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STUDIES OF CLOBAZAM AND CAR-DRIVING

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1 The methodology used in studies to assess the effects of drugs on car-driving performance is reviewed.
2 Clobazam 20 mg, diazepam 10 mg or placebo were administered daily for 3 d to 24 male students with a high neuroticism score (on the Cattell Personality Factors Questionnaire).
3 Car-driving performance was assessed on the second day in real traffic conditions; tests of attention and concentration and subjective assessments were made on the third day.
4 Diazepam 10 mg significantly impaired braking reaction time in comparison with clobazam 20 mg and placebo ($P<0.01$). Subjects also reported feeling more 'depressed' and lethargic after diazepam.

Introduction

THERE have been many attempts to measure the effects of psychotropic drugs on driving performance. The studies which have been carried out may fall within three categories depending on the methodological approach:
(1) Laboratory studies where psychological tests are used as indicators of car-driving performance.
(2) Laboratory studies with simulators where a car-driving situation is reproduced as realistically as possible.
(3) Field studies using cars in test areas without normal traffic. The variables are either measured by special apparatus and/or recorded by observers in the car. The subjects are sometimes given special tasks, such as parking in a small space, passing between two markers placed close together, manoeuvring, and so on. The time required to complete the task, or the number of attempts made, is used for scoring purposes.

Such methods have already been used in investigations involving clobazam. Ballus-Pascual & Montserrat (1977) investigated the effects of clobazam and diazepam in comparison with placebo on car-driving as a function of neuroticism, and Hindmarch *et al.* (1977) studied the effects of repeated doses of clobazam for 6 d on driving ability.

There are criticisms of each of these three methods, the most important being the validity of the different measures used. What do the variables measured tell us about driving performance in the normal driving situation? And what does a change in one of the variables under the influence of a drug mean with respect to its effects on driving performance?

Even if we knew the answers to these two questions there remains another one: What does a given variation in driver performance mean as far as 'safety' is concerned? This is the crucial concern for patients who take psychotropic drugs.

If studies of the effects of drugs on driving performance were restricted to using only measures which have been shown to correlate highly with actual car-driving performance, almost all parameters used in such studies up to now would be excluded. However, there may be a difference in the validity of a particular test when looked at from an individual's, as compared with a group viewpoint. It is quite probable that a change within an individual, such as an increase in reaction time, would be reflected in that individual's driving performance, whereas it has been shown that inter-individual differences in changes in reaction time do not correlate well with driving performance.

Even when looking at changes within an individual, how they should be interpreted in respect to driving performance is not clear. For example, what does it mean if a subject under the influence of a tranquillizer has the following test results: reaction times are 5 ms longer than usual; the number of completed items in a concentration test is ten more within half-an-hour than usual; mood is rated more calm and passive than usual? Does it mean that the same subject if driving would react too slowly? Would he drive with poor concentration but more calmly and passively? Any such assumptions would be speculative only, even if they seemed to be logical and valid (see Huntley *et al.* (1972), who studied changes in reaction time due to alcohol both in the laboratory and in a driving situation).

Another criticism of all of the three methods mentioned above concerns the motivation of the subjects. In the laboratory and when solving driving problems on a test track, a drug-induced decrease in performance can be compensated for by a higher level of motivation. Drug-induced changes in mood such as euphoria will affect performance in the laboratory less than in the field situation. This factor is especially relevant when considering the validity of studies in

which performance has been assessed but mood changes have not been monitored. This particular aspect of the evaluation of the effects of drugs on driving performance has been discussed by Clayton (1976) and, with special reference to the effects of clobazam, by Hindmarch *et al.* (1977).

Because of the unsatisfactory methodology discussed above, the only fully reliable information on the relationship between the effects of drugs and safety of driving performance has been provided by epidemiological studies. However, the epidemiological approach is not practicable with *new* drugs, and the vast size of such studies, the complexity of drug assay methods and the costs involved have meant that this approach has hardly ever been adopted, even with established drugs.

With these considerations in mind we set out to study the effects of clobazam in comparison with diazepam and placebo on driving performance in the normal situation of the driver in everyday traffic conditions. The main difficulties with such a study were as follows:

(1) legal and ethical problems involved when driving with subjects under the influence of drugs in normal traffic.

(2) control of the experimental conditions: How could they be kept constant?

(3) which variables should be measured?

(4) How could they be measured with sufficient objectivity?

(5) Could these variables be measured reliably and in a reproducible way, that is, independently of the time of observation?

