Whereas alcohol-induced impairment of driving skills and consequent increment in accident risk are generally accepted facts, effects of licit drugs on traffic safety are controversial. There is a dearth of epidemiological data concerning the role of drugs in accidents. Furthermore, a recent collaborative study documented large cross-national differences in the patterns of use of sedative anxiolytics. The dosages, duration of intake, and prevalence of use are highly variable from one country to another (Balter et al., 1983; Table 1). Such differences render it difficult to apply estimates concerning the incidence of accidents associated with the use of these widely-prescribed drugs to other drugs. Moreover, antidepressants and, even, neuroleptics are used in some countries for the treatment of anxious outpatients. Thus, cross-national differences will probably be found once the epidemiological studies concerning the role of these drugs in traffic accidents are conducted.

Currently, benzodiazepines are the only group of prescription drugs whose use has been associated with an increased risk of traffic accidents (Bo et al., 1976; Honkanen et al., 1980; Skegg et al., 1979; Warren et al., 1981). It is not certain, however, whether the benzodiazepines or the disorders for which they have been prescribed are the major contributor to the increased accident risk. In the laboratory, diazepam 10 mg (but not 5 mg) t.i.d. impairs skilled performance of severely anxious patients, who are slower than age- and sex-matched healthy volunteers to learn the tasks (Linnoila et. al., 1983). Doses of diazepam often used for the treatment of anxiety disorders in the U.S.A. (Kahn et. al., 1981) have similar...
deleterious effects on performance of both anxious patients and healthy volunteers (Linnoila et al., 1974; 1983). Anxiety per se does not seem to impair the maximum level of performance; rather, it impairs the rate to achieve that level.

There are 2 trends in U.S.A. which may alter effects of licit psychotropic drugs on traffic safety: 1) The number of prescriptions written for antidepressants has increased tremendously while the number of prescriptions for the traditional 1, 4-benzodiazepines, such as diazepam, has decreased slightly (Mellinger & Balter, 1981). Because of the increased risk of traffic accidents associated with the use of diazepam (Honkanen et. al., 1980; Skegg et. al., 1979; Warren et. al., 1981) a switch from anxiolytics to antidepressants for the treatment of anxiety disorders could be beneficial to traffic safety. Recent research has revealed that antidepressants demonstrate superior long-term therapeutic effect to benzodiazepines in many anxiety disorders (Johnstone et. al., 1980; Kahn et. al., 1981). Thus, a switch from benzodiazepines to antidepressants in the treatment of anxiety is also medically indicated. 2) A new class of antidepressants, relatively specific serotonin reuptake inhibitors, will soon be marketed in several countries. Zimelidine, a member of this new class of antidepressants, has been investigated in our laboratory. We have found that it is remarkably free of effects resulting in impairment of skilled performance. Zimelidine has, however, been withdrawn from human use because it caused dangerous allergic reactions in some patients. If other drugs of this class do produce as little impairment of skilled performance as zimelidine their use, instead of the tertiary amine tricyclic antidepressants, could improve to traffic safety. Because of their general lack of toxicity, they would also be a significant advance in the treatment of depression.

New anxiolytics, which do not have antidepressant potency, are also being developed. Agents, such as buspirone, may prove to be less of a safety hazard than some of the traditional benzodiazepines. To complicate the outlook, new benzodiazepine derivatives which have antianxiety, antipanic, and some antidepressant potency, will soon be introduced. The first of these drugs, alprazolam, is already available. The introduction of these drugs will undoubtedly be beneficial for the treatment of psychiatric patients, but there is a lack of knowledge concerning the effects of these new substances on skilled performance. Yet, the cost of studies to gain such knowledge is a minuscule proportion of the development cost of a new medication for human use in the U.S.A. (less than 0.1%). The results of such studies can be used to rank
order potential traffic and occupational safety risks produced by various antidepressants and anxiolytics. Because these drugs are used very commonly by out-patients, such a ranking, used as a basis for regulating drug use and driving, could contribute to improved public health by reducing the number of traffic accidents. To exemplify the potential increase in safety provided by the new drugs, we will review 2 studies comparing effects of buspirone (an anxiolytic) and zimelidine (an antidepressant) with commonly prescribed standard drugs on skilled performance of healthy volunteers.

**BUSPIRONE VS DIAZEPAM**

Two groups of healthy male volunteers, each containing 12 subjects, participated in the double-blind, cross-over, split-plot design experiment. One group received single doses of buspirone (10 and 20 mg) as well as of diazepam (10 mg) with placebo drinks. The other group received ethanol (0.8 g/kg body weight) with the drugs. A battery of psychomotor tests was administered to the subjects (Erwin et al., 1978; Erwin et al., in press; Linnoila et al., 1978) to assess their brain functioning, mood, and performance. The first battery of tests was completed prior to administration of drugs which was followed by administration of drinks. The tests were then repeated between 2 and 3 hours and between 4 and 5 hours after the drug ingestion.

