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LABORATORY INVESTIGATION OF EFFECT OF ACUTE DOSES OF NOMIFENSINE ON A SIMULATED ASPECT OF NIGHT-TIME CAR DRIVING PERFORMANCE

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1 Six healthy volunteers received single doses of either nomifensine 100 mg, nomifensine 50 mg or placebo at weekly intervals in a randomized double-blind crossover study.

2 Subjects were subjected to a simulated test of car driving at night.

3 Testing lasted about 1.5 h and consisted of measuring responses to light stimuli, a modification of a test designed by Baker & Theologus (1972).

4 Nomifensine 100 mg reduced the latency of response significantly when compared with placebo ($P<0.05$). Nomifensine 50 mg had no significant effect.

5 It was concluded that nomifensine was unlikely to impair night driving performance.

Introduction

Numerous reports in the literature (Milner, 1972) have indicated that acute doses of psychoactive compounds cause a significant impairment of various psychomotor functions and skills, including those important in driving a motor vehicle. Recent studies have shown (Pentillä *et al.*, 1975) that the pronounced side-effects of certain psychotropics are instrumental in disturbing coordination and sensory processing of information.

It has long been established that imipramine, and related tricyclic antidepressants, produce marked atropine-like side-effects of nausea, blurred vision and fatigue (Grunthal, 1958), and Kibrick & Smart (1970) have shown such drugs to severely impair car driving performance in certain individuals.

There are certain legal and ethical objections to investigating the effects of acute doses of psychoactive substances in actual car driving situations but it is possible to simulate certain aspects of car driving skill in the laboratory and then extrapolate these findings to the real life situation. As Betts *et al.*(1972) have indicated, however, there are problems in extrapolating results from laboratory studies to real life driving situations.

This study reports an investigation into an aspect of car driving performance which is difficult to monitor in the real life driving situation, that is, a sustained night driving task.

Methods

The night driving task was adapted from that used by Baker & Theologus (1972) in their studies on the effects of caffeine on visual monitoring.

Apparatus

The apparatus consisted of two five-eighth inch diameter red bulbs mounted horizontally on a matt black display board placed vertical to the subject's line of sight some four yards in front of him. Small electric motors enabled the lights to be brought together or moved apart along the horizontal axis. This apparatus was installed in a dark room free from reflective surfaces and objects. Subjects viewed the display board down a screened tunnel and received white noise through headphones during the experiment to mask the electric motor and other extraneous noise. Electronic timers recorded the time which elapsed between the horizontal movement of the stimulus lights and the subject noticing the movement and responding by pressing a hand-held toggle switch. The geometry of the viewing conditions corresponds to a driving situation in which one vehicle follows 60 yards behind another. The rate at which the stimulus lights separate is equivalent to what the driver of the following vehicle would perceive, with respect to the tail lights of the lead vehicle, should he close on the lead vehicle at approximately 0.92 m.p.h.

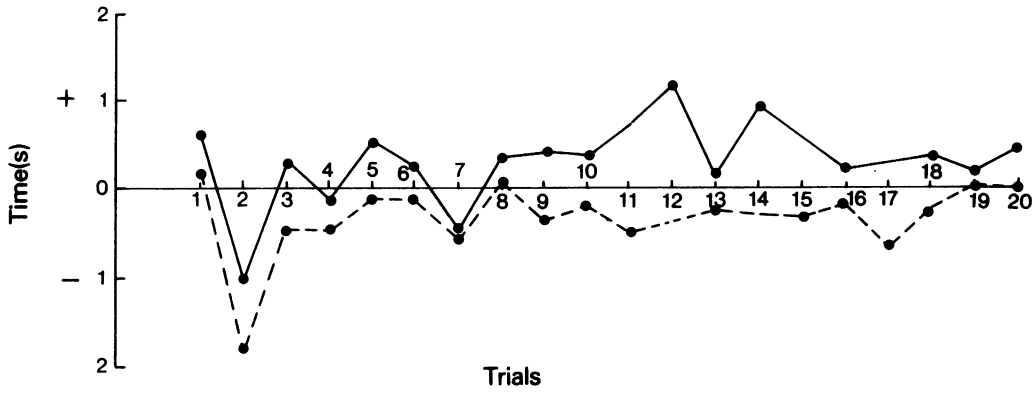

Figure 1 Mean response latency changes with respect to placebo produced by an acute dose of nomifensine 50mg—or 100 mg (. . . . . .).

