

Slow-release caffeine as a countermeasure to driver sleepiness induced by partial sleep deprivation

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Accepted in revised form 30 May 2001; received 11 December 2000

SUMMARY The effect of partial sleep deprivation (PSD) on driving abilities, as measured with a driving simulator, and the value of slow-release caffeine as a countermeasure to the expected performance decrements, were studied. Twelve subjects, between 20 and 25 years of age, underwent four experimental conditions, 4.5 or 7.5 h time in bed (TIB) with 300 mg slow-release caffeine or placebo, according to a Latin square design. Driving performance was measured twice by a 45-min driving task on a simulator. Subjective sleepiness/alertness and mood were assessed four times, by means of the Stanford Sleepiness Scale (SSS) and Profile of Mood States (POMS). After 4.5 h as compared with 7.5 h TIB lane drifting and speed deviation were higher, but only the effect on the first variable reached significance. In the placebo condition at 13.00 h, accident liability increased after PSD. Subjective sleepiness was higher in the 4.5 h TIB group. Caffeine intake gave rise to a decrease in lane drifting and after PSD it led to a smaller speed deviation and accident liability. The findings suggest that a lack of sleep can lead to a significant driving performance impairment, with drivers having problems to maintain an appropriate road position and a posted speed and more drivers getting involved in an accident. Secondly, the results indicate that caffeine – more specifically slow-release caffeine – can serve as a valuable countermeasure to these performance decrements, in the absence of any important side-effects, especially when its application is of an acute nature and when there is no opportunity to take a nap.

KEYWORDS caffeine, driving simulator, driving, partial sleep deprivation, sleepiness, traffic safety

INTRODUCTION

During the last decade excessive sleepiness among car and truck drivers is generally accepted as a relevant risk factor to traffic safety. Looking at the prevalence of sleepy drivers and of sleepiness related traffic accidents, the reason for this becomes obvious. A postal questionnaire in the United Kingdom, showed that 29% of the respondents had felt close to falling asleep at the wheel in the last year (Maycock 1996). Sleepiness related accident rates coming from self-report studies range from 4 to 16.1% among automobile drivers to 24.8% among truck drivers (Arnold *et al.* 1997; Fell 1995;

Lyznicki *et al.* 1998; Rizzo 1999). The fact that these accidents are more often serious and have in about 28% of the cases deadly outcomes (Philip *et al.* 1997), points to the significant human and financial costs that go together with it. An important risk factor for getting involved in a sleepiness related accident, next to circadian factors and sleep/wake disorders, is a lack of sleep, even a partial one (Fell and Black 1997; Philip *et al.* 1997; Rizzo 1999).

Driving simulator studies, which assess the impact of total sleep deprivation (TSD) on driving behavior experimentally, generally show clear qualitative and quantitative decrements in driving abilities (Alloway and MacLean 1999; Arnedt *et al.* 2000; Fairclough and Graham 1999; Lenné *et al.* 1998; Peters *et al.* 1999; Thorne *et al.* 1999; Verwey and Zaidel 1999). The reported changes in driving performance after partial sleep deprivation (PSD) are less consistent. Some studies demonstrate an increase in accident liability after a restriction of

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sleep to 3 h time in bed (TIB) (Thorne *et al.* 1999); others conclude that a reduction to 4 h TIB has no influence on this driving parameter (Fairclough and Graham 1999; Peters *et al.* 1999; Roehrs *et al.* 1994). The same conclusion can be made for lateral deviation, a second major indicator of driving performance: Fairclough and Graham (1999) report an increase in lateral deviation after 4 h TIB; Peters *et al.* (1999) and Roehrs *et al.* (1994) found no changes under that condition.

Once the problem of drowsy driving is clearly stated, the challenge remains to identify useful countermeasures. Among the different countermeasures that have been proposed, naps and caffeine are the most promising. The psychopharmacological action of caffeine on attention suggests it can be useful to optimize performance on a driving task, which is in essence a complex psychomotor vigilance task (Smith *et al.* 1991; Zwyghuizen-Doorenbos *et al.* 1990). The number of driving simulator studies examining the value of caffeine as a countermeasure to driver sleepiness is small, but the results confirm what could be expected considering its psychopharmacological action: a caffeine dose of 150–200 mg improves driving performance after 5 h PSD (Horne and Reyner 1996; Reyner and Horne 1997). Specifically, a decrease in the number of major incidents – vehicles leaving the road – can be noticed (Horne and Reyner 1996; Reyner and Horne 1997). The number of minor incidents – a car-wheel crossing lane markings – also decreases in some studies (Reyner and Horne 2000); other research results indicate no effect of caffeine on this parameter (Horne and Reyner 1996; Reyner and Horne 1997). These previous studies however, did not use a control group of non-sleep deprived subjects, so the usefulness of caffeine to increase driving performance under more optimal conditions, remains unknown.

