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THE INTERACTION BETWEEN ALCOHOL AND MARIJUANA

A Dose Dependent Study of the Effects on Human Moods and Performance Skills

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A DOSE DEPENDENT STUDY OF THE EFFECTS ON HUMAN MOODS AND PERFORMANCE SKILLS

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EXECUTIVE SUMMARY

1. A study was designed to examine the effects of marijuana and alcohol when taken alone and in combination on human skills performance and mood.

2. Four dosage conditions were employed for each drug (placebo and three active doses). All possible combinations of these dosage conditions were tested (ie 16 dosage groups).

3. Twenty subjects were used for each dosage group, the experiment employing 320 subjects in all. Each subject attended the laboratory on one occasion only.

4. Data collected were for psychomotor performance using a battery of computer-presented tests, mood effects, subjective assessments of the nature and degree of intoxication, and the subjective assessment of the effects of the drugs on driving skills and willingness to drive a motor vehicle.

5. The performance battery included tests of human skills related to those considered necessary to drive a motor vehicle with safety.

6. The population sample were recruited by advertisments on two Sydney "Rock music" FM radio stations. All volunteers were non-naive as regards marijuana use and were indeed heavy to very heavy users of this drug. The extent of alcohol use by the volunteers was considered to be within the normal range of use of this drug within the community.

7. The attitudes expressed concerning the dangers associated with the use of the two drugs indicated that the population sample was heavily biased against alcohol and in favour of marijuana.

8. The subjective assessment of the doses of each drug employed indicated that they were comparable. The subjects assessed the degree of intoxication by marijuana as being of a similar intensity as that produced by alcohol. The doses selected therefore appear to be relevant to those used within the social experience of the volunteer population.

9. Both drugs produced significant dose-dependent effects on the performance measures, on the intoxication rating scales and on some of the mood measures.

10. However, there were both quantitative and qualitative differences between these effects, both on the performance measures and on the subjective mood effects of the two drugs.

11. By far the major effects on these tests were those produced by alcohol.

12. The effect on skills performance of alcohol and marijuana when taken in combination was essentially one of addition. Marijuana tended to increase the intensity of the performance impairment produced by alcohol. However, there was evidence to suggest that the lowest dose of marijuana produced a degree of antagonism of the effects of alcohol.

13. Marijuana had no effect on the absorption or metabolism of alcohol. The blood alcohol concentration was not affected by any of the doses of marijuana used.

14. The results of this study indicate clearly that alcohol and marijuana are distinctly different drugs. The effects produced on the performance measures were qualitatively and quantitatively different. In addition, the differences in the nature of the drug-induced subjective intoxication and the self-reported changes in mood effects such as anxiety and alertness, strongly suggested different drug actions.

14. The ability to discriminate and assess the degree of intoxication with alcohol was not affected by marijuana. However, the ability to assess the intoxication due to marijuana was greatly affected by alcohol. The subjective intoxication produced by marijuana appears to be of a more subtle nature than that produced by alcohol.

15. Evidence is presented which suggests that under the influence of alcohol, subjects engage in a "speed-accuracy trade-off". They are prepared to make a hasty response to a question rather than to spend more time to ensure a correct answer. This effect could be related to a risk-taking behaviour. The results with marijuana on the other hand suggested a slower and more careful approach to the problem, though, as with alcohol, an increased error rate in responses was recorded.

16. Evidence is presented which suggests that marijuana produces periodic attentional lapses.

17. The results strongly suggest that the performance deficits and mood changes produced by alcohol are of a greater magnitude than those produced by marijuana.

18. Recommendations for directions of further research are made.

RECOMMENDATIONS

1. Further studies should be conducted to clarify the differences between the effects of alcohol and marijuana. The present study indicates that they are drugs with quite different modes of action. Studies should be designed to elucidate differences in their action on various performance skills. In addition, studies should be undertaken to clarify the differences between the effects produced on mood states.

2. Alcohol and drug involvement in road crashes not only involves effects on skills performance but also on mood and motivational changes such as the willingness to take a risk. Evidence presented in this study as well as in others strongly suggests that a difference exists in the changes in mood effects and risk-taking behaviour produced by alcohol and by marijuana.

It is strongly recommended that studies of the effects of each drug on performance tests designed to measure risk-taking behaviour should be undertaken. The correlation of these drug effects with measures of personality and other individual differences should be sought.

3. The differences between the two drugs on specific measures such as attention and tasks requiring a division of attention should be further clarified.

4. Further studies are required to elucidate the influence of the marijuana-induced postural hypotension on tasks which require the subject to stand still for a period of time.

It is suggested that the use of marijuana by a worker who is engaged in an activity which requires him/her to stand still might increase the risk of an accident by causing dizziness and fainting. An investigation should be undertaken to determine if any correlation exists between marijuana use and industrial accidents of this type.

5. Evidence provided by this study and by others indicate that alcohol is the drug of major concern for traffic safety. Alcohol not only impairs performance skills, it also impairs the drivers awareness of the extent of this impairment. Indeed, the changes in mood produced by alcohol appear to be in the direction of increased confidence and an increase in the willingness to take a risk.

Further research must undoubtedly be undertaken with drugs other than alcohol for a further understanding of their role in road crashes. However, any reduction in the concentrated attention to the role of alcohol on the road, both by educational means and law-enforcement measures would be seriously counterproductive.

INTRODUCTION

The role of alcohol in road crashes has received considerable study over the last twenty years. As a result of these studies it has now been concluded that alcohol plays a contributory role in a significant proportion of road crashes and legislative approaches have been made in many countries in an attempt to reduce the incidence of alcohol-related crashes. The evidence which has led to these conclusions and upon which the drink-driving legislation is based has been derived from studies in a number of scientific disciplines. These include the sciences of pharmacology, psychopharmacology and epidemiology. From the science of pharmacology is derived the information that alcohol is a depressant of the function of the central nervous system and is a drug which would be expected to interfere with driving skills. Pharmacological studies have also described the manner of the absorption, distribution, metabolism and excretion of alcohol. From this information, the ability to measure the blood alcohol concentration by determining the concentration of alcohol in a breath sample has been derived. Psychopharmacological studies have described the nature of the effects of alcohol on human skills performance as well as the correlation between the blood alcohol concentration and the extent of the impairment of those skills (Perrine, 1973; Moskowitz and Austin, 1979). Epidemiological studies have indicated the proportion of road crashes which are alcohol-involved and have provided evidence

that the probability of a driver being involved in a road crash increases with increasing concentrations of alcohol in the bloodstream (Borkenstein et al 1964; Perrine et al 1971; Farris, 1977 ; McLean et al 1980).

In recent years concern has been expressed for the possible role of drugs other than alcohol in road crashes. Attempts have been made to determine the possible role of other drugs, including marijuana, in road crashes by using similar techniques to those described for alcohol. For a number of reasons, predominantly pharmacological, the task facing the researchers in this area is much more difficult than that encountered with alcohol (see Chesher, 1985). Epidemiological studies have been undertaken, but for methodological reasons have not included a control group as was the case with the alcohol studies. For this reason the data obtained are very difficult to interpret. An attempt at a control group has been made by the Canadian investigators, Cimbura et al (1980), who compared the incidence of drugs in blood samples of dead drivers who were considered to be at fault in the crash with the incidence of drugs in those drivers not considered to be at fault. This ratio (a culpability index) suggested an increased incidence of the presence of drugs in the "at fault" group. Marijuana was one of the drugs falling into the category with an increased culpability index. This technique is obviously dependent upon the accuracy of the assessment of the "at fault" driver.

In another extensive study of drivers killed in single

vehicle crashes, Mason and McBay (1984) have indicated that whilst they detected marijuana in the blood of these drivers, this drug seldom is found alone. In most cases marijuana is found together with alcohol and the concentration of alcohol is such that of itself is sufficient to account for its involvement in the crash. Other studies have confirmed the findings of multiple drug use and it is difficult to gain acceptible evidence for the role of any one drug as a causative factor in road crashes. A review of the evidence for the involvement of drugs other than alcohol in road crashes has been presented by Hendtlass (1985).

In view of the methodological difficulties encountered in the epidemiological approach, more emphasis therefore must be placed on studies of the effects of drugs on human skills performance in an attempt to understand the possible role of these substances in road crashes.

Marijuana, alcohol and driving.

Alcohol and caffeine are undoubtedly the most widely used of the social drugs in Western cultures. It is also clear that the illicit drug, marijuana is very widely used in the same populations, especially amongst the 18 to 30 year age groups. That alcohol is capable of producing an impairment of human driving skills performance is widely known. Studies of the effects of marijuana, taken by mouth or by smoking also indicate

quite clearly that this drug is also capable of impairing performance on a number of human skills. (for reviews see Austin & Moskowitz, 1979; Siemens,1980; Klonoff,1983). What is not clear however, is whether the use of marijuana is likely to present an equal, greater or lesser danger on the road than does alcohol. Furthermore, it is becoming increasingly apparent that both drugs are frequently being consumed in combination (Fishburne et al 1980; Johnstone et al 1980). It is of obvious importance therefore that the possible interactions between these drugs be fully understood.

A report from the Institute of Medicine, Washington D.C. U.S.A. '1982) concluded:-

"The issue of alcohol-marijuana interaction is an important one but currently few data are available. Clearly, more studies of marijuana interactions with alcohol and other commonly used drugs are needed".

The present study was designed to throw some light on this problem.

THE PRESENT STUDY

The purpose of this investigation was to examine the dose-response relationship, on a battery of tests of human mood, psychomotor and cognitive functions, of smoked marijuana and of orally administered alcohol, each drug given alone or in combination. The dose of marijuana is determined as the concentration of the main active constituent, tetrahydrocannabinol, in the material provided for smoking.

All tests were chosen to test skills related to those necessary for driving a motor vehicle. The marijuana was administered during the rising phase of the blood alcohol curve so that the testing time coincided with the peak of the effect of both drugs.

Four dosage conditions of each drug were employed and the experimental design presented sixteen experimental groups such that all of the possible combinations of drug dosages were tested. Twenty subjects were used for each dosage condition, there being three hundred and twenty subjects for the study. The design is illustrated in Table 1.

TABLE 1

THE DOSAGE GROUPS

ALCOHOL	THC: 0	THC: L	THC: M	THC: H
0	1	2	3	4
L	5	6	7	8
M	9	10	11	12
H	13	14	15	16

Note: 0 = placebo; L = low dose; M = medium dose; H = high dose

This experimental design provides the ability to obtain an answer to the following questions:

(i) Is the drug exerting an effect on skills performance or on the subjects mood states?

(ii) What is the effect of one drug upon the other?

(iii) What is the nature of the interaction between these two drugs?

(iv) Are the effects produced by alcohol greater or less than those produced by marijuana?

THE EFFECTS OF ALCOHOL AND MARIJUANA TAKEN TOGETHER:

The present status of knowledge.

In view of the widespread social use of both of these drugs and the knowledge that they are often used in combination, there have been surprisingly few studies to examine their interactive effects. In an extensive literature search only fourteen published reports were found in which both drugs were given in combination. Of these, eight involved tests of human skills on laboratory-based tests and six examined the effects of the drug combination on a driving task either in a real vehicle on a closed course driving circuit or in a driving simulator. A seventh study involving closed course driving has been undertaken in Canada, but no data are yet available.

The studies were carried out in different laboratories involving different conditions of set and setting as well as different methodology, tests and testing times in relation to drug consumption. For these reasons it is difficult to make a direct comparison and an overview of all of the results. More research is obviously necessary before a clear picture can be assessed.

Studies involving on-course driving.

The task of driving a motor vehicle is a complex combination of abilities and motivations which has so far defied those attempting to create a definitive and all-embracing model with which to work. Of the driving experiments reported to date which have studied the effect of alcohol and marijuana taken together, this lack of a suitable model has led to many different approaches and each study has its own particular emphasis. Naatanen and Summala (1976) and Casswell (1977) have emphasised their views that the behaviour of drivers involves two different classes of behaviour. The first being the guidance of the vehicle after procedures of search, identification and prediction of environmental events. The other behaviour concerns the motivation of the driver with the emphasis on the principle that driving is essentially a self-paced task. As well as the skills performance requirements associated with the first behaviour described above, driving also involves the driver in decision making with regard to the perceived risk and the amount of risk or emotional tension the driver is prepared to tolerate when controlling the vehicle. Drugs are likely to affect performance, perhaps even selectively, on these two behaviours. Most studies have addressed themselves primarily to the first of these behaviours. Casswell (1977) designed a study to examine both of these behaviours.

A closed circuit driving course was set up by Casswell

(1977) with a wide variety of driving situations, including a section of the track where the driver was required to perform an overtaking manoeuvre. The task required the driver to overtake at the last acceptable moment so as to return to the correct lane (the left side of the road in New Zealand) at a given point. The drivers received instructions via road signs and through headphones. Brake pedal, accelerator, steering movements and speed were all monitored. Volunteers were required to complete eight circuits of the course, a task which took approximately 35 minutes. Thirteen subjects were used in a within-subjects design. On each of six occasions, subjects received a drink (alcohol or placebo) and leaf material to smoke (active marijuana or placebo). The only drug combination condition studied consisted of alcohol sufficient to produce a BAC peak of 0.05g% and marijuana containing 3.12 mg THC. The other conditions were alcohol (BAC 0.1g%) plus placebo marijuana, alcohol placebo with marijuana containing 6.25mg THC, or the double placebo. The results indicated a large between-subject variability, an effect which Casswell considered might be due to individual differences in the drivers' perception or tolerance of risk and the interaction of these variables with the drugs given. Alcohol produced an increase in speed and an impairment of steering control. Marijuana alone reduced driving speed and also slowed response time to the orders given over the headphones. The drug combination tended to increase driving speed, impair steering control and to increase response times to the auditory

instructions. Casswell has suggested that under the influence of marijuana alone, drivers appeared to be aware of the adverse effects of the drugs on their driving skills and tended to compensate for these effects by reducing driving speed and maintaining control effort. In contrast, under the influence of alcohol alone, subjects appeared to behave in a more risky manner.

