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Driving performance under the influence of drugs: rationale for, and application of, a new test

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1 This paper offers the rationale for developing an over-the-road test for assessing drug effects on actual driving performance.

2 It describes the development of such a method and results obtained in three separate experiments where the method was applied.

3 The results support the claim that the test provides a valid measure of drug effects on one type of actual driving performance. The test may eventually find a place in the screening of psychoactive drugs for licensing.

Keywords drugs driving performance

Introduction

With the exception of the barbiturates, the earliest psychoactive drugs (e.g. MAO-inhibitors, phenothiazines) were intended for use by psychiatric inpatients. Drug interference with normal performance capabilities was of little practical concern since this patient population was already largely incapable of undertaking any of life's more demanding tasks.

The introduction of the minor tranquillizers in the 1960's radically changed this situation. Since then, psychoactive drugs have been widely used by fully ambulatory outpatients who are not only free to undertake all normal tasks, but are usually encouraged by their physicians to do so. Yet the same psychomotor tests which were developed mainly out of academic interest to assess the gross effects of the earlier drugs continue in use today for assessing the far more subtle effects of newer drugs. They were never specifically designed to predict performance impairments of practical consequence.

Numerous investigations employing batteries of laboratory tests have been undertaken to assess the effects of drugs on skills related to driving'. The assertion that what is measured by these tests was usually made with no empirical support whatsoever. Moreover, it is in defiance of the common belief of driving performance experts that *no* battery of laboratory tests provides single or composite measures which strongly predict safety-related performance of ordinary drivers (Naätänen & Summala, 1976).

Whether such tests can be used to predict unsafe driving performance under the influence of drugs is admittedly another question. In the extreme case, when a drug's effect is to render the subject incapable of performing any laboratory task, the prediction that this effect will extend into the driving environment is probably sound. However, minor tranquillizers and antidepressants have no such obvious effects. Neither do hypnotics, 9–24 h after ingestion. There is a real question as to whether laboratory test results are useful predictors of the practical performance effects of the newer drugs. This question has been raised repeatedly (Clayton, 1976; O'Hanlon, 1980, 1981; Silverstone, 1974) but it has never been answered by the proponents of the laboratory approach.

The use of staged driving performance tests conducted on a course closed to other traffic and of tests conducted in driving simulators seems more defensible. Performance under such circumstances resembles actual driving. Moreover, the achievable degree of experimental control and assurance of subject safety are factors which

argue for the application of these approaches. Yet it is true that no two teams of investigators employ the same closed-course or simulator test battery. Does this mean that all provide equally valid results, or does it simply indicate that every team uses the method it has available and justifies it, post hoc, the best it can? On rational grounds one would suppose that the most complex and realistic tests provide the better predictions of actual driving performance. Yet to retain absolute control and safety, closed-course testing can never approximate real driving, and for the moment, complete driving simulation is a technical impossibility. The question of test fidelity is therefore one of test validity. At what point does the artificial test enough resemble the real task so that the former's results become predictive of the latter? This is the first question which should be answered by proponents of either the closed-course or simulator approach but not the last.

All psychoactive drugs, and especially anxiolytics, have pronounced motivational effects in addition to those that might impair perceptual-motor or cognitive skills: the drugs reduce avoidance motivation. In real driving, the motivation to avoid hazardous situations is certainly as important as any other factor for determining performance. In 'completely safe' tests, this motivation is replaced by those to please the experimenters, achieve some idiosyncratic achievement criterion or avoid a reduction in pay. Is it reasonable to suppose, without evidence, that a drug's effect would be to reduce motivation in the real and artificial tasks to exactly the same extent? Is it not more reasonable to expect that the motiviation to avoid death or injury would be more resistant to change than any other? If this is the case, then no closed-course or simulator test, however realistic, can be expected to provide a valid measure of a psychoactive drug's effect on actual driving performance. This is a strong statement but if it is false, then it behoves the proponents of closed-course or simulator testing to refute it with evidence.