In the current study 300 mg of a new form of caffeine, the slow-release form, was used. Slow-release caffeine (Stinergetic[®], Sanofi-Synthelabo) offers some extra advantages in comparison with a regular caffeine solution (Lagarde *et al.* 2000). First, the pharmacodynamic effects are more prolonged, resulting in a smooth, long-lasting effect instead of the boost effect of caffeine solutions like coffee. Maximal plasma concentration is reached in about 4 h and elimination half-life is 5–6 h. Secondly, less deleterious side-effects in comparison with immediate-release caffeine can be expected. Thirdly, the amount of caffeine this new galenic substance contains, is constant. This is not the case for coffee or other caffeine beverages. Next, previous pharmacological research suggests 300 mg is an optimal dose: doses under 200 mg induce little or no effect (Smith *et al.* 1991) and doses exceeding 600 mg can lead to the onset of deleterious cardiovascular or neurological side-effects (Carillo and Benítez 1994; Lagarde *et al.* 2000).

This study was designed to assess the effect of PSD (TIB = 4.5 h) vs. a control situation (TIB = 7.5 h) on the performance on a low cost driving simulator. Secondly, as to new form of caffeine – the slow-release form – is available

today, we wanted to assess its value as a countermeasure to the experimentally induced sleepiness.

METHODS

Subjects

Subjects were recruited through advertisement placed around the campus of the Free University of Brussels. Seven males and five females between 20 and 25 years of age (mean = 22.5, SD = 1.6) were enrolled after they were informed of the protocol and gave their informed consent. Inclusion criteria were: a minimum of 2 years of car driving experience, a regular sleep–wake schedule and a good general health condition. All but one subject had a Pittsburgh Sleep Quality Index (Buysse *et al.* 1989) between 2 and 5, indicating that they were moderate to good sleepers. Exclusion criteria were medical problems that can be exacerbated by sleep deprivation, e.g. epilepsy, hypersensitivity to caffeine and an extremely high daily caffeine intake (more than six caffeine-containing beverages a day). The study was approved by the Ethics Committee at the Free University of Brussels.

Subjects were instructed to maintain a regular sleep–wake schedule and to consume alcohol and caffeine only in moderation during the course of the study. In addition, they were requested to abstain from caffeine and alcohol from 4 PM the day before the drive.

Experimental design

Two factors were manipulated: TIB the night before testing, being either 4.5 or 7.5 h, and the substance, 300 mg slow-release caffeine or placebo, which was administered double-blind. This gave rise to four experimental conditions, which each subject underwent with a 1-week washout and according to a Latin square design.

Procedure

The evenings preceding the testing days subjects arrived at the laboratory at 22.00 h. They were allowed to engage in recreational activities such as watching television, reading, conversation or playing round games. The first evening a 20-min test practice session on the driving simulator was performed. At 24.00 h, the subjects went to their rooms and lights were extinguished. According to the experimental condition, subjects were awakened at 04.30 h or 07.30 h, after which they had a caffeine-free breakfast. Again, free time could be spent at choice with work, homework or recreational activities, such as video, reading and games. At 08.00 h 300 mg slow-release caffeine or placebo was administered. Subjects completed the sleepiness and mood scales at 08.00, 10.00, 12.00 and 14.00 h. The 45-min driving test took place at 09.00 h and 13.00 h. A caffeine-free meal was scheduled at 12.00 h. Subjects were discharged after completing the sleepiness and mood scales at 14.00 h.

Measurements

Evaluation of driving performance

The computer program Drivesim 3.00 of the York driving simulator (York Computer Technologies, Kingston, Ontario, Canada), running on an IBM-compatible personal computer, was used to assess driving performance. The simulator was equipped with an accelerator, brakes and a steering wheel to control the simulated car. A forward view from the driver's seat of a motorway road scene, with standard lane markings and signs and signals appropriate to the road environment, was presented on a 21-inch computer screen. The two-lane route had no bends, no stop signs or traffic lights. During each session the subject's vehicle was taken over by two other cars. Subjects drove for 45 min and were instructed to stay in the right hand lane and to keep on driving the posted speed, 100 km per hour (km h^{-1}).