Sutton (1983) reported the results of an on-course driving study involving 9 students in a within-subject design using alcohol (BAC 0.06g%) or alcohol placebo and marijuana (amount unspecified, but described as 2% THC, which probably supplied 12.5mg THC) or marijuana placebo. All subjects received (on separate occasions) the four possible dosage combinations, there being of course, only one dose condition with the combination of the two active drugs. Driving performance evaluation was conducted by a safety manager from the American Automobile Association, a high school driving instructor and an off-duty patrol officer who followed each driver on the course in an unmarked vehicle to determine whether the driver was impaired enough in his opinion to warrant being stopped were it a real road situation. The ratings by all of the observers showed a significant effect when drivers had taken the combined drug dose, the patrol officer reporting that he would have stopped all of the drivers when in this condition. No such effect was found when drivers had taken either drug alone.

A study by Attwood and his colleagues in Canada of the effects of alcohol and marijuana taken alone and in combination has been undertaken and was referred to by Stein et al (1983). However, the present authors have been unable to obtain a copy of the report and the details cannot therefore be included in the present report.

Driving simulator studies

A study using a computerised driving simulator was reported by Smiley et al (1981). The simulator task required to drive a vehicle through a computer-presented simulated roadway and to encounter a variety of environmental conditions. These included road signs, sharp curves, wind gusts, and the sudden appearance of roadway obstacles. The computer recorded the following distance of the driver from a lead car as well as speed and lane position, the adequacy of emergency decisions and ability to respond to the road signs and monitored overtaking tasks. A reward/penalty system of payment was used to help maintain the subjects' motivation. Good driving was financially rewarded and bad driving, such as crashes were penalised. Three dosage conditions for each drug were used. The doses employed were: alcohol placebo and two doses of alcohol which produced

peak BAC of 0.045 and 0.075g%; and marijuana placebo and two active doses, 100 and 200 ugTHC/kg. The experimental design employed three groups of volunteers (n=15, 10 and 10). All volunteers in each group were given all conditions of the marijuana dosage and only one of the alcohol doses.

Marijuana was found to impair driving performance on a wide range of measures including variability of lane position, speed control and inappropriate steering movements. On the other hand, drivers after taking marijuana became more cautious in the overtaking task and attempted overtaking less frequently. Alcohol effects were surprisingly slight. In the view of the authors, this was "because alcohol was a between subjects variable, comparing groups of 15, 10 and 10 subjects, it was less sensitive to treatment effects than was the marijuana variable, where results for 35 subjects were compared". There was also some evidence to indicate that there were initial differences among the alcohol groups.

The interactive effects of alcohol and marijuana were unclear, due, in the view of the authors, to the possible initial group differences indicated above, the problems associated with the experimental design and the order in which the groups were run.

Stein and colleagues have completed two studies of the effects of alcohol and marijuana alone and in combination, the first conducted between 1976-1978 and the second in 1983 (Stein

et al., 1983). The simulated drive, which was of 15 minutes duration, included winding roads, simulated accidents, wind gusts, obstacles on the road and speeding "tickets". Two dosage conditions of alcohol were employed, placebo and a dose to produce a BAC at peak of 0.1g%. Three conditions of marijuana were employed, placebo, and 50 and 100ug/THC/kg. Each subject completed a run, in a random order, with each of the six possible dosage conditions. Alcohol consistently and significantly impaired the control of the vehicle across a wide range of measurements. After alcohol, drivers had more simulated accidents and received more speeding tickets. The accuracy and speed of response to roadside signs was also impaired. Marijuana at the doses employed had "only an occasional effect". There was little evidence for any interaction between alcohol and marijuana when taken in combination. Although alcohol alone increased the incidence of accidents and speeding offences no evidence for such effects were noted for marijuana alone or for the alcohol-marijuana combination. There was however an enormous increase in between subject variability when subjects were tested in the combined dosage condition. The authors considered that this increase in the variability might have accounted for the inability to detect any effect in this condition.

These authors reported a second study using an updated version of the same driving simulator and using much the same experimental design, the same dose of alcohol, though using higher doses of marijuana (100 and 200 ug THC/kg).

In an attempt to maintain the motivation of the volunteers a system of rewards and penalties was used, the subjects earning extra money for completing the drive and for beating a reference completion time. Financial penalties were imposed for driving more slowly than the reference time, responding incorrectly to road signs, getting a speeding ticket and for having an accident. In addition to the simulator conditions used in the first study, a divided attention task was included in which the driver had to respond to signals by beeping the horn or pressing the dimmer switch in addition to attending to the other demands of the driving simulator task. The data were analysed by analysis of variance with levels of significance of $p< 0.05$ with $p<0.1$ described as of marginal significance. However, as there were 24 driving parameters separately examined by these procedures the Type I error rate was unacceptably high. With this criticism in mind, the data indicated an increase in hazardous driving with alcohol whilst the main effect for marijuana was to drive more slowly. The combined effects of alcohol and the high marijuana dose were seen as predominantly additive. With the lowest marijuana dose, evidence for both addition and some antagonism of the alcohol effects were described. On several measures (including the total number of accidents, reaction times to signs and in the reward/penalty performance) a significant interaction factor was recorded when the lower dose of marijuana when taken in combination with alcohol. The trend of this interaction was in the direction of an antagonism between the two drug effects.

Evidence for such an antagonism between alcohol and marijuana has been reported by others in laboratory-based tasks (MacAvoy and Marks,1976; Chesher et al,1977).

Laboratory studies of skills performance.

The first reported study of the effects of alcohol and marijuana in combination was that of Manno et al (1971). A within-subject design examined six dosage conditions, employing two dosage conditions of alcohol (placebo and 0.66g/kg) and three conditions of smoked marijuana (placebo, 2.5 and 5mg THC). These doses of THC were delivered by marijuana containing two times the amount of THC to allow for an estimated 50% loss by burning during smoking. Most other reports (including this one) state the marijuana dose in terms of the THC provided in the material to be smoked. Therefore, for direct comparison with other studies, the doses used by Manno et al were 5 and 10mg THC. Twelve healthy medical students were the subjects, each completing the tests under each dosage condition in a randomised design. The alcohol (the concentration of which was not stated) was consumed over a period of 30 mins at which time smoking began and performance testing began in another 30 mins (ie 1 hour after the beginning of drinking and 30 mins after the beginning of smoking). The subjects were either naive to marijuana use prior to the experiment or were only very light users, none were described as

daily users. Subject's drinking history was not reported. The experimental setting was a two bed hospital ward.

Drug effects on mental activity were assessed as a verbal performance task using delayed auditory feedback and motor performance was tested with a pursuit meter which had four different pursuit patterns of increasing complexity. The results showed there to be little difference between the degree of impairment produced by the two doses of marijuana. Alcohol produced a decrement on the verbal task but not on the motor test. When given in combination the two drugs produced an additive decrement in performance on both tasks.

A study by MacAvoy and Marks (1975) examined the effects of alcohol and THC in combination on a divided attention task. These authors studied 32 voluteers and compared the effect of the drugs on subjects who were naive to marijuana with experienced users (average consumption of 3 "joints" per week) of the drug. Marijuana users and non-users were matched for age and educational background. The subjects were not matched for their alcohol drinking history, but it was found at the time of analysis that the marijuana users were also comparatively heavier users of alcohol, drinking an average of 43 drinks per week to the non-marijuana users average of 18 drinks per week. This discrepancy possibly complicated the validity of the group comparisons.

Each subject received, on separate testing occasions, the four dosage conditions of marijuana which were no cigarette,

placebo cigarette, cigarette with 2.62 mg THC or cigarette with 5.24 mg THC. The alcohol conditions were no drink, placebo drink, and two doses which produced peak blood alcohol concentrations of approximately 0.048 $\pm$ 0.002 g% and 0.096 $\pm$ 0.006 g%.

The experiment really consisted of four separate within-subject designs, each utilizing eight volunteer subjects, all of which attended the laboratory on four experimental days each approximately one week apart. Each group of eight volunteers comprised four marijuana users and four matched non-users; each group of four was made up of two male and two females.

Each group of eight received one of the four alcohol doses for the four testing occasions and all of the dosage conditions of marijuana.

The divided attention task was similar to that used by Moskowitz and Sharma, (1974) and Moskowitz et al (1972). Subjects were required to attend to two tasks, a central light and to an array of peripheral lights. The subjects were asked to attend to a central blinking light and to respond by pressing a button when there was a discontinuity in the rate of blinking. Moskowitz on the other hand, altered the difficulty of the central task, requiring the subject either to attend only to a non-blinking central light or to maintain a count of the number of blinks. The second task required the subjects to press another button when they detected any of the lights which were placed in an arc either side of their visual field. Moskowitz reported that the effect of alcohol (alone) was dependent upon the demands of the

central task. Alcohol was without effects at BAC under 0.1g% when the central light was not flashing. When required to count the blinks, the detection of the peripheral lights by the subjects was significantly affected at BAC as low as 0.02g%. The relative insensitivity of the MacAvoy & Marks' task to alcohol was probably due to the low demands placed on the subject's attention to the central task. The main alcohol effect was a slight increase in false alarms. Marijuana on the other hand produced a significant decrement in the number of correct responses to both the centre and peripheral signals. This finding was in agreement with that of Casswell and Marks (1973) for the action of marijuana to impair the ability to divide attention between two tasks. A direct comparison of the effects of alcohol and marijuana on this task was not possible in view of the experimental design. The study of the effect of marijuana was a within-subjects design whilst that for alcohol was a between-subjects design. This design (as well as the nature of the test itself) was less sensitive to the effects of alcohol and more sensitive to those of marijuana (Winer, 1962).

The findings by MacAvoy and Marks (1975) indicated that the effects of the interaction between marijuana and alcohol on this task were basically additive, as the analysis of variance of the data revealed no significant interactions. However, two other interesting findings were reported. Evidence was presented to suggest that amongst the experienced marijuana users, but not amongst the non-users, the interaction of this drug with alcohol

may have been antagonistic. A signal detection theory analysis indicated that the average sensitivity of the marijuana users after taking marijuana actually increased as a function of the amount of alcohol taken. This suggested to the authors that in the case of experienced users of marijuana, alcohol and marijuana have antagonistic effects on visual attention functioning. They further suggested that this antagonism must have occurred at a physiological level and did not involve voluntary control of behaviour, such as "being able to pull one-self together", a factor which has been described in marijuana studies (Cappell and Pliner, 1973; Casswell, 1975; Tart, 1971).

Other evidence also presented suggested a degree of cross-tolerance between the two drugs, however the confounding factors of the experimental design and the differing alcohol usage between the marijuana user and non-user groups render interpretation difficult. The authors conducted a second experiment using a within-subjects design to resolve this question and summarized their results in a "Note Added in Proof". In this second experiment there was no evidence for the cross tolerance suggested in the first experiment, although marijuana users tended to be less impaired than non-users under all drug conditions. Furthermore, as with their first experiment, they found, amongst the marijuana users, a trend for the antagonism between alcohol and marijuana to occur at the low doses.

Studies conducted for the Le Dain Commission in Canada by Hansteen et al (1976) included a laboratory study of the

interactive effects of alcohol and marijuana on a compensatory tracking task in the laboratory. The tracking task was used with and without secondary tasks. The latter comprised a requirement that the subject respond to the appearance of the numbers 1, 2, or 3 by depressing the appropriate foot pedal. Twenty-two volunteers were used and three dosage conditions of alcohol employed; placebo, and doses to achieve blood alcohol concentrations of 0.03 and 0.07g%. Three marijuana conditions were used; placebo and 1.6 and 6.8mg THC. All drug combinations were not tested but six of them were used in a latin square design so that all subjects received all treatment combinations. However, the only alcohol-marijuana combination was that of the two lowest doses of each drug. The results indicated a dose-dependent decrement for the effect of alcohol and an effect only for the higher dose of marijuana. On the simple compensatory task, the effect of the drug combination was no greater than that of the alcohol alone. However, when the secondary task was added, each drug alone produced an impairment and the effect of the combination of the two drugs was greater than that of either drug alone, (presumably an additive effect). This study provides further evidence for the greater sensitivity of a task which involves the division of attention.

A series of experiments to investigate the interactive effects of marijuana and alcohol have been conducted in the laboratories of the Department of Pharmacology of the University of Sydney (Chesher et al, 1976,1977;Belgrave et al

1979a,1979b;Bird et al 1980). All of these studies, using essentially the same test battery used the same dose of alcohol (0.54g/kg) but used different doses of THC, in each case given as a capsule in sesame oil, and taken by mouth. The doses of THC were given according to body weight, on the basis of 10mg,15mg and 22mg per 70 Kg providing, in the different studies, 137, 214 and 320 ug THC/kg. (respectively Chesher et al 1976; 1977; Belgrave et al 1979a). A repeated measures design was used to assess any changes in the nature of the interaction across time. The fundamental findings of each study was that both drugs are capable of producing an impairment in performance on the test battery and that the interaction between alcohol and THC was one of addition. There was no evidence to suggest that the drug combination produced an effect which was greater than the addition of the effect of each drug. The effect of the increasing doses of THC across the three experiments indicated that a dose dependent effect was produced on a series of cognitive, perceptual and motor function tests. In one experiment (Chesher et al 1977) there was a suggestion for an antagonism between the effects of THC and alcohol which occurred approximately 1 to 3 hours after the ingestion of THC. There was no evidence for such antagonism in either of the other two studies.

