as coffee and energy drinks act as a psychostimulant. However, recent research has suggested that theanine, found in tea, acts as an caffeine antagonist and may have a negative effect on the alerting properties of caffeine.[36]

This paper has examined some caffeine studies that do not include driving. It may be that such studies are nonetheless very relevant to driving safety, as measures of vigilance may be just as important as measures of lane drift. As George[37] suggests, it is not necessary for a sleepy person to fall asleep at the wheel, for their inattentiveness is dangerous in itself. 'In traffic, even small performance decrements, which at first glance may seem rather trivial, can have meaningful implications for traffic safety'.[38] Given that driving simulator studies are inevitably time consuming and expensive, and therefore typically test relatively few participants, they may not provide the best context for detecting subtle, but potentially significant effects of caffeine on decrements in alertness and attention resulting from sleep restriction, work fatigue, or caffeine withdrawal.

On the other hand, the general public are more likely to trust the conclusions from driving studies. It is, therefore, important that any future studies should control for withdrawal effects. The most effective way of testing for caffeine withdrawal, as previously mentioned, is by comparing the effects of an acute dose of caffeine on overnight withdrawal versus long-term-withdrawn participants (in comparison with placebo). It would also be necessary to carry out these studies after a normal night's sleep and after a night of sleep restriction to increase our understanding of the effects of caffeine on driving *per se* and on drowsy drivers and in doing so increase our knowledge of the effects of caffeine on sleep. Finally, with the risk of drivers consuming very large quantites of caffeine to stay awake, and the potentially negative responses to higher doses, future studies should look at the effects on driving of high doses of caffeine.

It is important for caffeine consumers to continue to consume regular caffeinated drinks while driving, for any reasonable time, to avoid the symptoms (e.g. fatigue and headache) which accompany caffeine withdrawal. At best, positive effects of caffeine on driving are short lived. However, whether caffeine is a useful tool for drivers in the absence of caffeine withdrawal will remain questionable until appropriately designed experiments are accomplished and, therefore, it may be that advice given to the public should be adjusted accordingly.

Acknowledgement

I would like to thank Peter Rogers for his assistance.

References

1 Horne JA, Reyner LA. Driver sleepiness. J Sleep Res 1995; 4(Suppl. 2):23–9.
2 Philip P, Vervialle F, Le Breton P, Taillard J, Horne JA. Fatigue, alcohol, and serious road crashes in France: factorial study of national data. Br Med J 2001;322(7290):829–30.
3 James M, Lyznicki MS, Theodore C, Doege MD, Davis RM, Williams MA, for the Council on Scientific Affairs, American Medical Association. JAMA 1998;279:1908–13.
4 Royal Society for the Prevention of Accidents. Driver fatigue and road accidents a literature review and position paper 2001. Available from: http://www.rospa.com/RoadSafety/info/fatigue.pdf
5 James JE. Understanding caffeine: a biobehavioral analysis. London: Sage; 1997.
6 Maycock G. Sleepiness and driving: the experience of UK car drivers. J Sleep Res 1996;5:229–37.
7 Reyner LA, Horne JA. Evaluation of 'in-car' countermeasures to sleepiness: cold air and radio. Sleep 1998;21(1):46–50.
8 Royal Society for the Prevention of Accidents. Road safety information. Driver Distraction 2007. Available from: http://www.rospa.com/roadsafety/advice/driving/info/driver_distraction.pdf
9 Warburton DM. Effects of caffeine on cognition and mood without caffeine abstinence. Psychopharmacology 1995;119: 66–70.
10 Smith A. Effects of caffeine on human behaviour. Food Chem Toxicol 2002;40:1243–55.
11 James JE. Does caffeine enhance or merely restore degraded psychomotor performance? Neuropsychobiology 1994;30:124–5.
12 Rogers PJ, Martin J, Smith C, Heatherley SV, Smit HJ. Absence of reinforcing, mood and psychomotor performance effects of caffeine in habitual non-consumers of caffeine. Psychopharmacology 2003;167:54–62
13 Yeomans MR, Ripley T, Davies LH, Rusted JM, Rogers PJ. Effects of caffeine on performance and mood depend on the level of caffeine abstinence. Psychopharmacology 2002;164(3): 241–9.
14 Smith AP, Christopher G, Sutherland D. Effects of caffeine in overnight-withdrawn consumers and non-consumers. Nutr Neurosci 2006;1:63–71.
15 Childs E, de Wit H. Subjective, behavioural, and physiological effects of acute caffeine in light, nondependent caffeine users. Psychopharmacology 2006;185:515–23.