Three variables were analysed to assess driving performance: (1) lane drifting, the standard deviation of the road position in an arbitrary lane width of 3 m calculated in cm, (2) speed deviation, the mean of the differences in km h^{-1} of the speed of the vehicle from the posted speed limit, (3) accident liability, being 1 if the car left the road or hit another vehicle at least once during the 45-min drive, 0 if this was not the case. Speed and road position were sampled at intervals of 100 ms. Data of the first 15 min of the drive were not included in the analyses, to allow adaptation to the driving task to develop.

Evaluation of subjective sleepiness/alertness and mood

Subjective sleepiness was assessed by the Stanford Sleepiness Scale (SSS) (Hoddes *et al.* 1973) and two subscales of a Dutch version of the Profile of Mood States (POMS), vigor and fatigue (MacNair *et al.* 1971). Further assessment of mood was carried out by the three remaining scales of the POMS, anger, depression and tense.

In both the SSS and the POMS, higher scores are indicative of a higher intensity of the construct measured.

Evaluation of adverse effects

This was realized by stressing the subjects to report any experienced unusual effect.

Caffeine

We made use of 300 mg of slow-release caffeine (Stinerbic®).

Statistical analysis

The driving variables, lane drifting and speed variability were analysed using repeated measures ANOVA's in which TIB (4.5 h, 7.5 h), substance (placebo, caffeine) and time (09.00 h, 13.00 h) were extracted as within-subject variables. The anger, depression and tense scales of the POMS were analysed the same way, except for the time variable having four levels (08.00, 10.00, 12.00, 14.00 h). A MANOVA,

in which the TIB, SUBSTANCE and TIME factors were analogous, was performed on the three scales measuring subjective sleepiness/alertness (the vigor and fatigue scales of the POMS and the SSS). When appropriate further comparisons were carried out using Scheffé post hoc tests. The dichotomous variable accident liability was analysed by Fisher's Exact tests. The level of significance for all analyses was set at 0.05. Because of technical problems, the simulator-data of one subject in the 7.5 h TIB/placebo condition at 13.00 h was not evaluable.

RESULTS

Driving performance

Lane drifting and speed deviation

The ANOVA on lane drifting showed a significant main effect of TIB, indicating that lane drifting increased after 4.5 h, as compared with 7.5 h TIB ($F[1,10] = 10.53$, $P < 0.01$). Also, speed deviation was higher in the 4.5 h TIB condition, but this effect did not reach significance ($F[1,10] = 4.42$, $P < 0.10$). There was a statistically significant effect of the substance factor, with lane drifting ($F[1,10] = 20.91$, $P < 0.001$) and speed deviation ($F[1,10] = 10.24$, $P < 0.01$) being smaller in the caffeine condition, as compared with the placebo condition. No time of day effect was evident on both driving performance measurements. In the case of lane drifting, there was an interaction effect between substance and time ($F[1,10] = 5.84$, $P < 0.05$). For both dependent measures a marginally significant interaction between the factors TIB and substance was noticed (lane drifting: $F[1,10] = 3.60$, $P < 0.10$; speed deviation: $F[1,10] = 4.63$, $P < 0.10$). Figure 1 illustrates these interactions. For lane drifting, a TIB effect was only significant following placebo administration ($P < 0.05$), while caffeine intake eliminated this effect (NS). This same conclusion can be made for speed deviation, but here the TIB effect in the placebo condition was only marginally significant ($P < 0.10$). Moreover, the interaction effect on speed deviation signified that the caffeine effect was only apparent following 4.5 h TIB ($P < 0.05$). The caffeine effect on lane drifting was present in both TIB conditions (4.5 h TIB: $P < 0.01$; 7.5 h TIB: $P < 0.05$). Principal results are summarized in Tables 1 and 2.

No significant gender effects were observed in driving performance following both PSD and caffeine intake.