The alternative to all methods mentioned above is that of assessing drug effects in actual driving situations. In some societies this is prohibited by law (e.g. Sweden) or exceedingly difficult to accomplish owing to the threat of litigation and resultingly prohibitive insurance requirements (e.g. United States). Unfortunately for drug users in such places, their own national research possibilities are too restricted to provide them with complete assurance that the drugs they must use for medical reasons are also safe for use while driving.

In this author's opinion the final test of any psychoactive drug's potential for impairing actual driving performance must transpire in the actual driving environment. Naturally the test cannot represent every possible driving situation and some degree of control must be exerted to ensure reproducibility. It will also be artificial to some extent but less so than tests employed in any other approach. Stringent controls must be exerted to safeguard the subject's safety but the final responsibility for his (and the accompanying experimenter's) safety must reside with himself, as the driver. His motivation might be somewhat different than normal, but again, less so than as a participant in any 'completely safe' experiment.

Following these principles, we developed an over-the-road test for assessing driving performance under the influence of drugs. It was first applied in a limited pilot study (O'Hanlon *et al.*, 1982), and subsequently, in three completed experiments. Two more are in progress at this time. The remainder of this paper describes the method and some results from completed studies.

Method

The subject's task is to operate a specially instrumented vehicle around a 100 km primary highway circuit (50 km each way, on the same road, between fixed terminal points) while attempting to maintain a constant speed (95 km/h) and a steady lateral position of his own choosing between the delineated boundaries of the slower (right) traffic lane. He may deviate from those instructions only

1. in order to pass a slower vehicle and
2. at the mid-circuit, turn-around point where it is necessary to leave and re-enter the highway.

The subject is accompanied on the test by two experimenters; one whose task is to ensure ride safety, the other is to operate the equipment and record the occurrence of certain events of interest.

Speed and lateral position are continuously measured and recorded using apparatus and procedures described elsewhere (O'Hanlon *et al.*, 1983). These data are reduced by 10 km segments of the ride and separate values are averaged over the entire ride to yield the overall mean, standard deviation (SD), the standard index of skew and that of kurtosis for both variables, separately.

In all of our studies to date the most important performance measure has been SD lateral position. The sensitivity of this, or similar, measures

to changes in the driver's physical condition had been repeatedly demonstrated in studies of driver fatigue (see reviews by Harris & Mackie, 1972; Lecret, 1976). To cite one example, 12 normal drivers' mean SD lateral position increased progressively from 18 cm to 26 cm over the course of a 5 h continuous drive around a 56 km highway circuit (Riemersma *et al.*, 1977). Changes of a similar magnitude were observed for subjects in a simulator task after being treated 1h before with either diazepam 7.5 or 15 mg, or secobarbital 75 mg or 150 mg (Ziedman *et al.*, 1979). Finally, the observation of elevated lateral position variability ('weaving') by police was the most frequently cited reason for stopping drivers suspected of alcohol intoxication in a survey by Harris (1980).

Our three experiments completed since the pilot study are summarized in Table 1. All employed the basic procedure described above in 4- or 5-way, double-blind, cross-over experimental designs.

Experiments 1 and 2 employed different but highly comparable samples of female hypnotic drug users. These women had used some hypnotic drug for the relief of insomnia for periods of between 1 week and 8 years, although they had discontinued drug use sometime during a 2-year period prior to the respective studies. Data obtained from the subjects in reply to standard questionnaires indicated that, on the average, they still suffered from sleep disturbances. The purpose of both experiments was to determine whether there are residual effects of various hypnotics in tests administered in the morning (08.00–09.15 h) and in the afternoon (14.00–

Table 1 Summary of Experiments 1–3 with respect to subjects, treatment conditions, times of testing and times since last treatment.