Further studies in the Sydney laboratories examined the possible interactions between alcohol, THC, and cannabinoids other than THC which occur in the marijuana plant. Data have been presented to indicate that some other cannabinoids, such as

cannabidiol (CBD) and cannabinol (CBN), do possess pharmacological activity in experimental animals as well as showing interactive effects with THC (for refs see Belgrave et al, 1979b). In the first of these studies (Belgrave et al, 1979b), the effect of cannabidiol (320 ug/kg by mouth), alone and in combination with alcohol (0.54 g/kg) was studied. The effects were measured before and at 100, 160 and 220 mins after CBD ingestion (40, 100 and 140 mins after the beginning of alcohol consumption). Alcohol produced effects consistant with those previously demonstrated on the test battery. Cannabidiol produced no demonstrable effects, nor did its combination with alcohol produce any detectable differences in the alcohol-induced performance impairment or in the mood effects of alcohol. A second, larger study (Bird et al, 1980) was designed to examine the interactions between all of the possible combinations of alcohol, THC, CBD and CBN, all given by mouth. For this experiment a between-subject design was employed, using a total of 161 volunteers, each being used only once. Both alcohol and THC when given alone produced significant decrements in performance on the test battery. There was no suggestion of systematic effects involving CBD or CBN, either alone or in combination with alcohol or THC. The data were therefore described in terms of a model which referred only to the effects of alcohol and THC. Significant impairment on the test battery was demonstrated for both alcohol and THC. The combined effects of the two drugs were greater than those of either drug given

alone, an effect which was descibed in terms of an additive model. There was no statistical evidence for an interaction.

The effect of alcohol and marijuana on mood states

As can be seen from the above, the major emphasis in studies of the effects of marijuana and alcohol has been on measures of skills performance. However, it has been pointed out by Naatanen and Summala (1976) that despite the fact that driving is unquestionably a perceptual-motor task, the level of perceptual-motor skills possessed by drivers does not correlate well with the probability of being involved in a road crash. They propose that the demands of the drivers task are more a function of the driver's choice than the characteristics of the task itself. Therefore, if drugs can exert effects on the driver's mood and motivation, they could also influence driving behaviour. Evidence to support this contention has been outlined in the studies described above. For example, in on-course driving or in a simulator, alcohol has been described as increasing the driving speed and increasing risk-taking behaviour. Marijuana on the other hand has been demonstrated to decrease driving speed and to decrease risk-taking behaviour (Casswell,1977; Stein et al 1983; Smiley et al 1981; Dott 1972). Drug-induced changes in the motivational aspect of driving performance must be assessable by

psychological methods and it is surprising that so little emphasis has been given to this area of research. Alcohol-induced changes in mood, including alcohol induced aggressive behaviour is well documented in most textbooks of pharmacology (eg Ritchie, in Goodman and Gilman (1980). Similarly, the effects of marijuana on human mood has received close attention (Tart, 1971; Jasinski et al 1971;Salzman et al, 1974). However, these mood effects do not appear to have been considered in the context of driving behaviour. Nor has attention been directed to the study of the effect on mood of the combination of alcohol and marijuana.

METHODS

THE DATA COLLECTED

A. Non-repeated measures: descriptors of the volunteer population.

(i) Eysenck Personality Questionnaire (Although these data were collected they have not been incorporated in the present analysis).

(ii) Drug-taking history questionnaire (see Appendix 1)

(iii) Attitudes towards alcohol and marijuana (see Appendix 1)

(iv) Age, sex, weight and occupation.

B. Repeated measures. (ie collected on each testing occasion)

(i) Mood measures: (see Appendix 1)

In addition to the measurement of the effects on skills performance, it is important to determine the ability of the individual to assess the degree of subjective intoxication produced by the drug. This ability also relates to

the awareness by the intoxicated driver of the extent of the drug-induced impairment. Also one of the purposes of the present investigation is to examine similarities and differences in the effects produced by alcohol and marijuana on the subjective moods of the drug users. Subjects indicated the status of their mood, or the degree of their intoxication at the time of testing by placing a mark on the horizontal scale, where their present mood fitted within the poles of the moods described by the adjectives at either end of the line. The responses were quantified by measuring the distance in centimetres of the subjects mark from the left pole of the horizontal line.

The following mood scales were designed to collect information on these subjective effects of the drugs both alone and in combination.

(a) horizontal analogue scales as described by Ashton et al (1978) were used to describe the dimensions of "tension", "alertness", "depression", "detachment" and "anxiety". An additional scale to determine overall "feelings" was also used.

Subjects completed these scales before the administration of the drugs and on the two test occasions after the drugs had been taken (T2 and T3, see below)

(b) horizontal analogue scales to measure the intensity of drug effects and the subjects ability to distinguish between the effects of marijuana and alcohol were presented before the two post-drug testing times.

To assess the intensity of drug effects three scales were used. Scale 1 was intended to assess the specific effect attributed to each drug and for this purpose the "stone" or "drunk" scales were used. The subject was asked to indicate the degree of intoxication by placing a mark on a horizontal line within the extremes of "absolutely straight" or absolutely sober" to "as drunk (or 'stoned') as I have ever been. Scale 2 was intended to assess the overall degree of intoxication due to the drug combination. For this "overall affected scale the extremes were "absolutely unaffected" to "extremely affected". The third scale asked subjects to rate the effect of the drugs taken with the extremes being "not enough" to "too much" affected.

Questions concerning the awareness of drug-induced impairment of driving skills were presented in the format of a analogue scales. Two questions were asked, the first was "As you feel RIGHT NOW, how safely could you drive a car?" and the extremes were "absolutely certain I COULD NOT drive safely" and "absolutely certain I COULD drive safely". The second driving related question which required a YES or NO answer was "Would you drive a car as you are feeling now?".

(ii) Physiological/pharmacological measures:

(a) Blood alcohol concentration was recorded by means of a Draeger 7010 breathanalysis evidential apparatus. Determinations were recorded upon arrival at the laboratory and immediately before the beginning of each repeat of the performance measures on the test battery after drug consumption (see below, Procedure).

(b) Heart rate was recorded from the radial pulse within thirty minutes of arrival at the laboratory and again immediately before the beginning of each testing time on the battery of performance tests.

(iii) The performance measures.

All tests were presented by microcomputer (Apple //e) and data collected and stored on floppy disk. A brief description of each test is given below.

(a) Simple reaction time. The subject is required to press a button as quickly as possible whenever an "X" appears on the screen of a visual display unit (VDU). The signal "X" appears within a "box" approx. 30 cm square

which is continuously displayed during the test. Two versions of the test were used differing only in the interval between each stimulus. The "regular" stimulus presentation consisted of 50 stimuli which appeared at a regular rate of about one per two seconds; the irregular version presented twenty stimuli which appeared at random intervals with an average of about 15sec.

(b) Choice reaction time. A series of distinct stimuli are presented on the VDU at 4 second intervals. The subject is required to press, as quickly as possible, the appropriate key in accordance with a rule which has previously been displayed on the screen. Two degrees of difficulty were employed. First, the stimulus-response compatibility was high; ie the rule is displayed on the VDU three times during the trial as follows:-

NEW RULE: IF YOU SEE A	1	2	3	4
THEN PRESS A	1	2	3	4

The stimuli are digits between 1 and 4 (which appear in a "box" approx. 30 cm square which is continuously displayed during the test) and the response is to press the appropriate button labelled 1 to 4 on the subject keyboard. For each response the reaction time is separately recorded for correct and incorrect responses. Missed responses are also recorded. Thirty stimuli were presented.

The second degree of difficulty of the task is where

the stimulus-response relationship is incompatible. For example, the rule, which is displayed three times during the trial, may indicate:-

NEW RULE: IF YOU SEE A	3	8	5	2
THEN PRESS A	1	2	3	4

The rule for the low compatibility condition changes between testing occasions (repeats) but remains the same for each repeat. Thirty stimuli with the incompatible rule are presented at each repeat. Reaction times for both correct and incorrect responses are recorded as well as the number of correct, incorrect and missed responses. To control for the possibility that some low compatibility rules might be more difficult than others the presentations of rules are distributed such that each variant of the incompatible rule is randomly distributed between all subjects in all groups.

(c) The "Little men" test. This test is a mental rotation task and is a test of spatial abilities. The responses are also timed, and as the subjects were asked to respond as quickly as possible without making a mistake the task is also a measure of reaction time.

For each item a pair of cartoon-like stick "men" appear on the monitor, each holding a ball in one of their hands. Each little man may be presented as facing towards or away from the observer and may be oriented at various angles (ie on his

side, head down or head up). The subject is required to indicate whether the little men are holding the ball in the same or different hands. This is done by pressing as quickly as possible a YES or a NO button on the keyboard. The reaction times for both correct and incorrect responses are recorded and the percentage of correct responses calculated. This test has a timed duration of 7 minutes during which, according to the mental processing speed of the subject would result in the presentation of between 200 to 300 stimuli.

(d) Pursuit tracking task. A pair of brackets move from left to right across the VDU in a random fashion. The subject is required by means of a small "steering wheel" knob (4cm diam) to maintain a "car" within the brackets. This test has a timed duration of 7 mins.

(e) Forward digit span. A test of short term memory. A series of digits appear on the screen, one at a time. At the end of a series the subject is required to key in the digits in the same order as they appeared on the screen. If the subject responds correctly, the next series will be one digit longer; if an incorrect response is given the next series will be one digit shorter in length.

RATIONALE FOR THE TEST SELECTION AND DESIGN

The test battery was designed to satisfy a number of separate aims.

A. The tests were selected to span a variety of ability domains:-

(i) Reaction time (tests a, b and c)

(ii) Visio-motor co-ordination (test d)

(iii) Short term memory (test e)

(iv) Spatial ability (test c)

Note, tasks (a),(b) and (c) are essentially measures of reaction time with an increasing demand on the mental processing and cognitive functions. The subjects were instructed to perform the tasks as quickly as possible without making any mistakes. As the degree of demand on cognitive processes increases, so also does the reaction time as well as the inclination of the subject to make a "speed-accuracy trade-off". This measure may be considered as an index of "risk-taking" behaviour.

B. Whilst alcohol, in adequate dosage can be shown to adversely affect a number of aspects of skills performance, the functions most sensitive to the drug are those which involve some degree of central information processing. The tests presented in

this study are designed so that within each test as well as across the test battery the complexity of the items are systematically varied. This should enable an accurate comparison of the extent to which the two drugs will follow the same pattern with respect to the changing loads on information processing.

C. Although there have been few studies to qualitatively compare the effects on human skills performance of alcohol and marijuana, evidence currently available suggests some differences between the drugs. As indicated above, the effects of alcohol involve a slowing of information processing. It seems that an effect of marijuana is more associated with attentional distraction. Furthermore, whilst the role of alcohol in risk-taking behaviour has been well documented it seems that marijuana has not been shown to increase risk-taking, but rather to produce a more cautious attitude, at least on an overtaking task presented on a driving simulator (Dott 1972). Tests in the present battery should be sensitive to attentional deficits, and as indicated above, a speed-accuracy trade-off should be evident in the "little men" test and the choice reaction time tasks when the reaction times and the percentage of errors are examined.

THE DRUGS.

A. Alcohol. Ethanol absolute was diluted to contain 15% (v/v) ethanol with orange juice to which 0.2 ml peppermint oil had been added to mask the aroma and taste of the alcohol. The placebo beverage contained only orange juice with 2.0 ml concentrated peppermint water (as peppermint oil is insoluble in water). Approximately 0.5ml ethanol was floated on top of the placebo beverage just before serving to the subject. All beverages (all doses) were served chilled. The doses administered were 0 (placebo), 0.25, 0.5 and 0.75 grammes ethanol per Kilogram body weight. The doses given to female volunteers were 0.92 X the male dose, a conversion factor which was derived from previous studies (Martin, personal communication) to correct for male-female differences in adiposity, body weight and body water. The alcohol was consumed at a regular rate over a period of twenty minutes. To facilitate the regular rate of consumption of ethanol, the volume to be consumed by each subject was presented to them in two equal portions, each portion to be consumed over a ten minute period. The second portion was distributed ten minutes after the first.

B. Marijuana. Marijuana leaf supplied by The National Institute on Drug Abuse (N.I.D.A.) Department of Health and Human

Services U.S.A. was used and the doses of tetrahydrocannabinol (THC) administered were 0 (placebo), 2.5, 5.0, 10.0 mg. There was no attempt to adjust the dosage according to body weight. Subjects were provided with the same weight of marijuana leaf (approx 400mg), all samples were blended with placebo leaf to minimise the differences in appearance between samples. Subjects were requested to smoke the given quantity of marijuana leaf as they wished, with the only restrictions that the measured weight of marijuana provided should be smoked within fifteen minutes and that the cone of the water pipe should be packed such that each could be smoked with one inhalation. Smoking began five minutes after drinking had finished.