Diazepam and alcohol impaired standing steadiness on the first and second test (Fig. 1 and 2). Moreover, the high dose of buspirone had an additive deleterious interaction with alcohol on body sway on the first test. Tracking was impaired by diazepam, and diazepam and alcohol had a synergistic deleterious interaction on tracking at the second test (Fig. 3 and 4). Tracking was not adversely affected by buspirone. Diazepam also impaired divided attention performance (Fig. 5), but buspirone was free of such a deleterious effect. Both buspirone and diazepam impaired performance in the vigilance task (Fig. 6).

Thus, single doses of 10 or 20 mg buspirone (similar to those intended to be used for the treatment of anxious patients) seem to have similar sedative potency to 10 mg of diazepam (as indicated by the impairment of vigilance), but they impair divided attention less than diazepam. Furthermore, buspirone has a milder interaction with alcohol than diazepam. Therefore, it should offer a safety advantage over diazepam in out-patients operating motor vehicles.
ZIMELIDINE VS AMITRIPTYLINE

Single 200-mg doses of zimelidine were compared with 50 mg doses of amitriptyline, with and without alcohol (0.8g/kg), in 12 healthy male volunteers. Zimelidine was devoid of adverse effects on performance and did not show additive effects with alcohol, whereas amitriptyline impaired performance and had additive deleterious effects with alcohol (Fig. 7 and 8). Zimelidine has been withdrawn from the market because of dangerous hypersensitivity reactions. If other serotonin inhibitors exhibit zimelidine's lack of adverse effects on skilled performance they may become the drugs of choice, from a traffic safety point of view, for treatment of depressed out-patients.

CONCLUSION

Alcohol is clearly a major problem for road traffic safety, whereas the effect of licit psychotropic drugs is uncertain. Laboratory studies demonstrate, however, that many commonly prescribed psychotropics impair skilled performance of anxious and depressed patients as well as healthy volunteers. New anxiolytic and antidepressant drugs with only minor adverse effects on skilled performance and very mild interactions with alcohol have recently been developed. These drugs, if effective in the intended indications, may improve safe operation of motor vehicles by anxious and/or depressed out-patients.

REFERENCES


Figure 1. Change from the predrug baseline in total body sway, expressed in arbitrary units. Run 1 at 1 hour and Run 2 at 3 hours after drug administration. Comparisons with placebo; Student's t test, 2-tailed probability.

Figure 2. Body sway after the administration of alcohol. Alcohol had a significant main effect in the ANOVA; p less than .01.
Figure 3. Cumulative RMS error in the 2-minute tracking task. Diazepam had a significant effect during the second test time; $p$ less than .01, Student's $t$ test, 2-tailed probability.

Figure 4. Cumulative RMS error after the administration of alcohol. Alcohol had a significant effect in the ANOVA; $p$ less than .01. Diazepam and alcohol had a more deleterious effect than alcohol alone during the second test time; Student's $t$ test, $p$ less than .01.
Figure 5. Combined score (RMS error x incorrect responses) in the divided attention task. Diazepam had a significant deleterious effect during both times; Student's t test; \( p < 0.01 \).

Figure 6. Number of correct responses in the 30-minute vigilance test. Both buspirone and diazepam impaired performance compared to placebo during the first test time; Student's t test; \( p < 0.05 \) for buspirone 10mg and \( p < 0.001 \) for buspirone 20mg and diazepam 10mg.
Figure 7. Effects of single doses of amitriptyline (AMI), desipramine (DMI), and zimelidine (ZMI) alone and in combination with alcohol on body balance. Time indicated is after ingesting the drugs.
Figure 8. Effects of single doses of amitriptyline (AMI), desipramine (DMI), and zimelidine (ZMI) alone and in combination with alcohol on tracking.
TO PUNISH AND/OR TO TREAT THE DRIVER UNDER THE INFLUENCE OF ALCOHOL AND/OR OTHER DRUGS

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SYNOPSIS

This is a review of the reported incidences of driving under the influence (DWI) of alcohol and the efforts to rehabilitate drivers, in various countries. The reports from Europe have been accentuated because the language barriers have made the methods employed in Europe unknown to the scientists in the other, mainly English-speaking countries.

The basic problem is not the question of punishment vs treatment. If we accept the proposition that punishment is basic for crime prevention, we acknowledge that punishment is a prerequisite for the prevention of unsafe driving. The coordination of punishment with rehabilitation is the main issue in our efforts to make transportation safe.

The epidemiological data about driving under the influence (DWI) of alcohol in various countries give the impression that a certain percentage of drivers on the roads are driving under the influence, despite all efforts of the authorities--jail, fines, suspension of driving privileges--to keep the drivers involved "off the roads." Take, as examples, the figures from Sweden, Australia (Victoria), and the Federal Republic of Germany (FRG):

In Sweden, of approximately 3.5 million licensed drivers, about 18,000 each year are convicted for driving with illegal blood alcohol concentrations (above 0.5 permill or 0.05%).

In the State of Victoria (Australia), each year approximately 14,000 drivers are convicted for drinking-and-driving, from a total population of 2 million drivers.

In the FRG, the number is about 120,000 drivers convicted for drinking and driving with illegal blood alcohol levels, each year.

From the roadside surveys in various countries, we can state the results in a more positive way: a high proportion

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