16 Haskell CF, Kennedy DO, Wesnes KA, Scholey AB. Cognitive and mood improvements of caffeine in habitual consumers and habitual non-consumers of caffeine. Psychopharmacology 2005;179:813–25.
17 Rogers PJ, Hohoff C, Heatherley SV, Mullings EL, Maxfield PJ, Evershed RP, *et al.* Association of the anxiogenic and alerting effects of caffeine with ADORA2A and ADORA1 polymorphisms and habitual level of caffeine consumption. Neuropsychopharmacology 2010;35:1973–83.
18 Heatherley SV, Hayward RC, Seers H, Rogers PJ. Cognitive and psychomotor performance, mood, and pressor effects of caffeine after 4, 6 and 8 h caffeine abstinence. Psychopharmacology 2005; 78(4):461–70.
19 Rogers PJ. Caffeine – our favourite drug. Biologist 2009;56(3): 98–103.
20 Rogers PJ, Heatherley SV, Hayward RC, Seers HE, Hill J, Kane M. Effects of caffeine and caffeine withdrawal on mood and cognitive performance degraded by sleep restriction. Psychopharmacology 2005;179:742–52.
21 Reyner LA, Horne JA. Early morning driver sleepiness: Effectiveness of 200 mg caffeine. Psychophysiology 2000;37:251–6.
22 Horne JA, Reyner LA. Beneficial effects of an 'energy drink' given to sleepy drivers. Amino Acids 2001;20:83–9.
23 Reyner LA, Horne JA. Efficacy of a 'functional energy drink' in counteracting driver sleepiness. Physiol Behav 2002;75:331–5.
24 Heatherley SV, Mullings EL, Tidbury MA, Rogers PJ. Caffeine consumption among a sample of UK adults. Appetite 2006;47: 266.
25 D'Amicis A, Viani R. The consumption of coffee. In: Garattini S (ed.) Caffeine, coffee and health. New York: Raven Press; 1993. p. 1–16.
26 James JE. Caffeine and health. London: Academic Press; 1991.
27 James JE. Caffeine, mental performance and mood. In: Watson DH (ed.) Performance functional foods. Cambridge: Woodland Publishing Ltd.; 2003. p. 168–94.
28 Rogers PJ, Richardson NJ, Elliman NA. Overnight caffeine abstinence and negative reinforcement of preference for caffeine-containing drinks. Psychopharmacology 1995;120:457–62.
29 Kaida K, Takahashi M, Akerstedt T, Nakata A, Otsuka Y, Haratani T, *et al.* Validation of the Karolinska sleepiness scale against performance and EEG variables. Clin Neurophysiol 2006;117(7):1574–81.
30 Smit HJ, Rogers PJ. Effects of low doses of caffeine on cognitive performance, mood and thirst in low and higher caffeine consumers. Psychopharmacology 2000;152:167–73.
31 Brice C, Smith A. The effects of caffeine on simulated driving, subjective alertness and sustained attention. Hum Psychopharm Clin 2001;16(7):523–31.
32 Heatherley SV, Hayward RC, Hill J, Smit HJ, Cater KF, Rogers PJ. Effects of caffeine and caffeine withdrawal on simulated driving performance. J Psychopharmacol 2004;18(3):A29.
33 Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. Psychopharmacology 2004; 176:1–29.
34 Sanchez-Ortuno M, Moore N, Taillard J, *et al.* Sleep duration and caffeine consumption in a French middle-aged working population. Sleep Medicine 2005;6:247–51.
35 Karacan I, Thornby JI, Anch M, Booth GH, Williams RL, Salis PJ. Dose-related sleep disturbances induced by coffee and caffeine. Clin Pharm Ther 1976;20:682–9.
36 Rogers PJ, Smith JE, Heatherley SV, Pleydell-Pearce CW. Time for tea: mood, blood pressure and cognitive performance effects of caffeine and theanine administered alone and together. Psychopharmacology 2008;195:569–77.
37 George CFP. Driving simulators in clinical practice. Sleep Med Rev 2003;7(4):331–20.
38 De Valck E, Cluydts R. Slow-release caffeine as a countermeasure to driver sleepiness induced by partial sleep deprivation. J Sleep Res 2001;3(10):203–09.