Accident liability

At 13.00 h a significantly higher accident liability was found in the 4.5 h TIB, as compared with the 7.5 h TIB condition, at least in the placebo group ($P < 0.05$). A TIB effect was not found in any other condition. A significant effect of substance was observed after 4.5 h TIB at both testing moments (09.00 h: $P < 0.05$; 13.00 h: $P < 0.05$), that is after 4.5 h TIB the accident liability was smaller in the caffeine than in the

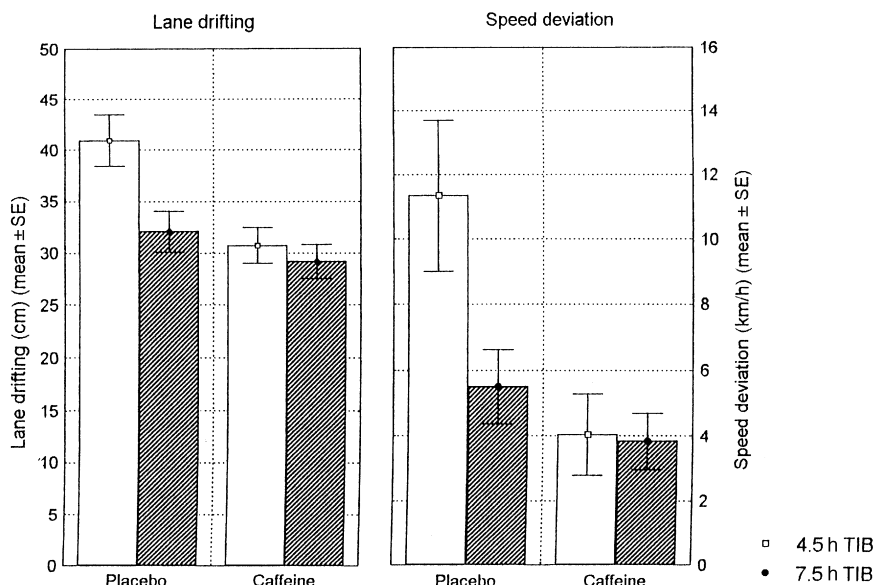


Figure 1. Interaction effect between TIB (4.5 h/7.5 h) and substance (placebo/caffeine).

Table 1 Means of the 2 (TIB) × 2 (Substance) × 2 (Time) design for lane drifting and speed deviation

	Lane drifting (cm)	Speed deviation (km h ⁻¹)
Time in bed (TIB)		
4.5 h	36.06	7.82
7.5 h	30.66	4.63
Substance		
Placebo	36.66	8.56
Caffeine	30.06	3.90
Time		
09.00 h	32.76	6.33
13.00 h	33.96	6.12

Table 2 Summary of the three-way repeated measures ANOVA's of lane drifting and speed deviation and of the MANOVA of subjective sleepiness (fatigue, vigor, sleepiness)

	Lane drifting		Speed deviation		Subjective sleepiness	
	F	P	F	P	Rao's R	P
Time in bed (TIB)	10.53	0.009	4.42	0.062	4.56	0.033
Substance	20.91	0.001	10.24	0.009	4.79	0.029
Time	2.50	0.145	0.08	0.779	4.42	0.124
TIB × Sub	3.60	0.087	4.63	0.057	20.18	0.001
TIB × Time	0.01	0.915	0.98	0.345	1.30	0.459
Sub × Time	5.84	0.036	0.06	0.810	2.91	0.206
TIB × Sub × Time	0.01	0.926	3.02	0.113	6.27	0.079

Values in bold are statistically significant.

placebo condition. When subjects were allowed to sleep 7.5 h, caffeine had no effect on the accident status, neither at 09.00 h (NS), nor at 13.00 h (NS). In none of the conditions Fisher exact tests showed an effect of time on the accident liability.

Table 3 shows the percentage of sessions in which at least one accident occurred in the various conditions.

Table 3 Percentage of sessions in which at least one accident occurred in the various conditions

	Placebo	Caffeine	Average
4.5 h TIB			
At 09.00 h	50	8	29
At 13.00 h	50	8	29
Subtotal	50	8	29
7.5 h TIB			
At 09.00 h	25	8	17
At 13.00 h	9	8	9
Subtotal	17	8	13
Average	34	8	21

Subjective sleepiness/alertness and mood

Subjective sleepiness/alertness

A MANOVA with the vigor and fatigue scale of the POMS and the SSS as dependent variables, indicated statistically significant main effects of TIB (Rao's $R[3,9] = 4.56$, $P < 0.05$) and of substance (Rao's $R[3,9] = 4.79$, $P < 0.05$). Mean values indicated higher levels of fatigue and sleepiness and lower levels of vigor in the 4.5 h TIB condition and in the placebo condition, as compared with the 7.5 h TIB condition and the caffeine condition, respectively. There was no significant effect of time (Rao's $R[9,3] = 4.42$, NS). Table 2 presents the MANOVA outcome and Table 4 the mean sleepiness/alertness scores in the various conditions.