Methods

Twenty-four male students (not psychology students) aged 18–24 yr took part in the study. Subjects were admitted to the study only if, on the Cattell Personality Factors Questionnaire, they had a neuroticism score higher than that which would be recorded for 85% of the general population. This was an attempt to select a group of subjects which would be representative of the patient population which is actually prescribed tranquillizers. Each subject was tested three times and the test was carried out at the same time of day and on the same day of the week on each occasion. Subjects were randomly allocated to treatment with clobazam 20 mg, diazepam 10 mg or placebo.

The drugs were taken each morning for 3 days. On the second day the driving tests were carried out and on the third day laboratory tests, all in double-blind conditions. Assessments in the laboratory were:

(1) the pentobarbital, chlorpromazine and alcohol group variability pattern (Haertzen, 1966) scale (PCAG) (from the Addiction Research Centre Inventory), which is an indicator of subjective tiredness.

(2) a labyrinth test consisting of 10 labyrinths, each of which was projected on to a screen for 30 s (subjects had to follow as many as possible of the nine lines of each labyrinth and write down the number at the end of the line).

(3) The Fleckenstein Rating Scale to provide scores for depression, activation and tension. This scale consists of 33 pairs of bipolar adjectives, separated by eight equal intervals.

(4) The concentration performance test of Düker & Lienert (1959). This is a timed concentration test involving fairly complex mathematical tasks. Three scores are derived: (a) number of correct items; (b) number of incorrect items; (c) percentage of incorrect items.

This battery of four tests and eight variables is comparable to that used in many studies of drug effects on driving ability and assesses concentration, visual performance and subjective mood.

The driving test will now be described in relation to the five problem areas mentioned above.

Legal and ethical problems involved The risks were minimized with the use of a car with dual controls, one of which was operated by a driving instructor. The instructor was the responsible driver in law but the subjects were not aware of this. The 72 tests were carried out without mishap, but the driving instructor had to intervene on two occasions to avoid an accident.

Control of experimental conditions All subjects had to drive in the same car on the same route at the same time of day with the same instructor and observer. Furthermore, each subject served as his own control to minimize the factor of individual driving style as a source of error. The most important factor which could not be controlled was the influence of the weather. Unfortunately, during one week we had an unusual spell of wintry weather with snow, ice and slippery roads. This circumstance certainly increased the total variance of the drivers' performance. However, this influence was distributed equally over the three drug conditions.

Selection of the dependent variables Aside from the practical problem of the ease of measurement of the variables, they were selected from the viewpoint of safety and the adjustment of driving style to traffic flow. Our method was based on that developed by Klebelsberg *et al.* (1968) for observing driving behaviour. The various measures of driving behaviour devised by Klebelsberg *et al.* are designed to facilitate classification into a meaningful system. The following items were marked on nine-point rating scales independently by the two observers:

overtaking: decisive – indecisive

behaviour while waiting at stop sign: patient – impatient

conduct at junctions: careful– careless

resuming a straight line: oversteering – understeering

lateral proximity to overtaken vehicles: wide – close

one-handed driving: frequent – infrequent

readiness to brake: frequent – infrequent
use of rear-view mirror: frequent – infrequent
criticism of others: frequent – infrequent
engaging of clutch: smooth – jerky
anticipation: good – bad
adaptation to engine speed: good – poor
changing gear: dragging – smooth
talking: much – little
posture: relaxed – tense
general impression: good – poor.

In addition, the observers recorded the frequency of:
being overtaken
overtaking
ratio 'being overtaken' to 'overtaking'
dangerous manoeuvres
engine with more than 3500 r.p.m.
turning head
traffic violations.

The car speed was recorded using a graph speedometer which also showed the time taken to complete the driving test. Also noted were:
speed on a bend
average speed in a certain stretch of road
number of times 60 m.p.h. was exceeded.

Acceleration, deceleration and lateral movement were monitored using a 'V-Gerät' (Klinger, West Germany). Altogether, there were 29 variables to measure driving performance.

Objectivity of the measurements This question concerns only those variables which were dependent on subjective ratings. With regard to the observer ratings, from earlier similar studies it is known that two well trained observers show a high level of agreement in their ratings, if the route is sufficiently long and varied to provide adequate opportunity for observation. Each variable was assessed independently by the two observers, who agreed on the final score after discussion.

Reliability of the measurements The fact that the test route was repeated three times means that repeat effects can be filtered out by analysis of variance. Test reliability can be assessed for those items not affected by the drugs. Aside from this, it soon became clear that reliability varied greatly from variable to variable and that it could be improved in future tests by: (a) having a longer practice phase without drugs; (b) increasing the length of the test route; (c) having a third observer to record only frequency and speed; (d) only carrying out the tests in comparable weather conditions. The implementation of these points depends, of course, on the resources available.