Experiment number	*Subject population*	*n*	*Treatment conditions*	*Time(s) of testing*	*Time(s) since last treatment*	*References*
1	Former hypnotic drug users, female (25–40 years)	24	Flurazepam 30 mg (d.d.), 2 nights	08.00–09.15 h	10.00–11.15 h	O'Hanlon *et al.* (1983)
			Flurazepam 15 mg (d.d.), 2 nights	and	and	
			Secobarbitone 200 mg (d.d.), 2 nights	14.00–15.15 h	16.00–17.15 h	
			Placebo, 2 nights			
2	Former hypnotic drug users, female (25–40 years)	16	Loprazolam 2 mg (d.d.), 2 nights	0.800–09.15 h	10.00–11.15 h	Volkerts *et al.* (1983)
			Loprazolam 1 mg (d.d.), 2 nights	and	and	
			Flunitrazepam 2 mg (d.d.), 2 nights	14.00–15.15 h	16.00–17.15 h	
			Placebo, 2 nights			
3	Healthy volunteers, male (22–32 years)	20	Amitryptiline 25 mg (t.i.d.), 1 day	19.00–20.15 h	01.00–02.15 h	Louwerens *et al.* (1983)
			Doxapine 25 mg (t.i.d.), 1 day	or		
			Mianserin 10 mg (t.i.d.), 1 day	21.00–22.15 h		
			Oxaprotiline 25 mg (t.i.d.), 1 day			
			Placebo (t.i.d.), 1 day			

15.15 h) after two consecutive nights of drug or placebo ingestion (22.00 h).

Experiment 3 employed healthy male volunteers for determining the acute effects of several antidepressants upon driving performance in a single test conducted either from 19.00 h to 20.15 h or 21.00 h to 22.15 h (half of the group during each period). The drugs or placebo were administered in three equal doses over the day, 1, 5 and 9 h prior to the beginning of the tests.

In all experiments, the subjects were licensed drivers who owned and operated their own vehicle for at least 5000 km/year. They were all trained in a 'dress rehearsal' of the test. They were treated in full accordance with the Declaration of Helsinki as amended in Tokyo in 1975. They were aware of the known side-effects of the drugs used in their particular experiment and of suspected effects upon driving performance, in general. They were also advised of the fact that under Dutch law, they and not the accompanying experimenters are primarily responsible for ride safety. Legally, they are not permitted to continue driving while feeling themselves under the influence of a drug to the extent of compromising safety. Their decision to quit under such circumstances was encouraged. They were further told that one of the experimenters (a licensed driving instructor) would intervene, using alternate controls if necessary, in the event that he judged the subject's performance to be deteriorating toward a dangerous level.

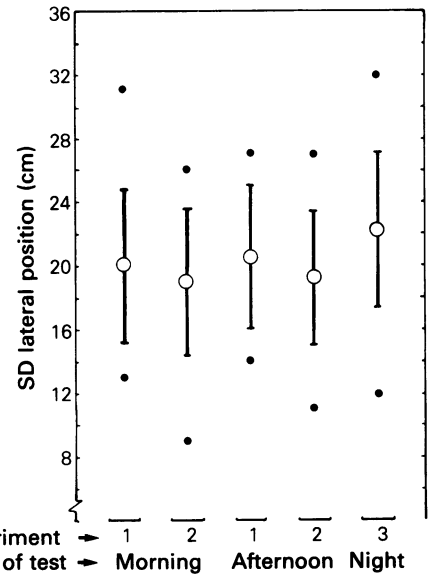

Figure 1 Means, s.d. and extreme scores of SD lateral position as measured in placebo treatment conditions in three separate experiments.

Results

Figure 1 shows the groups' placebo performance levels over the entire tests administered in each of the three experiments. The group average SD lateral position varied little between tests conducted in Experiments 1 and 2 but was slightly higher in Experiment 3. Distributions of individual scores were comparable between tests, and overall, their range extended from 9 cm to 32 cm. This may be considered as the 'normal range' for purposes of evaluating drug effects on SD lateral position.