A significant interaction effect for TIB and substance, Rao's $R[3, 9] = 20.18$, $P < 0.001$, revealed that caffeine led to a decrease in fatigue ($P < 0.001$) and sleepiness ($P < 0.05$) only if subjects slept 4.5 h. In the 7.5 h TIB condition, caffeine had no influence on fatigue and sleepiness (NS). Regarding the vigor scale, the only significant post hoc difference was between the caffeine/7.5 h TIB and the placebo/4.5 h TIB condition ($P < 0.01$).

Table 4 Means of the 2(TIB) × 2(Substance) × 4(Time) design for fatigue, vigor (POMS) and sleepiness (SSS)

	Fatigue	Vigor	Sleepiness
Time in bed (TIB)			
4.5 h	11.6	14.7	2.8
7.5 h	8.4	17.9	2.2
Substance			
Placebo	11.1	15.0	2.9
Caffeine	8.9	17.6	2.1
Time			
08.00 h	11.1	15.4	2.9
10.00 h	10.1	15.9	2.6
12.00 h	8.2	18.3	1.8
14.00 h	10.5	15.5	2.6

Anger, depression and tense

Regarding the dependent variables anger, depression and tense of the POMS three separate 2(TIB) × 2(substance) × 4(time) ANOVA's were performed. Only a significant main effect of TIB on the depression score was found; that is, the score was higher in the 4.5 h TIB condition ($M = 8.97$) than in the 7.5 h TIB condition ($M = 8.45$) ($F[1,11] = 6.83$, $P < 0.05$).

Adverse effects

Out of 12 subjects 11 did not report any side-effects that could be linked to the caffeine intake during the study period. One female subject reported some minor gastro-intestinal, nervousness and sweating complaints in the 7.5 h TIB/caffeine condition starting 3 h after caffeine ingestion. It is known from previous studies that the gastro-intestinal system is sensitive to caffeine and that women react more intensively to the drug as compared with men (James 1997).

Another female subject in the 4.5 h TIB/caffeine condition suffered from a headache at 05.00 in the morning. However, this could not be considered as an adverse effect of the drug, as the complaint started 3 h before caffeine intake.

DISCUSSION

Effects of partial sleep deprivation on driving performance

This study clearly demonstrated the negative impact of 4.5 h TIB as compared with 7.5 h TIB on simulator driving performance. An increase in lane drifting was evident in the PSD relative to the control group. Furthermore, an increase in speed deviation, not yet reported in the context of PSD, was noticed. We found an effect of PSD on accident liability that was rather modest. Accident liability in the placebo condition did rise significantly in the afternoon session (13.00 h), but not in the morning session (09.00 h), as a result of a lack of sleep. In accordance with numerous previous studies (Brendel *et al.* 1990; Hill *et al.* 1996; Pilcher and Walters 1997), we found an increase in subjective sleepiness after PSD relative to the 7.5 h

TIB conditions. This confirmed that PSD led to the intended induction of sleepiness.

Questions can be raised regarding the extent to which these clearly demonstrated performance decrements lead to meaningful safety risks in real traffic. As qualitative extrapolation of simulator data generally is assumed to be valid (Hoyes *et al.* 1997; Tornros 1998), we can conclude that drivers experience more difficulty in maintaining an appropriate lane position and a posted speed after a lack of sleep. On the contrary, quantitative extrapolation of simulator data is considered to be invalid (Tornros 1998). Concerning accident liability, we think the operationalization of the variable is crucial in this context. Contrary to previous investigators who used the number of accidents as a parameter for their analysis, we made use of a dichotomous variable, indicating whether or not the subject had at least one accident during the 45-min drive. In essence, what we are trying to measure is whether or not the driving performance is declined to the extent that it will lead to an accident. The number of accidents a person is involved in during a simulator drive is less relevant, for during real driving it is virtually impossible to have for instance three car accidents in a 30-min period. The relevant literature also indicates that the number of accidents on a simulator is far in excess from the number of accidents that can take place in real traffic during the same time period (Lenné *et al.* 1997; Reyner and Horne 1998). This is why we propose that defining accident liability as a dichotomous variable is more useful and benefits the external validity of the resulting findings.