PROCEDURE

1. The enlistment of the volunteer population.

Only subjects over 18 years of age and non-naive to marijuana were used. Volunteers were enlisted by advertisements on Sydney radio stations 2MMM and 2JJJ. The advertisements, informally delivered by the announcer-on-duty indicated that the experiment involved the study of the effects of alcohol and marijuana when taken together on various laboratory tasks of skills related to those required for driving a motor car. The respondents indicated their interest in smoking free marijuana

legally and most were interested in the purpose of the study and were eager to see the results of their performance tests. A particular effort was made to interest each volunteer in the experiment and all were told that the study was being conducted at the request of the Australian Government. Subjects were not given information about the doses of the drugs which were to be used but were told "I want you to spend the day knowing nothing about how much of each drug you received. In that way we will get a measure of how affected you really are and not a measure of how affected you expect you ought to be. At the end of the day you will be told exactly how much of each drug you received". The decision to instruct the volunteers in this manner was taken after the pilot study when the complete 4 X 4 design was explained before the experiment began. With this information the subjects tended to compare one with the other their assessment of intoxication with their knowledge of the doses of each drug in the study and to spend too much effort on this subjective evaluation. It was our belief that this knowledge produced a degree of subjective bias which could have produced an additional variable to the study.

2. The procedure each experimental day

Subjects were requested to arrive at the laboratory at 9.00am having consumed a light, non-fatty breakfast. On arrival, subjects were weighed and "breathalyzed" and given a description

of each of the computer-based tests. After a pulse rate had been recorded each subject completed the full test battery (T0). At the completion of this repeat, the mood scales, Eysenck Personality Questionnaire and the personal drug-taking history and attitude questionnaires were completed. A second (T1) repeat of the performance battery was then completed, and these data constituted the base-line data for the pre-drug measures. On the completion of T1 subjects were provided with the alcohol (or placebo) drinks which were consumed over a period of twenty minutes as described above. Five minutes after the alcohol beverage had been consumed, smoking of the marijuana leaf began. This was smoked as indicated above. Fifteen minutes after smoking had begun, pulse rates and blood alcohol concentrations were determined, the mood scales were completed and the first post-drug repeat (T2) of the test battery was commenced. At the completion of T2 a light lunch of bread, cheese, tomato and decaffeinated coffee was provided. Two and a half hours after the beginning of the T2 performance measures the final T3 repeat of the test battery was commenced. This was preceded by the collection of data from the mood scales, the pulse rate, blood alcohol concentration. At the completion of T3, all subjects were "breathalyzed" again and were released from the laboratory if and when their BAC was less than 0.04g%.

The allocation of the dosage of both drugs and the order of presentation of the tests within the test battery was

effected by means of a previously prepared table (see Appendix 2). The subjects were allocated a number sequentially according to the time of arrival at the laboratory.

A description of the population of volunteers is given under Results.

DATA ANALYSIS

Preliminary remarks.

The experiment is a three factor design with repeated measures on the last factor (time of testing). The factors are:-

A. Alcohol dosage

a1 to a4 for the four dosage conditions

B. Marijuana dosage

b1 to b4 for the four dosage conditions

C Time of testing

t1 to t3 for the testing occasions

Note in the analysis presented in this report only the difference between testing occasions T1 and T2 (ie "change scores") have been examined. This represents the reponses before and after drug taking, with T2 representing as near as possible to the peak of the effects of both drugs.

The experimental design for dosage groups is shown in Table 1 (p.6).

The information sought

1. Is the drug exerting an effect?

A basic principle in pharmacology is that most (if not all) drugs exert effects that are graded. That is to say that as we increase the dose taken so the effect produced by the drug is increased. In this study the term "drug effect" is defined as a dose-dependent change in the subjects' abilities or moods between testing times before (T1) and after (T2) the drugs had been taken. These effects have been examined in this study by the contrasts (comparisons) C1 and C2 described below. They examine the effects of alcohol in the presence of the various doses of marijuana, including the zero marijuana (placebo) condition. These data are described as "alcohol effects". The effects of marijuana in the presence of the various doses of alcohol may similarly be described and termed the "marijuana effects".

2. What is the effect of one drug upon the other?

The prime purpose of the study is to examine the effects of the drugs in combination. In this report the data which describe the drug combinations are expressed (eg. in the Figures 1 to 8) as the effect of the different doses of marijuana

when taken in combination with alcohol.

3. What is the nature of the interaction between these drugs?

Is the combination of alcohol and marijuana additive, supra-additive or antagonistic?* These questions are addressed by the interaction contrast analysis (C3) described below.

4. In the doses used and with the present test battery, are the effects produced by alcohol greater or less than those produced by marijuana?

This question is addressed by the "difference" contrast (C4) described below.

.....

*Footote: Additive implies that the effects of the drugs in combination are as would be expected by simple addition; eg 1 + 1= 2. Supra-additive implies that the effect of the drug combination is greater than one would expect from the simple addition of drug effects; eg 1 + 1 = 3. Antagonistic implies that the effects of the drug combination is less than one would expect from the simple addition of drug effects; eg 1 + 1 = 0.1.

The analysis.

First, for each performance measure, and for each subject, "change scores" were calculated. The "change scores" are the change in the performance measure after taking the drug. These were calculated by subtracting the score after (T2) from the score before the drug (T1). These were then standardized by dividing each by the standard deviation of scores in the double placebo condition. Thus for each measure the magnitude of the standardized change scores are relative to the 'natural' extent of variation in that measure. All subsequent measures were performed on these standardized change scores.

Also, composite variables were calculated by combining the Z-scores of a selection of the performance measures (the global means and standard deviations were used in the calculation of the Z scores). The composite (centroid) may provide an indication of the effects of the drugs on the test battery as a whole. The performance measures from which the composite (centroid) was derived are described in Table 12. In all sixteen measures were used for the determination of the centroid. The signs of the accuracy scores were reversed so that more positive values represented a decline of the performance measures. Reaction time scores remained unchanged.

For each performance measure and for the composite,

the following group-contrasts were calculated. Also each was statistically tested against the null hypothesis that the contrast was equal to zero.

1. C1 = C (alcohol linear). The linear trend contrast across groups of increasing alcohol doses.

2. C2 = C (THC linear). The linear trend across groups of increasing THC doses.

3. C3 = C (alcohol linear X THC linear). The interaction contrast between the above two alcohol and THC linear trend group contrasts.

4. C4 = C (alcohol linear - THC linear). The difference contrast between the above two alcohol and THC linear trend group contrasts (ie C1 and C2).

The contrast coefficients for the above four group contrasts (C1,C2,C3,C4) are given in the Table 2. The error term for statistical tests was the within-cell variance (this was calculated with both "pooled" and "non-pooled" estimates).

TABLE 2

TABLE OF CONTRAST COEFFICIENTS

DOSAGE GROUP	CONTRAST				CONDITION	
	C1	C2	C3	C4	Alcohol	THC
1	-3	-3	9	0	0	0
2	-3	-1	3	-2	0	L
3	-3	1	-3	-4	0	M
4	-3	3	-9	-6	0	H
5	-1	-3	3	2	L	0
6	-1	-1	1	0	L	L
7	-1	1	-1	-2	L	M
8	-1	3	-3	-4	L	H
9	1	-3	-3	4	M	0
10	1	-1	-1	2	M	L
11	1	1	1	0	M	M
12	1	3	3	-2	M	H
13	3	-3	-9	6	H	0
14	3	-1	-3	4	H	L
15	3	1	3	2	H	M
16	3	3	9	0	H	H

Note: 0=placebo; L=low dose; M=medium dose; H=high dose.

Explanatory Notes:

1. Contrasts 1 and 2 (C1 & C2) represent the extent to which performance (or mood) changes linearly with increasing doses of alcohol (C1) or of THC (C2), averaged across the different doses of each drug.

2. Contrast 3 (C3) represents the extent to which the linear effect of alcohol on mood and performance changes with varying doses of THC. That is to say, it is the interaction between linear effects of these two drugs.

3. Contrast 4 (C4) represents the extent to which the linear effects of alcohol are different from those of THC within the doses used in this experiment.

RESULTS

A. A description of the population sample.

The data presented have been collected from three hundred and twenty subjects, 264 males and 56 females, aged between 18 to 70 years (median 21 years, 91% of sample being under 30 years). A total of 356 volunteers presented themselves at the laboratory in response to the radio advertisements, and 36 were excluded for the following reasons:- 14 were excluded for their inability to understand the tests, 15 because they vomited after alcohol (14 of these had received the high dose (0.75g/kg) and 1 after 0.5g/kg). Two subjects could not complete the tests because of illness which was unrelated to the experiment (influenza), 1 was excluded for heroin use, and 4 "escaped" from the laboratory without completing the tests.

The volunteers were all marijuana users and the population sample, in view of the nature of its collection, was biased towards marijuana use. The responses to the drug use questionnaire are summarised in Table 3

TABLE 3

RESPONSES TO DRUG USE QUESTIONNAIRES

(a) Alcohol drinking history questions.

1. "On how many days last week did you drink alcohol?"

(i)	None....	11.4%
(ii)	1 or 2 days.....	37.5%
(iii)	3 or 4 days.....	38.1%
(iv)	5 or 6 days.....	7.0%
(v)	every day.....	6.0%

2. "On a day when you have a drink, how many drinks would you usually have?"

(i)	1 or 2 drinks....	19.6%
(ii)	3 to 5 drinks....	37.0%
(iii)	5 to 8 drinks....	23.7%
(iv)	9 to 12 drinks....	12.7%
(v)	more than 12 drinks.	7.0%

(b) Marijuana smoking history.

1. "On how many days last week did you smoke marijuana?"

(i)	None....	4.1%
(ii)	1 or 2 days....	19.7%
(iii)	3 or 4 days....	17.8%
(iv)	5 or 6 days....	17.2%
(v)	Every day.....	40.8%

2. "On a day when you smoke marijuana, how many sessions would you have?"

(i)	One.....	19.9%
(ii)	Two or three..	52.1%
(iii)	Four.....	11.7%
(iv)	More than four	16.3%

The mean duration of drinking (in years) was 4.8 ± 0.26 (s.e.m.) whilst the mean duration of smoking was 4.7 ± 0.006 (s.e.m.) years.

When assessed according to the N.H.& M.R.C. classification for alcohol consumption (National Heart Foundation, 1980) and an adaptation of this scale for marijuana (constructed by us), the comparisons of drug use within the population can be made as shown in Table 4.

TABLE 4

	N.H.& M.R.C.Classification (% of sample)			
DRUG	B	C	D	E
Alcohol	58.9%	24.7%	10.4%	6.0%
Marijuana	41.8%	28.8%	18.8%	10.6%

The classifications B-E are described as:-

B= Low risk female drinkers. No risk male drinkers.
(Average daily intake of less than three drinks; average of less than 6 sessions of marijuana per week).

C= Intermediate risk female drinkers. Low risk male drinkers.
(Average daily intake of 4 drinks or 9-12 drinks in any day; average of 6 to 13 sessions of marijuana use per week).

D= High risk female drinkers. Intermediate risk male drinkers.
(Average daily intake of 5 to 8 drinks or occasional excess; average of 13 to 30 sessions of marijuana use per week).

E= Very high risk female drinkers. High risk male drinkers.
(Average daily intake of 9 to 12 drinks or frequent or great occasional excessive intake; average of greater than 30 sessions of marijuana use per week).

As a further description of the volunteer population, the responses to the "attitude" questions were as follows:-

	Alcohol	Marijuana
1. ..is a safe drug	1.0%	30.5%
2...is safe for most people	27.9%	56.2%
3..bad for most in long run	54.6%	11.4%
4..harmful for all who use it	16.5%	1.9%

B. Mood measures.

(i) Self-assessment of intoxication

(a) The "drunk" and the "stone" scales. The contrast analyses (C1 & C2) showed there to be a significant dose-dependent linear effect for both alcohol and marijuana (see Table 5). The results for each drug alone, (ie alcohol with placebo marijuana and marijuana with placebo alcohol) are shown in Table 6. Here (with smaller group sizes, n=20 per group) it can be seen that the ratings for the doses of marijuana tended to be greater than those for alcohol.

An indication of the ability of the subjects to discriminate and distinguish between the effects of the two drugs when taken in combination may be determined by examining the mean scores on each of the specific drug scales ("drunk" or "stone"). These results are shown in Table 6(c). These data are the mean score values across all dosage groups of each drug in the presence of each dose of the other drug. In the case of the

TABLE 5

DOSE-EFFECT LINEAR CONTRASTS
(a) Intoxication ratings
Values at T2 only

MEASURE	ALCOHOL		MARIJUANA		INTERACTION		DIFFERENCE	
	Value	p	Value	p	Value	p	Value	p
*1 "Drunk"	45.37	0.000	-1.12	0.856	-8.12	0.556	23.25	0.000
*2 "Stone"	13.5	0.031	25.1	0.000	-28.5	0.042	-5.80	0.189
*3 "Overall affected"	39.35	0.000	18.75	0.001	-31.35	0.017	10.30	0.013
*4 "How rate effect"	13.8	0.020	6.3	0.287	-40.10	0.003	3.75	0.370

* The questions are as in Appendix 1:-
1. RIGHT NOW, how drunk do you feel?
2. RIGHT NOW, how stoned do you feel?
3. RIGHT NOW, how affected OVERALL do you feel by what you have taken?
4. How do you rate this effect?