The reliability of SD lateral position was determined in two ways from results obtained in placebo tests in Experiment 1. First, 'test-retest' reliability was determined from coefficients of correlation between morning and afternoon test scores. Then, 'split-half' reliability was determined from coefficients of correlation between means of SD lateral position obtained by alternate inclusion of data from successive 10 km segments from morning and afternoon tests. That is the first measure in the pair of scores obtained for each subject included all data from even-numbered segments in the morning test and those from the odd-numbered segments in the afternoon test. The second measure included data from the remaining segments. 'Test-retest' reliability was $r = 0.795$; 'split-half' reliability, $r = 0.987$.

Figure 2 shows the group's changes in SD lateral position from respective placebo levels to drug treatment conditions in Experiments 1 and 2. All of the mean changes for both morning and afternoon tests combined were found to be statistically significant when tested by multivariate analysis of variance. Significance levels varied from $P < 0.03$ (LOP 1) to $P < 0.0001$ (FLU 30 and SEC 200). There were significant ($P < 0.05$, or less) treatment condition × time of testing interactions for the following: FLU 30, SEC 200 and LOP 2. Various mean differences were also significant between drug treatment conditions and these are given in the respective reports of Experiments 1 and 2 (O'Hanlon *et al.*, 1983; Volkerts *et al.*, 1983).

Figure 3 shows changes in SD lateral position from the placebo level to drug treatment conditions in Experiment 3. Mean changes were significant in treatment conditions DOX MIA and AM1 ($P < 0.0007$, or less), but not in OXA. The latter produced relatively large changes in both directions for different individuals, indicating perhaps that oxaprotiline can either impair or improve driving performance. In any case, both

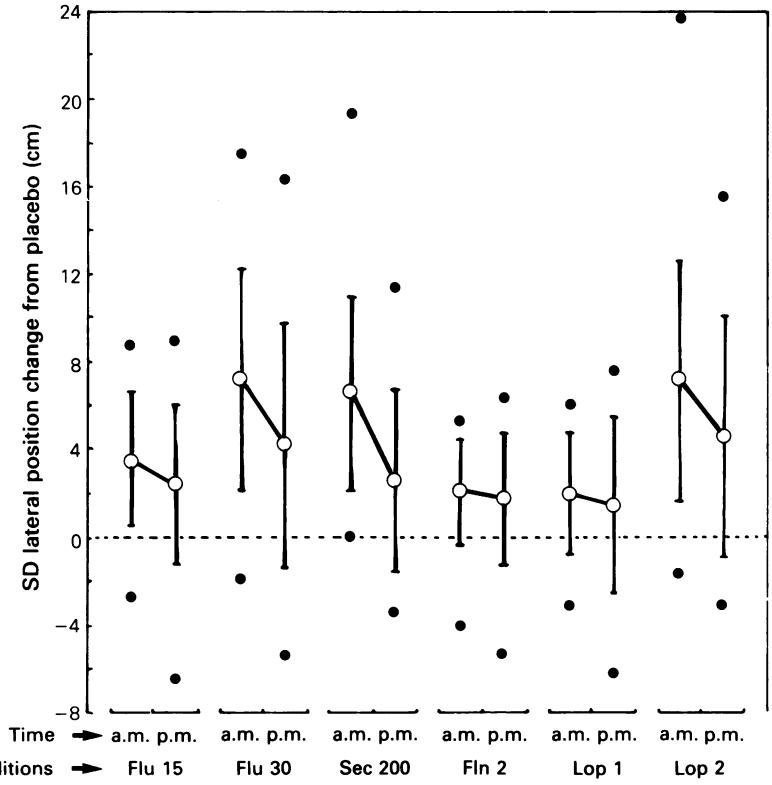

Figure 2 Means, s.d. and extreme scores of changes in SD lateral position from respective placebo levels after 2 consecutive nights of treatment with the following: flurazepam 15 mg and 30 mg, secobarbitone 200 mg, flunitrazepam 2 mg, and loprazolam 1 mg and 2 mg.

the drug's lack of a significant mean effect and its apparent tendency to produce performance changes in both directions were unique in our experience to date.