On the one hand, the limited effect of PSD on accident liability seems to support the idea of Fairclough and Graham (1999), purporting that PSD causes driving performance decrements, but not to the extent that it brings about a higher accident risk. Here, an explanation might be found in the asymptotic restorative function of sleep, which signifies that the most essential recuperation takes place during the first sleep cycles and to a less extent during later cycles (Horne 1988). On the other hand, we think that the consequences of the simulator performance decrements cannot be underestimated. In traffic, even small performance decrements, which at first glance may seem rather trivial, can have meaningful implications for traffic safety. This points to the necessity of more field studies to examine closely the relationship between performance on a simulated and a real driving task.

Caffeine as a countermeasure to driver sleepiness

The value of 300 mg of slow-release caffeine as a countermeasure to simulator driving performance decrements after PSD, was empirically supported. In the sleep deprived group (4.5 h TIB), the caffeine counteracted the increase in lane drifting and resulted in a lower speed deviation and accident liability. Furthermore, even under more optimal conditions (7.5 h TIB) caffeine intake went together with a performance improvement, though to a less extent. This was indicated by a decrease in lane drifting, while speed deviation and accident liability remained unchanged. The influence of caffeine on

accident liability after PSD has been reported elsewhere (Horne and Reyner 1996; Reyner and Horne 1997), but no previous studies were found regarding caffeine effects on the other driving performance parameters used here and after a 'normal' sleep duration.

The beneficial action of caffeine on driving performance was observed 1 h after administration and was still present after 5 h. This illustrated the prolonged action that is attributed to the slow-release form of caffeine. Although no other doses of this caffeine formulation were tested, the 300 mg dose showed to be an effective one in this study.

A second topic, next to the psychopharmacological action of caffeine, is its applicability in real traffic situations. The efficacy of the drug to improve performance from at least 1–5 h after intake, without any important side-effects, points to the usefulness of caffeine when driving performance needs to be optimised acutely, as a result of excessive sleepiness. However, its usefulness in drives of over 5 h in duration at this time is not explored. Among other things, future studies should look into the possible appearance of withdrawal sleepiness as well as into safety aspects of the effects of repeated intake.

Another countermeasure to sleep, planned naps, has an important advantage to caffeine as heavy and/or long-term use of caffeine can lead to the onset of health problems and tolerance to the effects of the drug (James 1997). On the other hand, some circumstances do not allow taking a nap. In these cases slow-release (SR) caffeine can have an important role. Fourteen percent of the car drivers and 69% of the truck drivers report using caffeine to counteract sleepiness at the wheel (Arnold *et al.* 1997; Maycock 1996). Undoubtedly, this is connected with the widespread availability of caffeine.

The usefulness of countermeasures to sleepiness, which have to be taken on one's own initiative, is dependent upon the extent to which the drivers are aware of their sleepiness state. It is evident that if they cannot estimate their level of sleepiness accurately, it is unlikely they will take appropriate countermeasures. However, most drivers seem to be able to judge their own sleepiness level quite correctly and only a minority of them do not realize the related risk of falling asleep (Reyner and Horne 1998).

Compensation theories suggest some caution in assuming that isolated safety measures will automatically lead to a safer traffic environment. They point to the possibility that when a situation is made intrinsically safer, people may behave riskier, because the overall risk they are willing to accept remains the same. This would be the reason why many safety measures miss their aim (Stanton and Glendon 1996). In the current context this would mean that in consequence of caffeine intake, drivers keep on driving for a longer time than they would without caffeine, so that the eventual accident risk is not reduced. However, the following alternative reasoning gains some empirical support as well. Compensation could result in drivers in suboptimal condition, trying to keep performance on a baseline level. Hockey *et al.* (1998) noticed that after one night TSD subjects succeed in keeping primary task performance on baseline level by putting more effort in it. This suggests caffeine

can be helpful when more effort is insufficient to counteract the driving performance decrements after sleep restriction.

It would be worthwhile to explore other beneficial applications of slow-release caffeine, for instance as a countermeasure to sleepiness induced by other medications such as antihistamines.

In conclusion, we found that speed deviation is a variable, sensitive to sleepiness and caffeine. This points to its possible value for use in sleepiness detection devices. The consequences of a decrement in the ability to maintain a posted speed for traffic safety, are not yet clear and deserve further scientific attention. It could be hypothesized that an increase in speed deviation leads to problems in selecting a speed in accordance to the situational demands or to annoyance and hindrance of other road-users.

Furthermore, it was argued that the performance parameter accident liability would lead to more externally valid conclusions when defined as a dichotomous variable, indicating whether or not an accident did happen, instead of as the number of accidents a subject was involved in.

ACKNOWLEDGEMENTS

We would like to thank Danny Rouckhout for his technical assistance.

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