(b) Driving-related questions
Values at T2 only

MEASURE	ALCOHOL		MARIJUANA		INTERACTION		DIFFERENCE	
	Value	p	Value	p	Value	p	Value	p
*1 "How safely"	-33.35	0.000	-5.61	0.532	-1.63	0.935	-13.87	0.030
*2 "Would you drive"	3.26	0.001	0.57	0.559	-0.48	0.822	1.35	0.049

*The questions were:-
1. "As you feel RIGHT NOW how safely could you drive a car?"
2. "Would you drive a car as you feel RIGHT NOW?"

ability to detect the effect of alcohol, the values given in Table 6(c) are those scores on the "drunk" scale and constitute the mean of the totals of the columns of the experimental design as described in Table 2. For the ability to detect the effects of marijuana in the presence of the various doses of alcohol, the values given in Table 6(c) are those scores for the "stone" scale and constitute the mean of the totals of the rows in Table 2. In each case, if the ability to distinguish the effects of one drug from the other is complete, then one would expect that the mean assessments for each drug should independently co-vary. There should not be any difference in the assessments for one drug across all the doses of the other. As can be seen from the data in Table 6(c) the ability to discriminate the effects of alcohol was not affected by the various doses of marijuana. However, the ability to discriminate marijuana was influenced by the presence of alcohol. Indeed, the difference in the "stone" score for marijuana with the alcohol placebo was significantly different from the score when the highest dose of alcohol had been taken ($t = 2.8201; p<0.01$).

(b) The scale "How affected overall do you feel by what you have taken?". The contrast analysis (Table 5) showed a significant linear effect for both drugs. In addition there was a significant interaction between the two drugs and the "difference" contrast indicated a significant difference between the drugs, with alcohol having the greater effect. This

difference is also seen when the assessment for each dose of each drug alone is examined (Table 6).

(c) The scale "How do you rate this effect?". The results in Table 5 of the linear contrasts indicate a significant linear effect for alcohol but not for marijuana. The effect of each drug alone is shown in Table 6 where it can be seen that whilst the assessments for each drug are quantitatively similar, those for marijuana show little difference between doses.

(ii) The driving-related questions.

(a) "How safely would you drive a motor car as you are feeling now?"

A highly significant linear effect for alcohol was recorded for the responses to this question, but no such relationship existed for the marijuana effect (see Table 5). As can be seen from the "difference" contrast this difference was significant ($p=0.03$). The results for each drug alone are shown in Table 7 where it can be seen that the assessments for marijuana did not vary significantly from that made in the placebo condition. The effect of marijuana on the assessments in the "alcohol condition" ($n=80$) is shown in Table 7.

TABLE 6

THE INTOXICATION RATINGS

(a) Alcohol (alone,with marijuana placebo)(n=20)

SCALE	DOSE (g/kg) Placebo	0.25	0.50	0.75
"Drunk"	3.45 ± 0.51	5.65 ± 0.62	5.75 ± 0.69	7.75 ± 0.64
"Overall affected"	5.95 ± 0.23	10.20 ± 0.23	10.90 ± 0.17	11.75 ± 0.19
"Rate this effect"	4.00 ± 0.54	6.75 ± 0.64	7.40 ± 0.53	7.65 ± 0.74

(b) Marijuana (alone,with alcohol placebo)(n=20)

SCALE	DOSE (mg) Placebo	2.5	5.0	10.0
"Stone"	4.60 ± 0.49	7.05 ± 0.66	9.00 ± 0.65	7.00 ± 0.66
"Overall affected"	5.95 ± 0.0.32	8.30 ± 0.26	10.20 ± 0.21	8.85 ± 0.19
"Rate this effect"	4.00 ± 0.54	6.05 ± 0.71	7.00 ± 0.61	6.65 ± 0.61

TABLE 6 (continued)

(c) An estimate of the ability to distinguish the effects of one drug in the presence of the other.

(i) ALCOHOL: The mean of the assessment of the effect of alcohol on the "drunk" scale (mean of all doses) in the presence of the various doses of marijuana.

(ii) MARIJUANA: The mean of the assessment of the effect of marijuana on the "stone" scale (mean of all doses) in the presence of the various doses of alcohol.

DOSE	(i) ALCOHOL mean "drunk" score ± s.e.m. (n=80)	(ii) MARIJUANA mean "stone" score ± s.e.m. (n=80)
Placebo	5.65 ± 0.35	6.9 ± 0.35
Low	5.77 ± 0.37	8.1 ± 0.36
Medium	5.60 ± 0.38	7.8 ± 0.37
High	5.89 ± 0.38	8.2 ± 0.3

TABLE 7

DRIVING RELATED QUESTIONS

1. As you feel RIGHT NOW, how safely could you drive a car?
   Where a score of 1 = "absolutely certain I *COULD NOT drive safely*
   and a score of 15 = "absolutely certain I COULD drive safely.

(a) Effect of alcohol alone (with placebo marijuana) (n=20)

DOSE ALCOHOL (g/kg)	DRIVING SCORE ± s.e.m.
0.00	11.6 ± 1.04
0.25	8.6 ± 1.07
0.50	9.2 ± 0.97
0.75	8.3 ± 1.06

(b) Effect of marijuana alone (with alcohol placebo)(n=20)

DOSE THC (mg)	DRIVING SCORE ± s.e.m.
0.00	11.6 ± 1.04
2.50	11.0 ± 0.89
5.00	10.6 ± 0.90
10.0	11.4 ± 0.97

(c) Effect of marijuana on the alcohol effect.
(alcohol effect=mean of all doses of alcohol)(n=80)

DOSE THC (mg)	DRIVING SCORE ± s.e.m.
0.00	9.42 ± 0.53
2.50	10.14 ± 0.46
5.00	8.82 ± 0.54
10.00	9.74 ± 0.48

TABLE 7 (Continued)

2. Would you drive a car as you feel RIGHT NOW?
(scored as yes=1; no=2)

(a) Effect of alcohol alone (with marijuana placebo)(n=20)

DOSE ALCOHOL (g/kg)	DRIVING SCORE
0.00	1.16 ± 0.08
0.25	1.42 ± 0.11
0.50	1.50 ± 0.11
0.75	1.50 ± 0.11

(b) Effect of marijuana alone (with alcohol placebo)(n=20)

DOSE THC (mg)	DRIVING SCORE
0.00	1.16 ± 0.08
2.50	1.25 ± 0.10
5.00	1.20 ± 0.09
10.00	1.16 ± 0.08

(c) Effect of marijuana on the alcohol effect
(alcohol effect = mean of all doses of alcohol)(n=80)

DOSE THC (mg)	DRIVING SCORE
0.00	1.40 ± 0.06
2.50	1.31 ± 0.05
5.00	1.44 ± 0.06
10.00	1.30 ± 0.05

(b) "Would you drive now?" A significant linear effect was demonstrated for alcohol towards a negative answer to this question was obtained and is shown in Table 5. No such effect was demonstrated for marijuana. The effect of each drug alone is shown in Table 7 and the effect of marijuana on the assessments in the alcohol condition is shown in Table 7.

(iii) The mood scales.

The mood scales are reproduced in Appendix 1 and the results summarized in Table 8. The main descriptors for each mood state are given below, however Appendix 1 provides the adjective check lists for each of these scales to indicate the actual nature of each of the mood measures.

(a) "Anxiety". A significant linear drug effect on this dimension was recorded for marijuana in the direction of an increase in self-reported anxiety. Alcohol showed a trend towards a reduction in anxiety but this failed to reach significance (see Table 8). The "difference" contrast showed that these differences in the two drugs was significant at the p=0.006 level.

TABLE 8

DOSE-EFFECT LINEAR CONTRASTS
Mood measures
Change scores, T2-T1

MEASURE	ALCOHOL		MARIJUANA		INTERACTION		DIFFERENCE	
	Value	p	Value	p	Value	p	Value	p
Anxiety	-7.55	0.168	13.85	0.012	0.25	0.984	-10.7	0.006
Detachment	-10.3	0.337	14.6	0.173	-4.9	0.838	-12.5	0.101
Depression	-0.05	0.994	9.35	0.147	-8.45	0.557	-4.7	0.302
Alertness	-18.6	0.017	9.00	0.244	25.1	0.147	-13.8	0.012
Tension	7.85	0.270	20.05	0.005	12.45	0.434	-6.1	0.225

TABLE 9

BLOOD ALCOHOL CONCENTRATIONS AND PULSE RATES

Contrast analysis for linear effect on dose.

MEASURE	ALCOHOL		MARIJUANA		INTERACTION		DIFFERENCE	
	Value	p	Value	p	Value	p	Value	p
B.A.C.	1.062	0.000	-0.005	0.775	0.002	0.951	0.534	0.000
Pulse Rate *	93.09	0.002	274.09	0.000	-91.38	0.175	-90.5	0.000
Estimated B.A.C.	0.485	0.000	0.030	0.588	-0.182	0.146	0.227	0.000

* Change in pulse rates, T2-T1.

(b) "Detachment". Neither alcohol nor marijuana produced a significant drug effect on this dimension. However the trend in this mood dimension for each drug was in opposite directions with alcohol tending towards a reduction in the detachment scale and marijuana towards an increase. The difference contrast between the two drugs approached but did not achieve significance ($p=0.101$).

(c) "Depression". Neither drug produced a significant effect on the self-reported mood scale. Alcohol was completely without effect whilst marijuana the trend was towards an increase in depression ($p=0.147$). The difference contrast indicated that there was no difference between the two drugs.

(d) "Alertness". The drug effects were in opposite directions on this mood scale with the effect of alcohol producing a significant ($p=0.017$) reduction in alertness. The trend for marijuana, though not significant ($p=0.244$) was in the direction of increased alertness. The difference between the two drugs on this mood scale was significant ($p=0.012$).

(e) "Tension". Marijuana produced a highly significant effect to increase the level of self-reported tension ($p=0.005$) whilst the effect of alcohol, although in the same direction of an increase in tension, was not significant ($p=0.270$). There was no significant difference between the drugs

on this mood dimension.

C. Physiological measures.

(i) The blood alcohol concentrations.

A highly significant linear effect of alcohol dose on the BAC was recorded ($p=0.000$) (see Table 9). The mean BAC achieved ($\pm$ S.E.M.) for each dose of alcohol is provided in Table 10. Marijuana had no effect on these values (Tables 10 and 11).

(ii) The change in pulse rate.

Both alcohol and marijuana produced a linear increase in pulse rate with increasing doses (Table 9). The increase produced by marijuana was significantly greater than that produced by alcohol ($p=0.000$).

(iii) Subjective assessment of blood alcohol concentration. At the completion of the first post-drug tests on the test battery and after the breath analysis had been made each subject was asked to estimate their breath alcohol concentration. The subjects were not given access to the results of their breathanalysis, and had been given no information other than that described under "Methods", ie that

TABLE 10

BLOOD ALCOHOL CONCENTRATIONS: ACTUAL AND ESTIMATED

ALCOHOL DOSE (g/kg)	ACTUAL B.A.C ± s.e.m. (n) (with THC placebo)	ESTIMATED B.A.C ± s.e.m. (n) (with THC placebo)	ESTIMATED B.A.C ± s.e.m. (n) (over all THC doses)
0.00	0.000 ± 0.000 (20)	0.026 ± 0.050 (20)	0.033 ± 0.003 (80)
0.25	0.027 ± 0.002 "	0.052 ± 0.010 "	0.047 ± 0.003 "
0.50	0.050 ± 0.001 "	0.052 ± 0.010 "	0.058 ± 0.003 "
0.75	0.083 ± 0.003 "	0.073 ± 0.010 "	0.070 ± 0.003 "

TABLE 11

THE EFFECT OF MARIJUANA ON THE BLOOD ALCOHOL CONCENTRATION

Mean B.A.C across all doses of alcohol with each dose of THC

Dose THC	placebo	2.5	5.0	10.0
Mean BAC	0.040	0.040	0.039	0.038
± s.e.m.	0.003	0.004	0.004	0.003

they were to be given alcohol and marijuana. The means (± SEM) of these estimates for each dosage group are shown in Table 10.

D. Performance measures.

(i) The general effects on the test battery as a whole.

The results are summarised in Table 12. It can be seen that alcohol exerted significant dose-dependent effects on simple reaction time, complex reaction time, the "little men" (mental rotation) test and the pursuit tracking task. Alcohol was without effect on the overall mean of all digit spans in the short term memory test.

The effect of alcohol on the "little men" test was to increase the error rate. The alcohol effect on the reaction times did not achieve significance.

Marijuana produced a dose dependent effect on choice reaction time, but not on simple reaction time. It exerted an effect on the "little men" test in the reaction time for the incorrect items but not for correct items. It was without significant effect on errors in this test. Marijuana was without effect on the pursuit tracking task. This drug however had a

TABLE 12
DOSE-EFFECT CONTRASTS
Performance Measures

MEASURE	ALCOHOL Value	p	MARIHUANA Value	p	INTERACTION Value	p	DIFFERENCE Value	p
S.R.T.		**						
Reg. Mean	48.50	0.002	14.21	0.35	-1.76	0.960	17.14	0.113
Reg. S.D.	105.85	** 0.003	23.0	0.52	20.86	0.796	41.41	0.104
Rand.Mean	182.69	** 0.003	-19.82	0.74	-372.8	* 0.006	101.26	0.018
Rand.S.D.	341.17	0.027	9.18	0.94	-860.0	0.094	165.99	0.068
C.R.T.		**		*				
Dir. Mean	147.41	0.001	115.4	0.007	47.36	0.600	16.0	0.594
Dir. S.D.	63.97	0.154	73.69	0.100	149.50	0.130	-4.86	0.88
Ind. Mean	177.42	0.021	50.30	0.500	-74.80	0.700	63.55	0.239
Ind. S.D.	158.92	** 0.002	138.3	0.008	-83.00	0.46	10.32	0.777
L.M.T.								
Correct Mean	350.22	0.010	22.79	0.870	-82.70	0.79	163.71	0.090
Correct S.D.	188.62	0.052	155.10	0.410	-225.5	0.590	106.34	0.426
Incorr.Mean	456.73	0.154	1050.40	** 0.001	-663.00	0.360	-296.85	0.193
Incorr. S.D.	108.98	0.729	595.30	0.060	214.60	0.760	-243.18	0.275
% Correct	-37.75	** 0.002	-23.55	0.052	-1.4	0.960	-7.1	0.407
TRACKING		**						
1st Mo.	19.51	0.003	6.46	0.330	-3.5	0.810	6.53	0.164
2nd Mo.	33.29	** 0.004	13.86	0.227	-19.00	0.450	9.71	0.231
S.T.M.								
Overall				**				
Mean	-2.53	0.212	-8.15	0.000	4.17	0.360	2.81	0.051
CENTROID	75.00	0.000	31.2	0.011	-31.73	0.244	21.9	0.011

** p<0.05 (with Bonnferroni correction ie 0.05/ number of planned contrasts)
ie 0.05/16 = 0.003
* p<0.1/16 = 0.006
Dir.=high stimulus-response compatibility
Ind.=low " " " "

significant effect on short term memory.