One consistent negative result in all three experiments was that of no significant correlation between placebo levels of SD lateral position and changes due to the drugs' effects. It is apparently about as likely for normally 'good' drivers to react with a large elevation in SD lateral position as it is for 'bad' drivers.

Group mean levels of SD lateral position over entire tests in the various treatment conditions were related to other signs of impaired driving performance. This is shown in Table 2. Listed there are the treatment conditions in the order of ascending group mean SD lateral position (1–17). Other signs of group impairment are also indicated in terms of the percentages of the subjects showing particular signs. For example, the percentage of subjects having a total test SD lateral position greater than 30 cm in all placebo treatment conditions combined was 7%. Though lower percentages were found in several drug treatment conditions, there was a general tendency for a larger percentage to exceed the criterion the higher the group's mean SD lateral position. Eventually in treatment conditions where SD lateral position was highest (AM), about ⅓ of the respective group members exceeded the criterion value of 30 cm. The Spearman rank-order coefficient of correlations between these variables was rho = 0.74 over all treatment conditions, and rho = 0.92 omitting the anomalous OXA condition.

A more discriminating, but less sensitive sign of group impairment was the percentage of its members driving with a total SD lateral position greater than 40 cm. This only occurred in SEC 200 am, LOP 2 am, FLU 30 am and AM.

Similar results were obtained in comparing groups' total SD lateral position with, respectively, the percentages of members driving with SD lateral positions greater than 40 cm and 50 cm on their worst 10 km segment.

Excursions from the assigned traffic lane in both the right (road shoulder) and left (adjacent lane) directions were also measured in every

Table 2 Summary of performance correlates with group mean SD lateral position (Numbers in table are percentages of respective groups showing particular reactions).

Condition (in rank order by average, total SD lateral position)	n	*Total test SD lateral position*		*Worst 10 km SD lateral position*		*Out of lane*		*Stops*
		>30 cm	*>40 cm*	*>40 cm*	*>50 cm*	*R*	*L*	
1 PLA	60	7	0	3	0	28	17	0
2 OXA	20	20	0	10	0	45	20	10
3 LOP 1, pm	16	6	0	6	0	31	19	0
4 FLN 2, pm	16	0	0	0	0	38	19	0
5 LOP 1, am	16	0	0	0	0	31	19	0
6 FLN 2, am	16	6	0	6	0	13	25	0
7 FLU 15, pm	24	8	0	0	0	54	13	0
8 SEC 200, pm*	22	9	0	9	0	55	0	0
9 FLU 15, am	24	21	0	4	0	63	17	0
10 DOX	20	30	0	20	0	60	35	10
11 FLU 30, pm	24	25	0	17	0	54	29	8
12 LOP 2, pm	16	25	0	13	0	50	25	0
13 MIA	20	30	0	25	0	55	30	10
14 SEC 200, am*	22	32	9	27	9	68	14	0
15 LOP 2, am	16	25	6	19	6	63	38	6
16 FLU 30, am	24	38	8	29	8	71	29	4
17 AMI	20	35	5	35	5	80	35	30
Rank-order (rho) correlations with group-mean SD lateral position	with OXA	0.74	0.75	0.82	0.75	0.85	0.53	0.50
	without OXA	0.92	0.76	0.88	0.76	0.86	0.56	0.70

*Two subjects treated with secobarbitone suffered immediate medical reactions (dizzyness, vertigo, ataxia and nausea) which precluded the administration of driving tests.

experiment. The percentages of subjects who drifted out of lane to the right and left in all placebo treatment conditions were low: 28 and 17, respectively. More and more group members allowed the vehicle to drift onto the road shoulder when their groups' mean SD lateral position rose as a consequence of various drug treatments (rho = 0.85). And, a similar though weaker tendency was shown for in the opposite, more dangerous, direction (rho = 0.53).

