Highway driving safety the day after using sleep medication: the direction of lapses and excursions out-of-lane in drowsy drivers

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SUMMARY

The primary outcome measure of the on-road driving test is the Standard Deviation of Lateral Position. However, other outcome measures, such as lapses and excursions out-of-lane, also need to be considered as they may be related to crash risk. The aim of this study was to determine the direction of lapses and excursions out-of-lane (i.e. towards/into the adjacent traffic lane or towards/into the road shoulder). In total, data from 240 driving tests were re-analysed, and 628 lapses and 401 excursions out-of-lane were identified. The analyses revealed that lapses were made equally frequently over left (49.4%) and over right (43.3%). In contrast, excursions out-of-lane were almost exclusively directed over right into the (safer) road shoulder (97.3%). These findings suggest that drivers are unaware of having lapses, whereas excursions out-of-lane are events where the driver is aware of loss of vehicle control.

INTRODUCTION

An important issue in the development of hypnotic drugs is to examine possible next-day effects that may negatively affect daily activities, such as driving a car. A standardized method to examine the ability to drive is the Dutch on-the-road driving test. In this test, subjects drive 100 km on a public highway in normal traffic, and are instructed to maintain a constant speed of 95 km•h^{-1} and a steady lateral position within the right traffic lane (O'Hanlon *et al.*, 1982; Verster and Roth, 2011). Speed and lateral position are continuously recorded. Traditionally, the gold standard outcome measure in highway driving research is the Standard Deviation of Lateral Position (SDLP), i.e. the weaving of the car (Verster and Roth, 2011). A graphical representation of SDLP is given in Fig. 1.

Using SDLP as primary outcome measure, a series of on-road driving studies have investigated the effects of driving a car the morning following bedtime administration of benzodiazepine hypnotic drugs and zopiclone (Roth *et al.*, 2014). In addition to the performance impairment demonstrated in these clinical studies, epidemiological evidence revealed that patients who use benzodiazepine hypnotics have an increased risk for having motor vehicle accidents (De Mello *et al.*, 2013). It is thus of great importance to examine driving performance and possible accident risk of newly developed hypnotic drugs.

Although there is consensus that SDLP is an excellent measure of vehicle control to demonstrate potential drug-induced effects on driving ability (Verster and Roth, 2012), its relationship to the risk of having a traffic accident is less clear. Although comparative analyses have shown a high correlation between SDLP increment seen in on-road driving studies and traffic accident risk from epidemiological studies (Owens and Ramaekers, 2009), this does not prove that high SDLPs are the proximal cause of accidents. Many other factors may play a role in the occurrence of an accident including, but not limited to, inattention, micro-sleep and distraction.

In this context, excursions out-of-lane are events that have been related to increased traffic accident risk. Excursions out-of-lane can be examples of severe loss of vehicle control, which can be made into the left traffic lane or into the right road shoulder (Fig. 2).

However, they can also occur in relatively unimpaired drivers if a lateral position is chosen close to the road delineation. Hence, the frequency of having excursions out-of-lane is significantly related to the mean lateral position of the car. Therefore, there is debate about the usefulness of

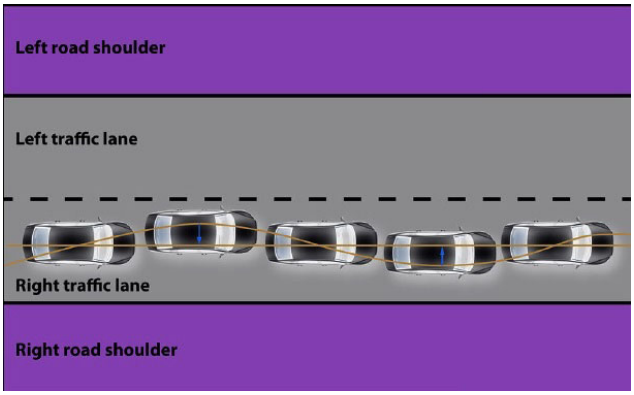

Figure 1. Schematic representation of the Standard Deviation of Lateral Position (SDLP).