As can be seen in Table 12 the interaction factor failed to reach significance ($p<0.05$) in any measure in any of the tests. The analysis on the centroid (see below) also indicated a non-significant interaction factor. The effect of alcohol and marijuana in combination is therefore one of addition of the effects of the separate drugs.

A trend towards an interaction (though not achieving significance at $p<0.05$) was observed in the simple reaction time (random items).

An analysis of the composite (centroid) of all measures was completed to determine the comparative effects of each drug on the performance battery as a whole. The results of this analysis are shown in Table 12 where it can be seen that both drugs exhibited a significant dose-response relationship on the test battery, with the interaction factor indicating that the combination of these two drugs is one of simple addition.

The dose-response relationship of alcohol alone and in the presence of each of the doses of marijuana is depicted graphically in Figure 1. The effect of the different levels of marijuana (THC) on performance is depicted in Figure 2. In this figure, (and for figures 3 to 8) the value graphed for each dose

level of marijuana represents the performance change for all subjects who had taken that marijuana dosage level, irrespective of their alcohol dosage level. The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The absolute height of the bars represent the combined marijuana, alcohol and other effects such as practice, fatigue etc., on the T2-T1 (after drug minus before drug) performance change scores.

The contrast to compare the effects of each drug (in the doses used) on the test battery indicated that the effect produced by alcohol was significantly greater than that produced by marijuana.

(ii) A closer examination of the drug effects on each test.

The above comments have provided an overall indication of the effects of the two drugs on the test battery. Below is a description of the results obtained for each test examined in isolation. The significance levels have not been submitted to the Bonnferroni correction.

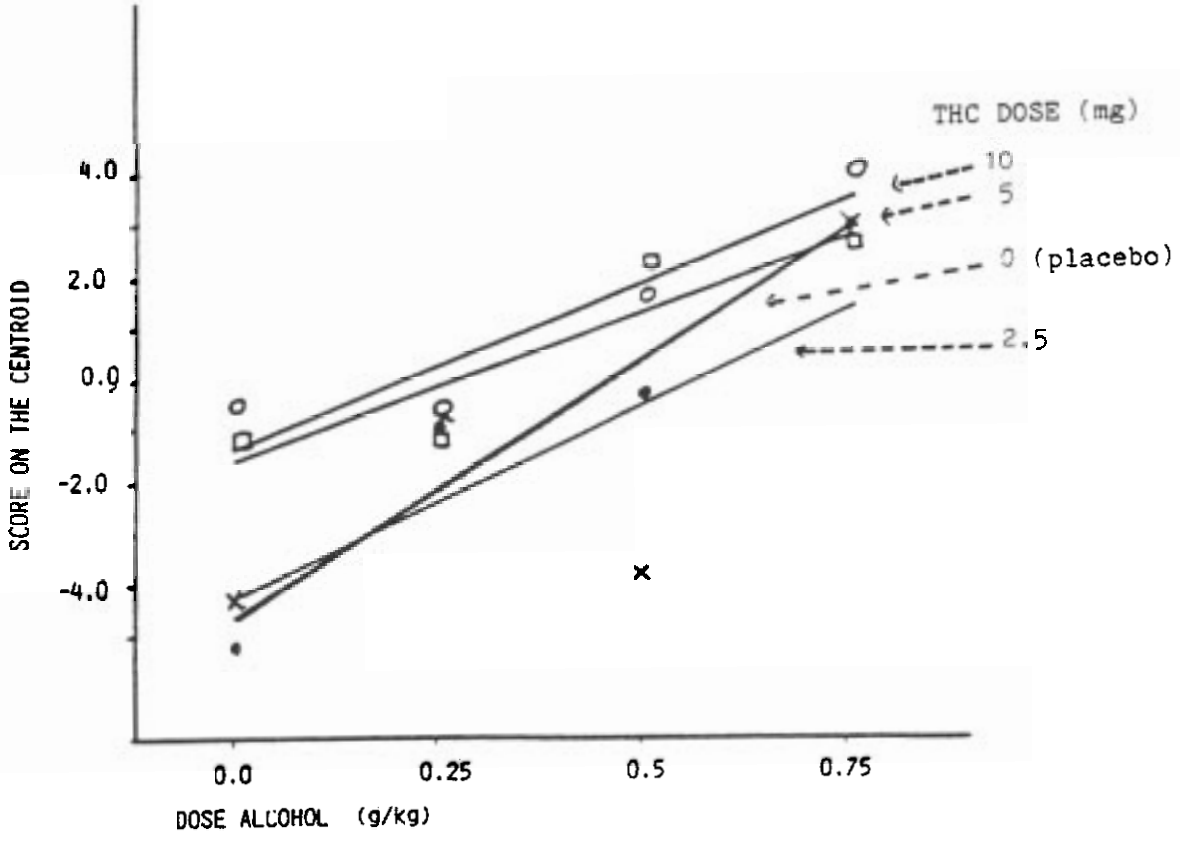

Figure 1 **The dose-response relationship of effect of alcohol** in the presence of each of the doses of THC. Response is expressed as the difference (T2 - T1) in the score on the centroid of the performance measures.

● = alcohol + THC placebo. × = alcohol + THC 2.5mg.
□ = alcohol + THC 5.0mg. ○ = alcohol + THC 10.0mg.

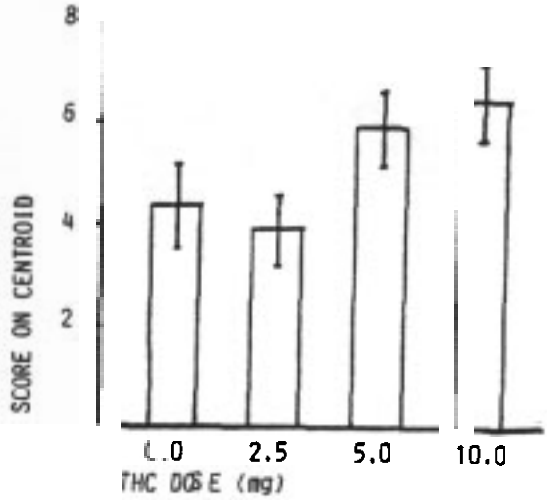

Figure 2 The Centroid. The effect of the different doses of marijuana on the difference (T2 - T1) in the performance score on the centroid. The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean.

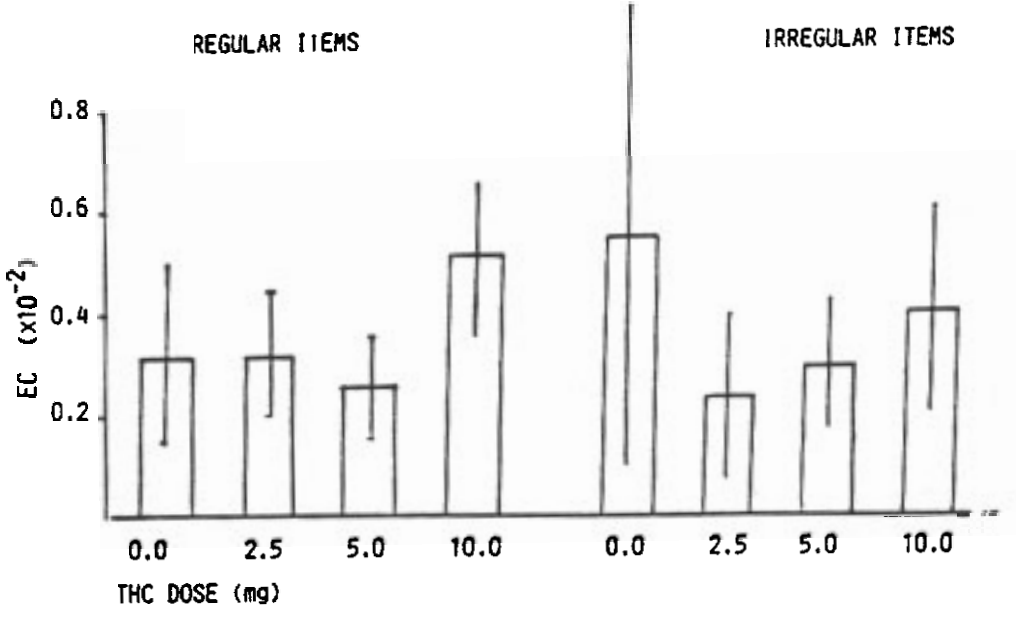

Figure 3 Simple Reaction Time. The effect of the different doses of marijuana on the difference (T2 - T1) in the responses to simple reaction time, to regularly and irregularly presented stimuli. The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean. The responses have been corrected for practice effect by subtracting from each drug combination score, the value (T2 - T1) for the double placebo group.

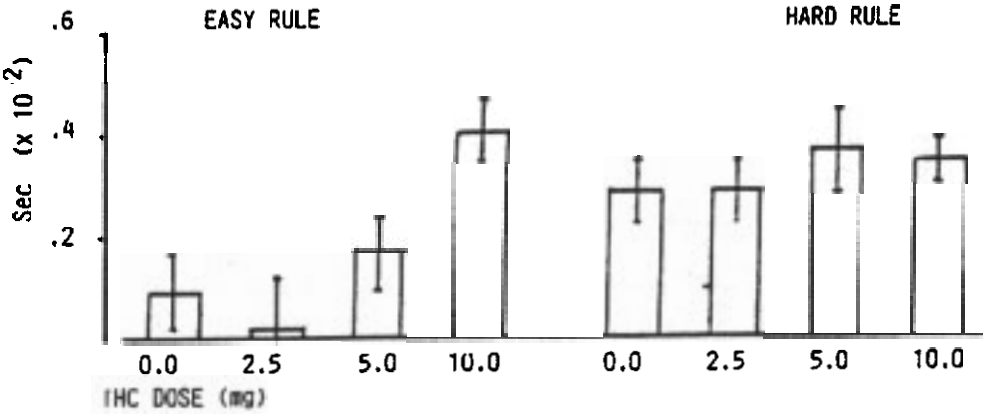

Figure 4 Choice Reaction Time. The effect of the different doses of marijuana on the difference (T2 - T1) in the responses to the choice reaction time. The change in the response times to stimuli with high compatability (Easy Rule) and with low compatability (Hard Rule). The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean. The responses have been corrected for practice effect by subtracting from each drug combination score, the value (T2 - T1) for the double placebo group.

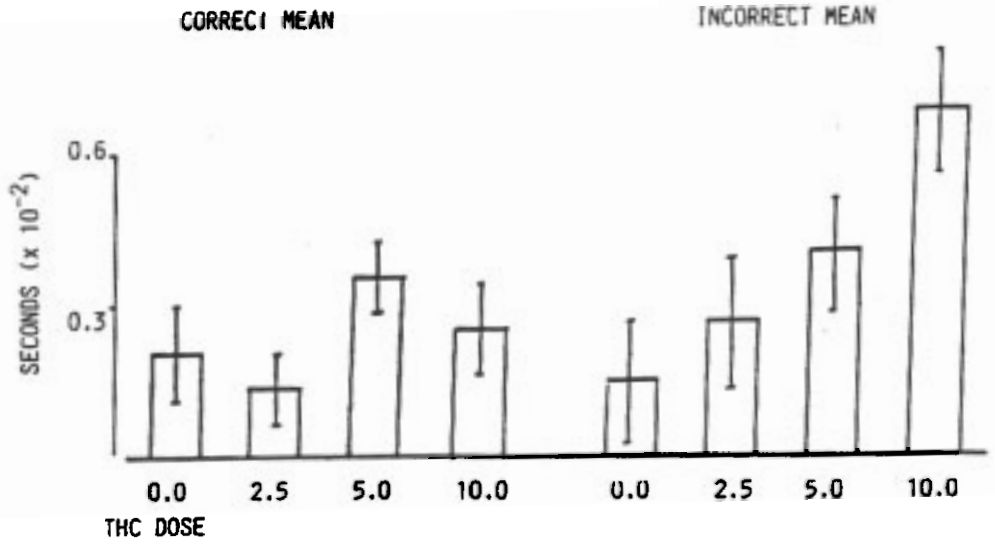

Figure 5 The "Little Men" test. The effect of the different doses of marijuana on the difference (T2 - T1) in reaction times for the correct items and incorrect items in the "Little Men" test. The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean. The responses have been corrected for practice effect by subtracting from each drug combination score, the value (T2 - T1) for the double placebo group.