Finally, while no subject failed to complete a test in any placebo treatment condition, 16 subjects either voluntarily stopped (10), or were stopped by the experimenter (6), before the completion of a test in the drug treatment conditions. The decision to stop a test was the least reliable correlate of total SD lateral position. Yet the relationship between percentage of subjects stopping and group mean SD lateral position was still rho = 0.50 over all conditions, and rho = 0.70 omitting OXA.

Test validation: SD lateral position and drug plasma concentration

Part of the results obtained in Experiment 2 deserves special consideration as it bears upon the question of whether SD lateral position is truly a valid measure of drug effects. Blood samples were routinely taken following each test's conclusion. These were assayed for the plasma concentrations of the drug administered beforehand. The results of the loprazolam assays are of particular importance since data were obtained from 15 subjects on four occasions (i.e. morning and afternoon following 1 mg and 2 mg loprazolam doses, administered the night before).

Even though individual plasma concentrations were not strongly related to lateral position changes from placebo levels in particular tests (r_s between 0.08 and 0.38), there was an obvious relationship between group mean values of the two variables. This is shown in Figure 4.

Mean SD lateral position change varied as an almost perfect power function of mean plasma loprazolam concentration: the correlation betwen log values of the variables approached unity (r = 0.99).

Discussion

The test described here is relatively new and still in a preliminary stage of development.

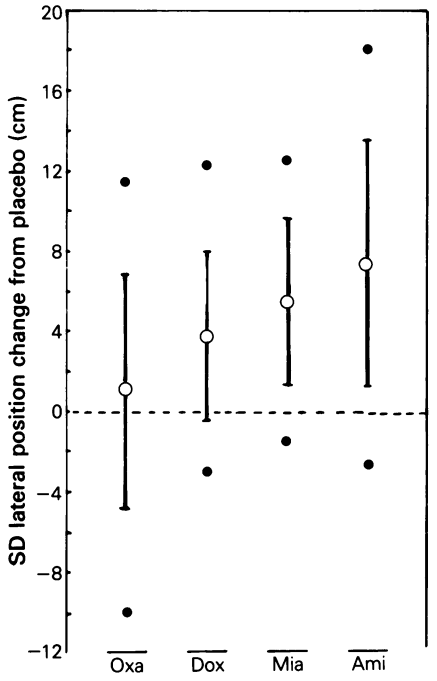

Figure 3 Means, s.d. and extreme scores of changes in SD lateral position from placebo levels after 1 day of treatment with the following: oxaprotiline 25 mg three times daily, doxapine 25 mg three times daily, mianserin 10 mg three times daily and amitryptiline 25 mg three times daily.

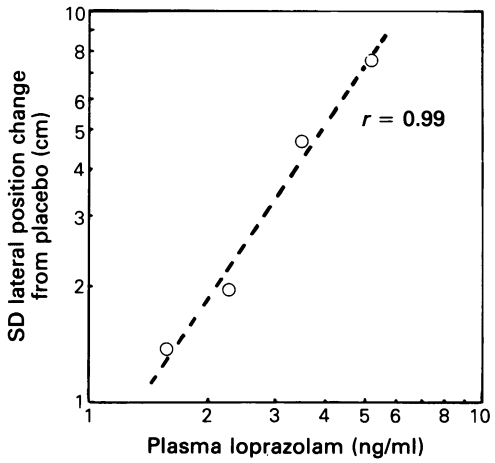

Figure 4 Log mean change in SD lateral position as a function of log mean plasma loprazolam concentration. From top to bottom, values were measured after morning and afternoon tests following treatment with loprazolam 2 mg, and at the same times following treatment with loprazolam 1 mg, on separate days (n = 15).