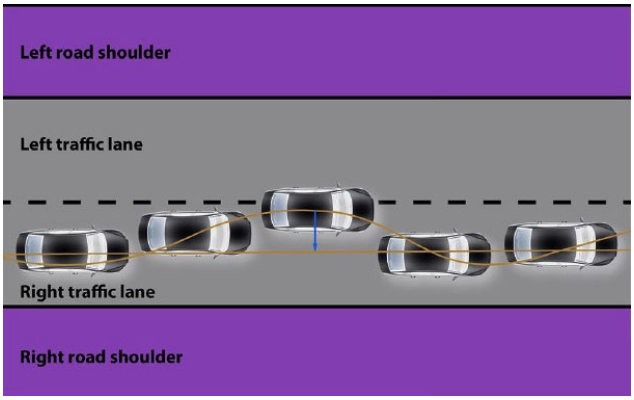

Figure 2. Schematic representation of an excursion out-of-lane.

excursions out-of-lane to distinguish impaired from unimpaired drivers (Verster and Roth, 2014a).

This limitation has facilitated the search of alternative outcome measures of highway driving tests, such as lapses (Fig. 3).

A lapse is defined as a deviation from the steady lateral position of at least 100 cm for at least 8 s. Recent analyses have shown that the number of lapses is a useful measure to demonstrate dose-dependent residual effects of hypnotic drugs (Verster *et al*., 2014). Alternatively, performance improvement was demonstrated in patients with attention deficit hyperactivity disorder (ADHD). While lapses were present in almost all patients when treated with placebo, when treated with their usual dose of methylphenidate lapses were virtually absent (Verster and Roth, 2014b). As inattention is a core deficit of patients with ADHD, this study demonstrated the usefulness and sensitivity of lapses, and the outcome supports the notion that lapses are in fact short periods of loss of vehicle control that are due to inattention or micro-sleep.

The aim of the current study was to directly compare the direction of excursions out-of-lane and lapses, in order to obtain indirect evidence on whether these are conscious events or without the awareness of the driver.

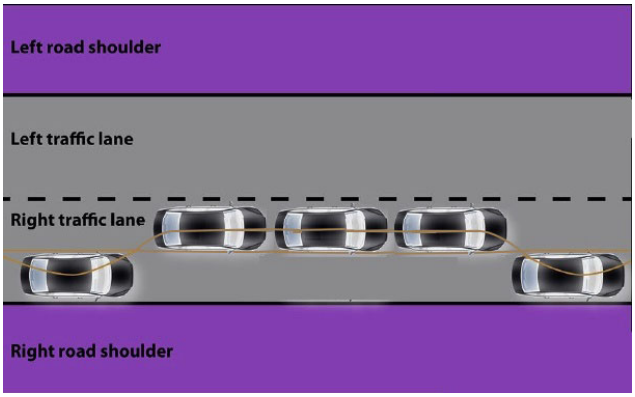

Figure 3. Schematic representation of a lapse.

MATERIALS AND METHODS

Data from two driving studies (Mets *et al*., 2011; Verster *et al*., 2002) were re-analysed. The first study examined the effects of the hypnotic drug zolpidem (10 and 20 mg), zaleplon (10 and 20 mg) and placebo, 4 h after middle-of-the-night administration (Verster *et al*., 2002). The second study examined the effects of the hypnotic drugs ramelteon (8 mg), zopiclone (7.5 mg) and placebo, 8.5 h after bedtime administration (Mets *et al*., 2011). In both studies, participants completed the 100 km on-the-road driving test (Verster and Roth, 2011), 1 h after waking up in the morning. The studies were chosen because in those studies it was found that several drivers were significantly impaired after treatment, and overall zolpidem (10 and 20 mg), ramelteon and zopiclone significantly impaired driving performance (as assessed with SDLP as outcome measure) relative to placebo, which increased the likelihood of having lapses and excursions out-of-lane in the data set. The study protocols were approved by the Medical Ethics Committee of the University Medical Center Utrecht, and informed consent was obtained from all participants.