Results

Significant drug effects were demonstrated for only 3 of the 37 variables. (Figures 1, 2 and 3). Nevertheless, these effects are consistent. With clobazam, subjects were more ready to brake than with diazepam

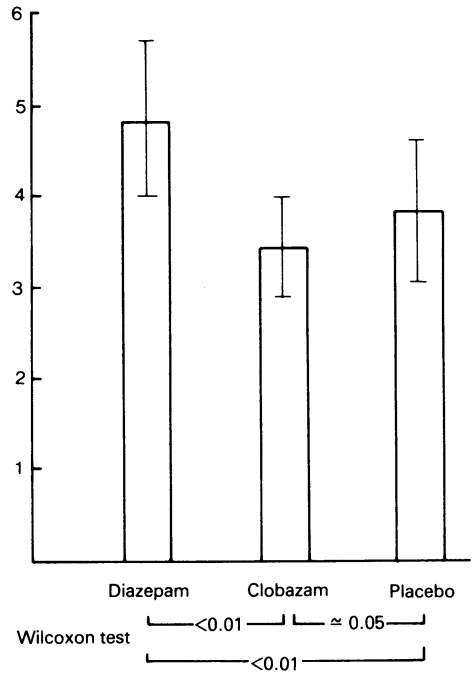

Figure 1 Readiness to brake (scale 1–9; frequent→infrequent).

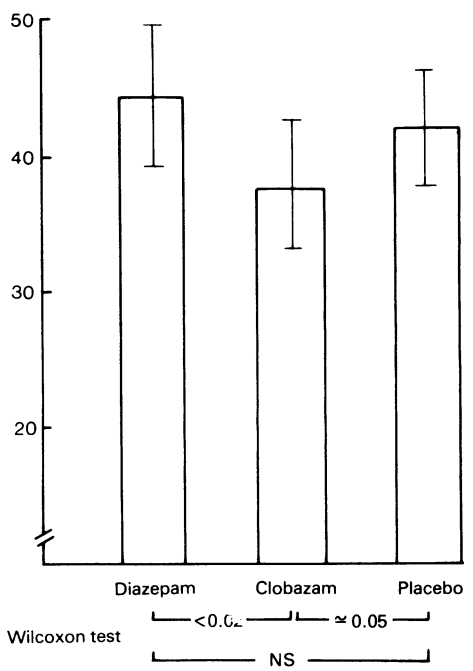

Figure 2 Ratings for depression.

($P<0.01$) or placebo ($P<0.05$). At the same time they subjectively felt more active with clobazam than with

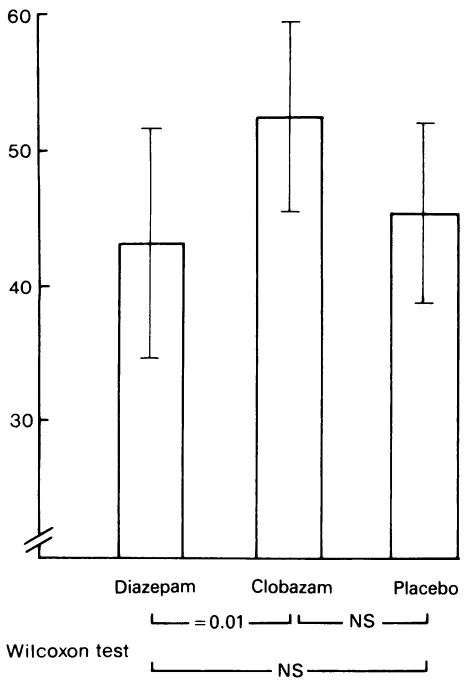

Figure 3 Ratings for activity.

diazepam ($P<0.01$) and their mood was less depressed than with diazepam ($P<0.02$). With diazepam, readiness to brake was impaired compared with both clobazam and placebo ($P<0.01$). The subjects felt more 'depressed' and their activity was reduced in comparison with clobazam. In comparison with placebo, no statistically significant mood changes were observed. Clobazam therefore differed significantly from diazepam in showing less impairment in both subjective feeling (depressed mood, activity) and objective behaviour (readiness to brake).