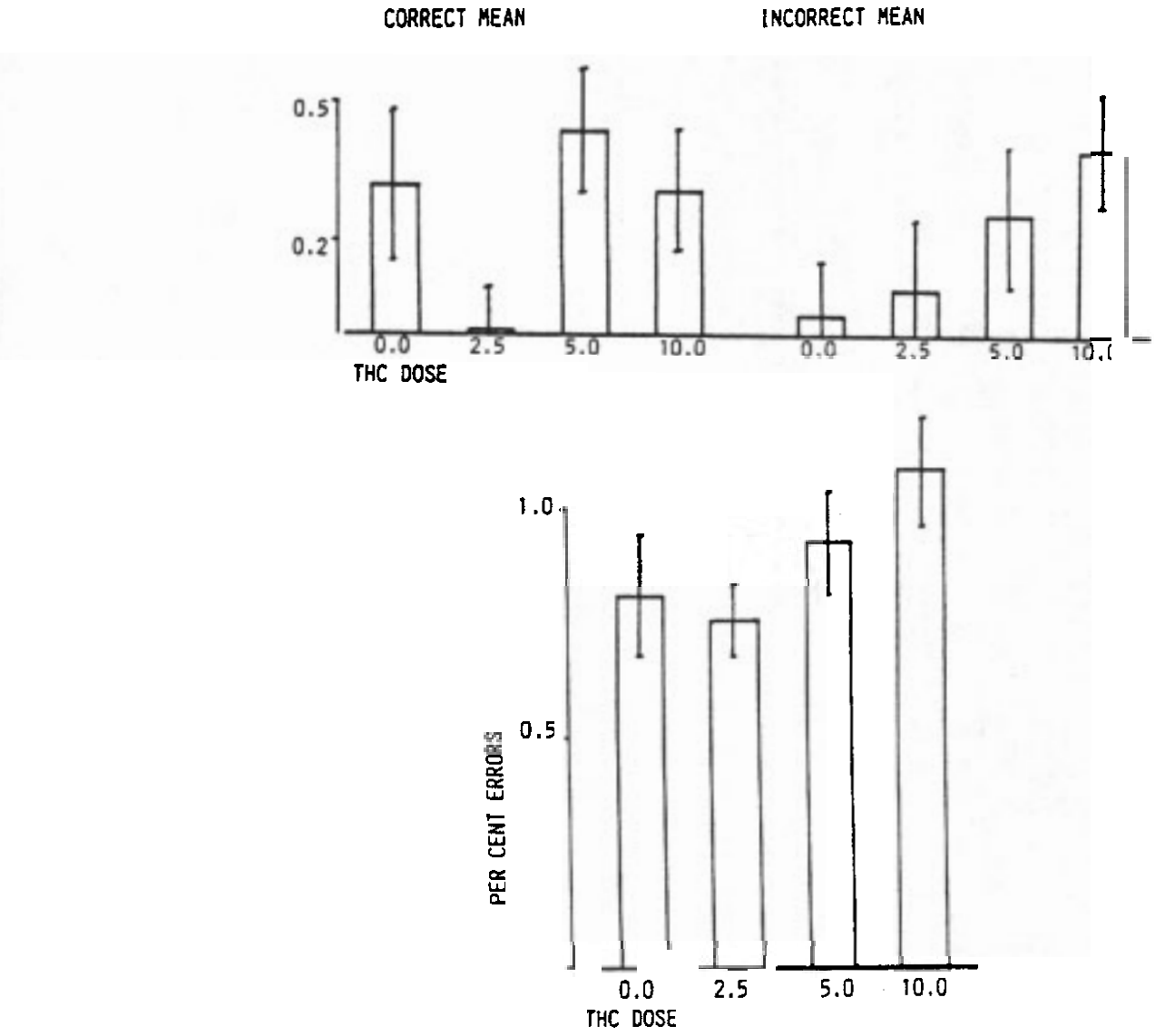

Figure 6 The "Little men" test: the standard deviation of responses. The effect of the different doses of marijuana on the difference (T2 - T1) in the standard deviation (the scatter about the mean) for reaction times to correct and incorrect responses (above) and the percentage error rate in responses (below). The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean.

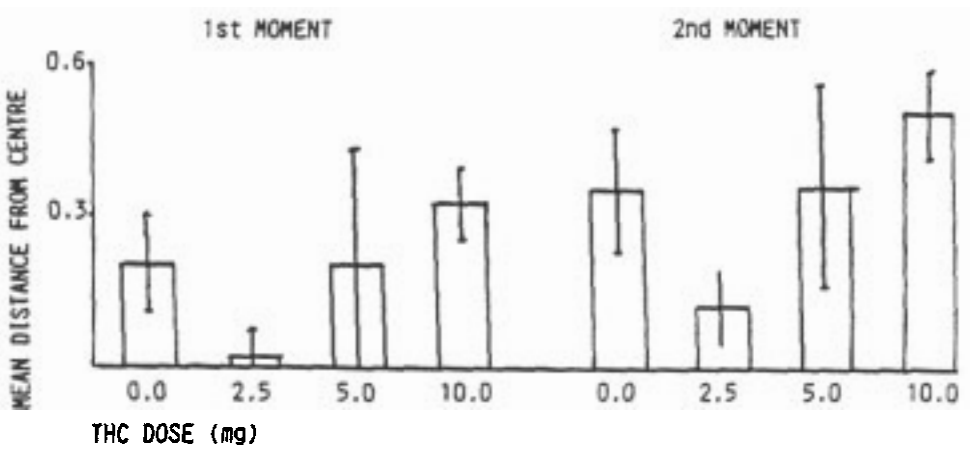

Figure 7. Tracking. The effect of the different doses of marijuana on the difference (T2 - T1) in the mean distance from the centre of the brackets during the tracking task. Results shown are the first and second moments. The relative height of each bar represents the overall effect of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean. The responses have been corrected for practice effect by subtracting from each drug combination score, the value (T2 - T1) for the double placebo group.

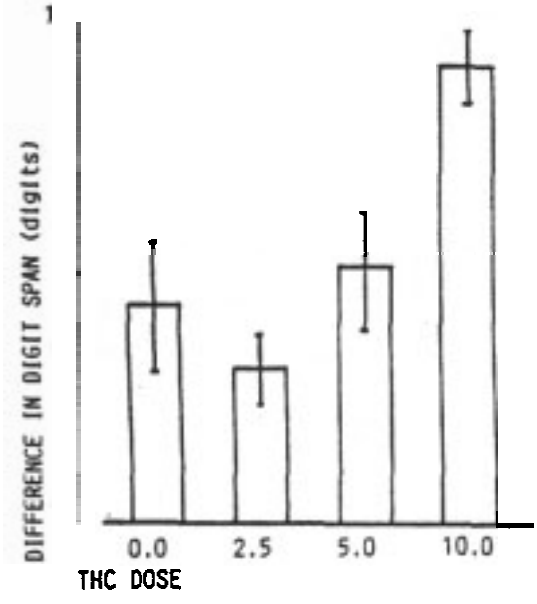

Figure 8. Short Term Memory. The effect of the different doses of marijuana on the difference (T2 - T1) in the overall mean of correct digit span recall. The relative height of each bar represents the overall effect (the reduction in the number of digits recalled) of the different marijuana doses when taken in combination with the varying doses of alcohol. The vertical bars represent the standard error of the mean. The responses have been corrected for practice effect by subtracting from each drug combination score, the value (T2 - T1) for the double placebo group.

(a) Simple reaction time

A significant dose-dependent effect for alcohol was demonstrated for simple reaction time, both for the regular and the randomly presented items. A significant dose dependency was also demonstrated for the standard deviation in the regular, but not the random items (see Table 12).

The actual extent of the effect is indicated by Table 13 which shows the change in reaction time ($\pm$ S.E.M.) between the measures recorded at T1 (before drug administration) and T2 (after drug administration). It can be seen that with the randomly presented items alcohol 0.5 and 0.75 g/kg doses significantly increased reaction times; $p<0.025$ for each contrast. With the regularly presented items, only for the highest dose (0.75 g/kg) was there a significant increase in reaction times ($p<0.01$).

Marijuana, on the other hand was without effect on this measure. Indeed there was a non-significant trend towards an improvement in reaction time after the drug on the irregular mean (see Table 12). This trend was no doubt the reason for a significant interaction contrast ($p=0.006$) for reaction time means and ($p=0.003$) for the standard deviation (S.D.) about these means.

The overall effect of the various doses of marijuana

TABLE 13

SIMPLE REACTION TIME

(a) The dose-dependent alcohol effect.
(across all doses of marijuana:Row totals; differences T2-T1)(n=80)

ALCOHOL DOSE	REGULAR ITEMS Mean ± s.e.m.	IRREGULAR ITEMS Mean ± s.e.m.
0.00	0.250 ± 0.10	-0.144 ± 0.45
0.25	0.017 ± 0.12	0.242 ± 0.11
0.50	0.355 ± 0.14	0.390 ± 0.15
0.75	0.765 ± 0.16	0.977 ± 0.45

(b) The dose-dependent marijuana effect .
(across all doses of alcohol:Column totals; differences T2-T1)(n=80)

THC DOSE	REGULAR ITEMS Mean ± s.e.m.	IRREGULAR ITEMS Mean ± s.e.m.
0.00	0.314 ± 0.17	0.545 ± 0.45
2.50	0.312 ± 0.12	0.234 ± 0.16
5.00	0.248 ± 0.11	0.294 ± 0.12
10.0	0.513 ± 0.14	0.394 ± 0.20

(in the presence of varying doses of alcohol) on the simple reaction time performance is shown in in Figure 3. The trend (though not significant) towards antagonism is seen in reaction times for both the regularly and irregularly-presented items.

(b) Choice reaction time

Both alcohol and marijuana exerted a significant dose-dependent slowing of the choice reaction time to the directly compatible rule, whereas neither drug produced a significant slowing of the reaction time to the indirectly compatable items. Both drugs however exhibited an effect on the standard deviation of the indirectly compatible items but had no effect on the variability of responses to the directly compatable stimuli. (Table 12).

The overall effect of marijuana dosage level on choice reaction time performance, in the presence of the varying doses of alcohol can be seen in Figure 4. There is little indication of any effect of marijuana on the reaction times to the "hard" rule (low compatibility) but a suggestion of first an antagonism with the lower marijuana dose and an increase in the reaction times with the higher doses with the "easy" rule (ie high compatibility).

(c) The "Little men" test.

These data are shown in Table 12. There were no significant dose-dependent changes produced by either drug in the overall reaction times for those stimuli for which the correct responses had been given. There was however a trend towards an increase in reaction times in the alcohol condition, but this failed to reach significance within the conditions of this analysis ($p=0.01$). On the other hand the reaction times for stimuli for which the response was incorrect showed a significant dose-response relationship for marijuana, but not for alcohol ($p=0.001$ and 0.157 respectively). Similarly, the error rate of the responses showed a dose dependent increase which was significant for alcohol ($p=0.002$) but not for marijuana ($p=0.052$).

The effect of the increasing doses of marijuana on the mean for all doses of alcohol are shown in Figures 5 and 6. The effects of marijuana on the reaction times to correct and incorrect items are shown in Figure 5 and the effects on the standard deviation of these responses are shown in Figure 6. A striking difference was observed in the effect of marijuana for the correct and incorrect responses. There was a trend towards an antagonism of the alcohol effect by the lowest dose of marijuana both to the reaction times and the standard error of these responses when the responses were correct. However, when the responses were incorrect both the reaction times and the standard

errors of these responses were increased by increasing doses of marijuana.

The effect of marijuana on the error rate in the responses in this test are shown in Figure 6. With the exception of the lowest dose of marijuana, there is a trend for an increase in the error rate with increasing doses of marijuana.

(d) Tracking

A significant linear dose-dependent decrement effect for alcohol was recorded on this task. There was no evidence for a linear relelation between dose of marijuana and the performance on this task. (see Table 12)

The effect of marijuana on the alcohol effect is depicted in Figure 7 where it can be seen that the antagonistic effect of the lowest dose of marijuana achieved significance. With the higher doses of marijuana the effect was towards one of an addition with that of alcohol.

(e) Short term memory

A highly significant linear relationship ($p=0.000$) exists between dose of marijuana and the effect of a reduction in the overall mean of the items successfully remembered in the forward digit span test. No such relationship was shown with alcohol ($p=0.212$). The difference between the two drugs ($p=0.051$)

failed to achieve significance within the Bonnferroni correction employed in this analysis. (see Table 12).

However the effect of marijuana on that produced by alcohol indicated an interesting trend (though non-significant) for an antagonism with the lowest marijuana dose. The highest dose was additive to the alcohol effect.

DISCUSSION

1. Introduction and overview.

The present experiment was designed to examine the dose-dependent relationship of the effects on performance and mood, produced by alcohol and marijuana when taken in combination. A basic principle in pharmacology is that drugs exhibit increased effects as one increases the dose. The dose dependency of alcohol is well documented (see Kalant, 1971). In two studies completed in this laboratory, the dose dependency of alcohol on a laboratory based test battery has been demonstrated (Franks et al 1976; Chesher et al 1984). Similarly the dose dependency of marijuana on a test battery in the laboratory has been demonstrated (Chesher et al 1984;1985). The analysis in these cases indicated that there were no significant departures from linearity in the regression of performance on dose. Therefore the first analysis of the data in the present experiment was to examine the linear effects of this regression. The interpretation placed on a finding of a significant linear effect is that this constitutes a significant drug effect.

The design of this experiment, with four dosage conditions for each drug and with cell groups to examine all of the possible interactions between these dosage conditions has produced data which contains a vast potential of information

awaiting the appropriate analysis. In view of our previous experience with these drugs, the analysis presented here should provide a general overall view of the nature of these interactions.