Participants were healthy volunteers, aged 21–65 years old. The participants' health status was thoroughly screened before the start of the study, including verification of the absence of any sleep disorder. In addition to physical examination, screening included blood chemistry, haematology, urinalysis and electrocardiogram. They were included only if they had sufficient driving experience (i.e. driving more than 5 000 km per year for at least 3 years). A detailed description of the inclusion and exclusion criteria and screening procedures can be found in Verster *et al.* (2002) and Mets *et al.* (2011). Participants were trained on the driving test and familiarized with the test circuit. In both studies, subjects slept under supervision, and driving tests were performed the next morning.

In both studies, a 100 km standardized driving test (O'Hanlon *et al*., 1982; Verster and Roth, 2011) was performed on a primary highway in actual traffic, between the Dutch cities of Utrecht and Arnhem. Participants were instructed to drive with a steady lateral position within the

right traffic lane while maintaining a constant speed of 95 km•h^{-1}. They were allowed to overtake slower moving vehicles. A licensed driving instructor had access to dual controls and assured the safety during the test. The vehicle's lateral position and speed were continuously recorded, digitally sampled at 2 Hz, and edited off-line to remove data that were disturbed by extraneous events (e.g. overtaking manoeuvres). Thereafter, for each driving test, the number of excursions out-of-lane and lapses, including their direction, were determined.

An excursion out-of-lane was defined as crossing (either full or partly) the left or right lane delineation. A lapse was defined as a continuous change in lateral position of greater than 100 cm, lasting for at least 8 s. The direction of lapses was determined by inspecting the areas above and below the mean lateral position. The biggest area above or below the mean lateral position at that moment determines the direction of a lapse. Lapses were thus classified as over left, over right, or in both directions.

Statistical analyses

For each drug and placebo, the number of excursions over left and right and the number of lapses over left versus right were counted. For all treatments combined, overall sum scores and corresponding percentages were computed. The N–1 Chi-squared test for proportions was used to assess the statistical significance of each comparison (e.g. proportion of lapses over left versus proportion of lapses over right). Differences were considered statistically significant if $P < 0.05$.

RESULTS

In total, data from 240 driving tests were re-analysed. Over all conditions summarized, 628 lapses were made and 401 excursions out-of-lane occurred. Results from the two studies are summarized in Table 1.

The analyses revealed that lapses were made more or less randomly to the left (49.4%) or right direction (43.3%, $P = 0.14$). In contrast, excursions out-of-lane were almost all directed over right into the (safer) road shoulder (97.3%, $P < 0.0001$). Inspection of the data further revealed that lapses occur significantly more often than excursions out-of-lane (626 versus 401 events, respectively, $P < 0.0001$). The frequency of experiencing lapses seems related to the sedative properties of a drug, as they are seen significantly more often after administration of hypnotic drugs when compared with the placebo conditions (545 versus 83 lapses, $P < 0.0001$). Also, a clear dose–response relationship for the number of lapses can be seen. When compared with the low dosages of these drugs, lapses are significantly more common after the high dosages of zaleplon (29 versus 53 lapses, $P = 0.0002$) and zolpidem (111 versus 210 lapses, $P < 0.0001$). For excursions out-of-lane, this dose effect was not significant.

Table 1 Driving test results

	Lapses			*Excursions out-of-lane*	
Treatment	*Left*	*Right*	*Both*	*Left*	*Right*
Study 1					
Placebo	24	14	5	1	3
Zaleplon 10 mg	13	15	1	0	4
Zaleplon 20 mg	25	27	1	0	3
Zolpidem 10 mg	58	49	4	2	36
Zolpidem 20 mg	88	91	31	4	114
Study 2					
Placebo	20	18	2	1	54
Ramelteon (8 mg)	41	19	1	0	80
Zopiclone (7.5 mg)	41	39	1	3	60
Overall	310	272	46	11	390
% of total	49.4	43.3	7.3	2.7	97.3

Total number of lapses and excursions out-of-lane, as well as their direction: left=towards/into adjacent traffic lane; right=towards/into the road shoulder.