Testing

Subjects were seated and connected to the headphones, and allowed a half-hour to dark adapt. Experimental instructions, through the headphones, told them to press the response switch when they noticed any horizontal displacement of the two red lights. The lights were initially separated by 6 inches, and at random intervals from 90 to 210 s they were made to move apart at a rate of 12.65 inches/min until the subject stopped the procedure by pressing the toggle switch. The lights then returned to their starting separation of 6 inches and the process began again. Each testing session lasted until 20 trials had been completed (approximately 1.5 hours).

Measures

Each response time, that is, the time between the onset of the horizontal movement of the lights and the subject indicating the detection of the same, for the 20 trials was averaged and the mean response latency recorded as the response measure.

Medication

Three treatment conditions were used: nomifensine 100 mg, nomifensine 50 mg and matching placebo. An hour before dark adaptation subjects received one of the three treatments, presented as four identical capsules: 4 x 25 mg nomifensine, 2 x 25 mg nomifensine + 2 x 25 mg placebo, or 4 x 25 mg placebo.

Design

The six consenting volunteers had a mean age of 27.5 yr (3 male, 3 female) and all received treatment with each of the medications, the order of presentation being balanced to avoid order effects. Testing took place at weekly intervals with the medications being taken between 1700 and 1800 hours.

Results

The mean changes produced in response latency by nomifensine 50 mg and 100 mg when compared with placebo are presented in Figure 1. Since the present sample population totalled six individuals, a non-parametric analysis of variance was carried out on the raw data for the three treatment conditions (Siegal, 1956). The Friedman two-way analysis of variance gave an Xr^1—7 and thus a probability of obtaining such results, P —0.029. A Wilcoxon matched pairs signed ranks test was then used to compare each active condition with placebo. The changes produced by nomifensine 50 mg when compared with placebo were not significant, but the response latency was significantly reduced, compared with placebo, following an acute dose of nomifensine 100 mg ($P<$ 0.05, two tailed).

Discussion

A preliminary (unpublished) acute dose study with nomifensine 50 mg and the continuous performance task showed the drug to possess a small degree of centrally stimulating activity, since the frequency of task errors attributable to 'commission' increased following medication with nomifensine. Mirsky *et al.* (1959) and Kornetsky (1972) have argued that the continuous performance task is a sensitive indicator of drugs having action on cortical or subcortical centres controlling arousal. Central activity due to the

administration of nomifensine has been reported (Hoffman, 1973) following laboratory studies with the drug, and further confirmation of its central action is to be found in the results of this present study.

The simulated night driving task used here is essentially a long-term visual monitoring task in which the stimulus configuration lacks any short-term novelty, thus fulfilling criterion for being a 'boring' task without any intrinsic satisfaction (Berlyne, 1960). In 'boring' conditions, there is a tendency for the overall level of central arousal to fall, resulting in a reduction of the accuracy of psychomotor performance (Parrott & Hindmarch, 1975). The real-life corollary of this present situation is a night-time driving situation in which lapses in attention or reduced arousal level could precipitate an accident.

It can be seen from Figure 1 that an acute dose of nomifensine 50 mg, when compared with placebo, produces no significant effect on the response latencies for detection of change in the visual array. Following treatment with nomifensine 100 mg there is a reduction in response latency which reaches significance when compared with placebo values ($P < 0.05$). This later finding implies that although there may not be incontrovertible evidence that nomifensine 100 mg improves long-term visual monitoring performance there is no evidence that performance of the task is impared.

In any long-term visual monitoring task there sometimes occurs a phenomenon known as a 'response block', a severe lapse of attention in which the subject does not notice the lights separate and has to be reminded to press his switch when the lights have reached their extreme positions (Baker & Theologus, 1972). There was only one instance of a response block noted in this experiment (for subject 6 with nomifensine 50 mg) but the relatively short duration of the testing session would have kept the frequency of such events low. An interesting extension to this study would involve subjects in the task situation for several hours to investigate the effects of nomifensine on the frequency of occurrence of response blocks.

Conclusions

In a simulated aspect of night driving, acute doses of nomifensine did not impair the latency with which subjects could recognise a small change in the visual array. An acute dose of nomifensine 100 mg produced a significant improvement in the response measure when compared with placebo, and it is concluded that similar dose levels will not be detrimental to night-time driving or other tasks involving visual monitoring.

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Discussion

DR OSWALD emphasized the importance of the age of the subjects in sleep studies. Although young people slept well, had little scope to improve, and were less sensitive to circumstances which could impair sleep, people in later life, possessed more scope for improvement and were sensitive to drugs like caffeine which could make sleep worse.

DR HINDMARCH (Leeds) said that his subjects were aged between 20 and 40 yr, with a mean age around 35 - 40 yr.

PROFESSOR TURNER, enlarging on Dr Oswald's important point, suggested that a positive internal control drug was insufficiently often used in normal