Psychometric characteristics of the test have yet to be rigorously defined. Yet its application over a series of experiments have met success in every case. Measurements of SD lateral position have discriminated between the effects of practically all of the drugs studied and the placebo, between effects of different drugs in the same study and between those of different doses of the same drug. The sensitivity of the test to drug effects seems therefore amply demonstrated.

In Experiment 1 we were able to clearly show the hazard posed by the residual effects of flurazepam 30 mg and secobarbital 200 mg. We further demonstrated that flurazepam 15 mg also produces a persistent residual effect but that its magnitude is not sufficient to preclude its use by drivers. It may be important to note that the residual effects of the lower flurazepam dose have never been so clearly and systematically defined in previous research, however conducted.

In Experiment 2 we measured a striking difference between the residual effects of 1 mg and 2 mg of loprazolam. The former dose may apparently be taken in complete safety by drivers but the latter, not. Flunitrazepam 2 mg, which has had a relatively bad reputation for producing residual effects had a relatively benign effect in this study. Though the latter result did not meet our expectations based upon the drug's reputation, it did conform with pharmacokinetic comparisons of flunitrazepam with other benzodiazepine hypnotics (Jochemsen, 1983; Pierce & Franklin, 1983). Our results indicate that flunitrazepam's reputation is undeserved and that it should be used by drivers in preference to longer acting hypnotics, such as flurazepam.

In Experiment 3 we found exceedingly large differences in the acute effects of different antidepressants. The classic and widely used antidepressant, amitryptiline, not only produced the largest effect upon SD lateral position of any drug studied to date, it also rendered about ⅓ of the subjects unable to complete the test. This result was in stark contrast to those typically reported from laboratory research. Until now amitryptiline has appeared to be devoid of serious side effects that could impair driving performance, except when taken in combination with ethyl alcohol (see Louwerens *et al.*, 1983). This view must now be sharply questioned on the basis of our more realistic test results.

The new antidepressant, oxaprotiline, was found to have different effects on different subjects. On the whole, it seems relatively safe for drivers' use. However, we did observe both impairment and improvement of driving performance in different individuals under the influ-

ence of oxaprotiline. These results suggest that our test may be used to identify psychoactive drugs which improve driving performance as well as those which impair it.

Perhaps the most promising result to emerge from our studies was the demonstration of a very precise relationship between one benzodiazepine's (loprazolam's) plasma concentration and the degree of performance impairment produced by the drug. If this result can be repeated for other benziodiazepine drugs and/or their active metabolites many benefits should follow. Because the plasma pharmacokinetic profiles of most of these agents are known, it is possible to define what average plasma concentrations would be present in a group of drivers at all times after drug ingestion. Each average concentration would have a predictable average effect upon driving performance. One might set some criterion for acceptable impairment, and by so doing, define the recommended waiting period after drug ingestion before it would again become safe to drive. This information could then be provided to prescribing physicians and the patients themselves by the drug manufacturers. Of course, the relationship between benzodiazepine plasma concentration and performance impairment might change with repeated doses as the result of the development of pharmacological tolerance. If so, it will be necessary to take this factor into account while providing information for drug users.

Future perspectives

The new test represents a major step toward the achievement of a standard test for assessing drug effects upon driving performance. It is too soon to tell whether the results of the test actually predict the potential of drugs for producing overall unsafe driving performance that leads to traffic accidents. Yet there can be little doubt concerning the test's sensitivity to drug effects upon one type of driving performance. In so far as SD lateral position is related to other performance parameters the test will predict overall driving performance impairment. Then, in so far as overall performance impairment is related to unsafe driving behaviour the test also predicts the accident-causing potential of a drug.

The achievement of a drug-sensitive, over-the-road test was the first requirement. Now that is accomplished. Work is under way toward expanding and validating that test as a predictor of unsafe driving behaviour. When this too is accomplished it is not too much to suppose that the licensing of all new psychoactive drugs will incorporate testing along the lines described here.

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