DISCUSSION

The analyses revealed clear differences between the nature of lapses and excursions out-of-lane. The direction of lapses was approximately equally divided over left (into the adjacent traffic lane) and over right (into the road shoulder). In contrast, excursions out-of-lane were almost exclusively directed over right into the (safer) road shoulder.

We hypothesize that if a driver is aware of being drowsy, in the case of loss of vehicle control with awareness, the driver will try to direct his car more towards the safer road boundary instead of the adjacent traffic lane (as other traffic may be driving in this lane). In contrast, during periods of inattention, it can be assumed that directions of the car during vehicle loss may be random and equally frequent towards the safer lane boundary (over right) and over left (towards the adjacent traffic lane with other traffic).

In terms of traffic safety, it is much safer to drive into the road shoulder than into the adjacent traffic lane, as other traffic may be present in the latter. This suggests that excursions out-of-lane are conscious moments of loss of vehicle control, as in 97% of cases the driver directs the car into the safer road shoulder; in contrast, the direction of lapses seems random, suggesting that the driver is unaware of these events. If lapses are considered to be moments of micro-sleep, it is understandable that they go unnoticed by drivers. As lapses may ultimately also result in excursions out-of-lane, it is worrisome that about half of them are directed to the other traffic lane instead of the safer road shoulder.

If it is true that drivers are unaware of having lapses, this would explain why it is equally likely that lapses occur randomly in both directions (over left or right). To prove this hypothesis, additional research is needed in which electroencephalographic (EEG) measurements are made during

driving. Brain activity can then be related to lapses and excursions out-of-lane to determine whether these events show different EEG changes. One would expect greater EEG signs of drowsiness (e.g. alpha) relative to excursions out of lane. The clinical relevance of this observation is clear. We hypothesize that drivers that are unaware of their driving behaviour are at higher risk of becoming involved in accidents. To investigate this, it would be interesting to re-analyse driving simulator crash data to examine if crashes are proceeded by having lapses, or more frequently occur during lapses. Future research should investigate these issues, to improve our knowledge on the nature of lapses and excursions out-of-lane to better understand the evaluation of impaired driving and the associated risk of accidents.

In conclusion, the current findings suggest that drivers are unaware of having lapses, whereas excursions out-of-lane are events where the driver is aware of loss of vehicle control.

AUTHOR CONTRIBUTIONS

JV and TR designed the study; LM and AB conducted the analyses; JV drafted the article; all authors contributed to and approved the final version of the manuscript.

CONFLICT OF INTEREST

JV has received grants/research support from the Dutch Ministry of Infrastructure and the Environment, Janssen Research and Development, Nutricia, Red Bull, Sequential, and Takeda, and has acted as a consultant for the Canadian Beverage Association, Centraal Bureau Drogisterijbedrijven, Coleman Frost, Danone, Deenox, Eisai, Janssen, Jazz, Purdue, Red Bull, Sanofi-Aventis, Sen-Jam Pharmaceutical, Sepracor, Takeda, Transcept, Trimbos Institute, and Vital Beverages. TR has received grants/research support from Aventis, Cephalon, GlaxoSmithKline, Neurocrine, Pfizer, Sanofi, Schering-Plough, Sepracor, Somaxon, Syrex, Takeda, TransOral, Wyeth, and Xenoport; has acted as a consultant for Abbott, Acadia, Acoglix, Actelion, Alchemers, Alza, Ancil, Arena, AstraZeneca, Aventis, AVER, BMS, BTG, Cephalon, Cypress, Dove, Elan, Eli Lilly, Evotec, Forest, GlaxoSmithKline, Hypnion, Impax, Intec, Intra-Cellular, Jazz, Johnson & Johnson, King, Lundbeck, McNeil, MediciNova, Merck, Neurim, Neurocrine, Neurogen, Novartis, Orexo, Organon, Prestwick, ProctereGamble, Pfizer, Purdue, Resteva, Roche, Sanofi, Schering-Plough, Sepracor, Servier, Shire, Somaxon, Syrex, Takeda, TransOral, Vanda, Vivometrics, Wyeth, Yamanuchi, and Xenoport. The other authors have no conflicts of interest to disclose.

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