None of the laboratory tests of performance which have been shown to be sensitive to measures of drug effects was significantly affected by any of the drugs (Table 1). It is therefore not surprising that the tranquillizers only affected one driving test item as these have a much greater degree of inter-individual

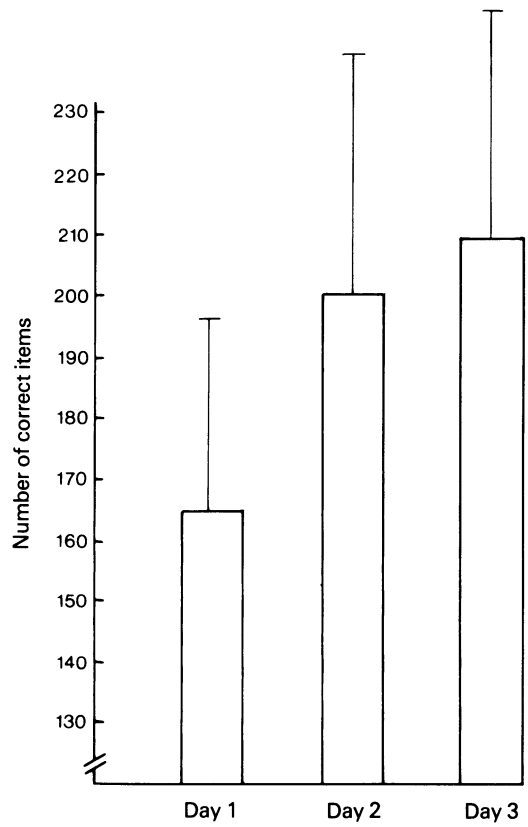

Figure 4 Training effect in the concentration performance test (KLT).

Table 1 Test battery

Overall comparison of drug and time effects in the laboratory performance tests and in three mood variables	*Difference between drugs*		*Difference between weeks 1, 2 and 3*	
	Friedman test		*Friedman test*	
	χ^2	P *(two-tailed)*	χ^2	P *(two-tailed)*
(1) ARCI/PCAG scale (tiredness)	0.44	NS	2.11	NS
(2) Labyrinth test	1.19	NS	12.03	<0.005*
(3) Concentration performance test (KLT) number of correct items	0.19	NS	24.69	<0.001*
(4) number of incorrect items	2.53	NS	3.69	NS
(5) percentage of incorrect items	1.44	NS	4.78	(<0.10)*
(6) Mood-rating depression	4.75	(<0.10)	0.58	NS
(7) Mood-rating tension	0.33	NS	2.33	NS
(8) Mood-rating activation	4.86	(<0.10)	2.53	NS

*All these results show a significant training effect in the course of the three week study period.

variance. The relative reliability of the measurement of these items was reflected in the significant effects shown in repeat measurements. Of the 37 items, there were 13 repeat effects ($P<0.01$), ten being from the driving test and three from the performance tests (for example, Figure 4). Thus, the study did show some drug effects, but the influence of the repetition of the test drive was greater than that of treatment with the two tranquillizers (for example, Table 1).

Conclusions

Subjects with a high neuroticism score were, when driving, less ready to brake after diazepam 10 mg. They felt more depressed and less active. The decrease in reported activity and readiness to brake may be related to the known muscle-relaxant effect of diazepam. The opposite picture was found with clobazam, both in comparison with diazepam and placebo. Clobazam seems to have no detrimental effects on subjects with high neuroticism scores either subjectively or in any of the performance tests. These results certainly require further validation before any general statement can be made. Nevertheless, by comparison with pure laboratory, simulator or test circuit situations, the method used here seems useful in bringing to light any drug effects on car-driving ability.

Translated from the German by Isobel Barnden and David Beattie.

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Discussion

DR J. T. SILVERSTONE (London) congratulated Dr Biehl on his study which had successfully overcome many of the objections to studying the effects of drugs on driving performance in real traffic conditions. The result was a most realistic model for the assessment of drug effects on car-driving ability. He pointed out that Dr Biehl had not covered in detail, in his review of the methodology involved in previous studies of this problem, the epidemiological approach which would perhaps be more relevant to the clinical situation.

It has yet to be established whether or not anxious patients who are prescribed anxiety-reducing drugs suffer more road accidents or drive less well than normal subjects given the same drugs, and this makes the interpretation of the results of volunteer studies in this area difficult.

Some surveys have been reported and one of the earliest took place in Florida, where it was found that patients taking chlordiazepoxide were ten times more likely to be involved in road traffic accidents (RTAs) (Murray, 1960). In a more recent study in Oslo, all patients admitted to hospital following a RTA had blood taken for screening for the presence of diazepam. Blood was also taken from a control group of patients admitted to hospital for other reasons. It was found that RTA victims were much more likely to have taken diazepam than the control group (B*ø et al.*, 1974).

DR BIEHL emphasized that although the subjects in his study were not clinically anxious patients, they had been selected on the basis of high neuroticism scores. He accepted that the validity of the variables which he had monitored was not established, and he would not be prepared to conclude from this evidence alone that, in general, clobazam or other similar drugs do not affect the safety of car driving.

DR P. NICHOLSON (Frankfurt) commented that it is important to ensure that subjects included in such studies have a reasonable standard of car-driving ability, in order for drug effects to be demonstrable.