As indicated in the description of the analysis, the dose dependent effects of each drug are expressed (unless otherwise stated) as the effects in the presence of all doses of the other drug. Reference to Table 1 will clarify these analyses; the dose dependency of alcohol in the presence of all doses of marijuana is indicated by a comparison between the mean values of the horizontal rows. The dose dependency of marijuana in the presence of all doses of alcohol is indicated by a comparison between the mean values of the vertical columns. All of the figures presented in this report are expressed in terms of the vertical columns and depict therefore the influence of each dose of marijuana in combination with the various doses of alcohol. The absolute size of each of the histogram bars represents the mean of the combined effects of a particular dosage of marijuana taken with the various doses of alcohol, as well as other effects (such as practice or fatigue) which could also affect the T2-T1 (*after drug minus before drug*) performance change in addition to the effects of the drugs. The relative height of each of the bars represents the overall or "main effect" of the various doses of marijuana, in the presence of various levels of alcohol and other non-drug factors. Should marijuana have produced no "main effect", these bars would all be of equal dimensions.

Previous studies of the effects of alcohol and marijuana, alone and in combination which were conducted in this laboratory (with a different battery of tests) provided data which indicated that a single composite measure, such as the centroid, was likely to be particularly sensitive to the effects of the two drugs on the battery as a whole (Belgrave et al., 1979; Bird et al., 1980). The measures from which the centroid (composite) in the present study was derived are those in Table 12. The analysis on the centroid indicated a significant linear regression of the performance measures with dose for each drug. As the interaction factor for this relationship was not significant, we can conclude that the effect of the two drugs when taken in combination is essentially one of the addition of the separate effects of each of the drugs. Results from this and previous studies (Chesher et al 1984, ; Belgrave et al., 1979; Bird et al., 1980) have indicated that both drugs have a general tendency to produce performance deficits. As can be seen in both Figures 1 and 2, there was a trend for the lowest dose of marijuana to exert an antagonistic effect on that of alcohol. Within the present analysis this effect was not significant. However the analysis for any departures from linearity of the regression of effect on dose has yet to be completed and cannot be presented in this report.

The analysis of data provided in Table 12 indicates

that the predominant drug effects on the test battery were produced by alcohol. Although the centroid indicates that marijuana produced significant dose dependent effects, these were quantitatively less striking and qualitatively different from those of alcohol. The effect of marijuana when taken in combination with alcohol on the performance measures are demonstrated in Figures 1 to 8 which show the effect of the increasing doses of marijuana. The main aspects of these drugs when taken in combination will be discussed below. First however, it is necessary to establish the equivalence in terms of social usage of the doses of each drug used as well as to point out the nature of the population of volunteers from whom these data were collected.

2. Were the drug doses used equivalent in terms of common social use?

In a study of this nature in which a direct comparison is to be made of the effects of two drugs it is of obvious importance that the doses chosen for each should, as far as possible, be of equivalent effectiveness on the measures tested. More specifically, the doses should produce effects of subjective intoxication which are as near as possible, equivalent. Of equal importance in dosage selection is the consideration of the social relevance of the dosages employed. The doses should be within

those commonly in social use. On both of these accounts the selection of doses for alcohol presents very few problems. There is an abundance of information concerning the nature of human performance deficit with various concentrations of alcohol in the blood (see Perrine,1973; Moskowitz & Austin,1979). In addition to this are the epidemiological data which indicates the increased probability of road crash involvement with increasing blood alcohol concentrations of the driver. The social relevence of alcohol dosage is also reasonably understood, primarily because alcoholic beverages are of standardized potency and the collection of drinking histories can be rapidly converted into a reasonably accurate estimate of alcohol intake.

The selection of the alcohol doses in the present study was dictated in the first place by the nature of the investigation. Being an interaction study the alcohol doses should not be so high as to obscure the hypothesised additive effects of marijuana, or to produce a degree of intoxication which was too great for the volunteers. The doses were chosen to be within those commonly used in social situations in this country and generally regarded as being moderate. The blood alcohol concentrations achieved confirmed these intentions, the highest dose producing a mean BAC of approximately 0.08g%.

Unfortunately, the equivalent information concerning marijuana to assist in the selection of socially relevant and equi-effective (to alcohol) doses is still inadequate. Whilst it has been consistently demonstrated that the drug is capable of

producing a decrement in human skills performance (Chesher et al 1976,1977,1984; Belgrave et al 1979; Bird et al 1980; Klonoff 1983), both in laboratory based tasks and on the road in a motor vehicle, the data available do not permit us to quantitatively compare marijuana with alcohol. An attempt to do this was undertaken in this laboratory (Chesher et al 1984) in a series of studies using a different test battery from that employed here. As a result of this study, and that of a pilot study (with computerised tests from which the present tests were derived) involving 50 volunteers, the present doses of THC were chosen. The previous study suggested that THC doses of 10, 15 and 20 mg produced effects on that test battery which were towards the peak of the dose-response curve. In the pilot study we encountered a high incidence of vomiting with the combination of 15mg THC with the 0.75g/kg alcohol dose. We therefore deleted the 15mg dose of THC and inserted the low dose of 2.5mg THC into the design.

It is a much more difficult task to justify the social relevance of these doses. Marijuana is an illicit substance and is not therefore subjected to quality control. Some idea of the doses socially used may be obtained from the analysis of street samples, usually those seized by law enforcement procedures. However, within recent years the potency of these samples has increased to a very significant extent. It is very difficult therefore to determine what the commonly employed doses of THC might be. One method, and that employed in this study, is to determine the subjective assessment of the effect of the doses

employed in relation to the previous experience of each volunteer with the drug. This was done by the use of the horizontal analogue "stone" scale. This scale records the subjects assessment of the drug's effect from that described as being no effect at all to the extreme of being "as stoned as I have ever been". A similar assessment with alcohol was used and the results indicated that the subjects rated the effects of the marijuana doses as being equivalent to, or of greater intensity than those of alcohol. We therefore may regard the dose selection to be of some social relevance and at acceptable levels for a comparison of the two drugs both alone and in combination.

3. The volunteer population.

The interpretation of the data derived from this, or from any study should be considered in the light of the population sample used. All subjects were non-naive as regards to marijuana use. In view of the size of the sample, volunteers were sought by advertisements on Sydney radio stations which specialize in contemporary "rock" music. Although all marijuana users, the population sample cannot necessarily be regarded as representative of marijuana users. One descriptor of the population was provided by responses to the drug-use questionnaire. However, honesty in the responses to the questions cannot be verified, nor did we attempt to do so. Nevertheless,

the data collected enable us to describe the population sample as being moderate users of alcohol and, heavy to very heavy users of marijuana. The distribution of subjects to dosage groups was conducted according to a previoulsy prepared random table as described in Methods. A distribution analysis for the various items of self-reported drug use history indicated that the distribution according to these variables was homogenous throughout all groups.

4. Responses to the intoxication rating scales.

As indicated above, the results of the "stone" and "drunk" scales (when each drug was taken alone i.e. the active drug in the presence of the placebo condition of the other) suggested that the doses employed of each drug were rated within the limits of the regular experience of the subjects, the mean scores being considerably less than the maximum of 15 which in each case represents the maximum effect ever experienced by the subject in their use of the drug(s) (Table 6a & 6b). Furthermore, there was a decided trend (on the "stone" and "drunk" scales) for the specific effect attributed to marijuana to be assessed as being greater than that to the doses of alcohol employed. On the "stone scale" the rating for the middle dose of marijuana (5mg THC) was significantly greater than that produced by the middle dose of alcohol (0.5g/kg).

However, other information provided in this study

indicates that this interpretation must be considered with caution. First, the responses to the two other questions designed to quantitatively rate intoxication ("How overall affected do you feel by what you have taken" and "How do you rate this effect") suggested that that alcohol alone (ie with placebo marijuana) produced a more profound subjective effect than did marijuana alone (ie with placebo alcohol). Possibly, the placebo response to the alcohol condition may have influenced this difference. The expectancy effects for both drugs in the study was high because subjects were given no information at the outset about the dosage groups of either drug. As all subjects were expecting to receive both drugs the placebo response in to both was quite high. A design of this nature has decided advantages as it provides some control of expectancy effects associated with the drug to be taken.

The question "how do you rate this effect" when put to the rather devoted population of marijuana users would be unlikely to be answered in the direction of being "too much affected". The volunteers were weighted towards heavy marijuana use and there could have been a reluctance to describe the effect in these terms. The attitudes of the population towards alcohol as exhibited in the drug attitude questions might similarly have influenced the responses to alcohol effects and inflated these values relative to those to marijuana. It is possible therefore that this question might have been affected by value judgements related to each drug as the population exhibited a decided

preference for marijuana.

5. The ability to distinguish the effects of alcohol and marijuana.

Also of interest was the comparative ability of the subjects to distinguish the effects produced by one drug when both had been taken in combination (Table 6 c). The presence of marijuana had no effect on the ability to rate the effect of alcohol on the "drunk" scale. However, the presence of alcohol had a significant effect on the ability of the subjects to rate the degree of marijuana intoxication on the "stone" scale.

Evidence provided by the "stone" scale (Table 6 b) also suggests that the subjective effect produced by smoked marijuana may be nearer in nature to an "all or none" effect. Although the linear contrast analysis indicated a significant linear relationship between the doses of marijuana, the scores for marijuana only (with alcohol placebo) dosage groups suggested little difference beteen the 2.5mg and 10mg doses. This, together with the apparent inability to distinguish the intensity of marijuana effects in the presence of alcohol suggests that the effect of marijuana is more subtle or elusive than that of alcohol and perhaps more susceptible to expectancy effects. This suggestion is supported by the findings of Ashton et al (1981). In describing the mood scales to the subjects it was clear that

there was no confusion as to the distinction between the terms "drunk" as describing the effect of alcohol and "stone" as it relates to the effects of marijuana.

6. The mood effects of alcohol and marijuana.

The mood scales devised by Ashton et al (1978) provide in five horizontal analogue scales, the ability to collect information in five mood dimensions described as "anxiety", "alertness", "depression", "detachment" and "anxiety" (see Appendix 1). Although greater reliability could have been obtained from the use of a greater number of questions for each of these scales, we believed that the simple form of the Ashton scales were much more easily understood by the intoxicated subjects. In some cases some effort and encouragement had to be given to the subjects (especially in the combination doses) to complete these scales. We cannot assess the extent to which this encouragement might have influenced the results. The intervention was necessary to overcome the subjects' conflict of interest between the task of completing the mood scales and to continue the enjoyment of the social interaction with other volunteers.

The mood effects, as with the performance data were analysed as the effects of the drug combinations as decribed in DATA ANALYSIS. The effects described as being due to marijuana are those to each dose of marijuana in the presence of all of the

various doses of alcohol; those described as alcohol effects are those in the presence of all of the doses of marijuana.

The results obtained have provided interesting information which points to the difference in the subjective effects produced by each drug. In all but the mood dimension "tension", each drug produced changes from the pre-drug assessments, the trends of which were in opposite directions. The effects for marijuana, which indicated a significant linear effect on dose were recorded on the scales described as "anxiety" and "tension", the effects in each case were an increase in each dimension. The adjectives describing these directions of change suggest a similarity of the mood effects for each. "Anxiety" was defined as "worried, jittery, afraid, no confidence" whilst "tension" was defined as "tense, impatient, on edge, restless, keyed up". The "difference" contrast analysis indicated that the difference between the two drugs was significant for the "anxiety" mood scale.

A significant linear effect was obtained for alcohol in producing a reduction in the "alert" mood scale. The trend for marijuana on this scale was towards an increase in alertness. The difference between the effects of the two drugs on this mood dimension was significant. The direction for the alcohol effect was described by the adjectives "lethargic, slow, muddled, bored, dopey".

Although not showing a significant linear relationship, marijuana indicated a trend ($p=0.173$) towards an

increase in the mood "detachment", which was defined by the adjectives "detached, uninvolved, impersonal, quiet".

The direction of change in these mood scales suggest that alcohol and marijuana are drugs with quite different mechanisms of action. The effects of alcohol are clearly those of a central nervous system depressant; those of marijuana appear to be of a different nature and have been described by some as being more in keeping with those of a mild hallucinogen. This suggestion is also consistent with the more subtle nature of this drug's effects and the ability of alcohol to interfere with the subjective identification of the effects of marijuana. They are also consistent with an interpretation of some of the effects of this drug on performance measures described in this and other studies (Sharma & Moskowitz, 1974) as being in the nature of an increase in distractability or a reduction in attention.

7. The driving-related questions.

Similar comments to the above might be applied to the results presented here of the responses to the driving related questions (Table 7). Whilst alcohol produced a significant linear relationship with dose of the assessment of one's ability to drive a motor car, and of the statement of intention of driving a vehicle "as you feel now", there was no such relationship for either question with marijuana. There are a number of

interpretations of these results but one which is consistent with the results discussed above relates to the subtle nature of the effect of marijuana and the apparent lack of the subjective mood effects which would be associated with a depression of the central nervous system. Alternative considerations must however be given to an interpretation of the answers to these questions. The public awareness of the effects of alcohol on driving-related skills has been greatly increased within recent years as a result of the drink-driving campaign and the introduction of the "Breathalyzer" legislation in N.S.W. It seems unreasonable to expect that this information would be without effect on the reponses made to the driving related questions.

The subjects were equally aware of the inability of the police to detect marijuana intoxication so the expectation of being caught and convicted is very low. Although many of the volunteers admitted to driving whilst "stoned" many agreed that the drug did affect their driving skills and that they "drove more carefully and slowly" on such occasions.

8. The performance measures.

The differences in the subjective effects of alcohol and marijuana described above are also apparent in the results on the performance measures. The predominant effect on these tests was undoubtedly exerted by alcohol. The approximate equivalence of the doses of alcohol and marijuana in subjective terms has been discussed above and the social relevance of the differences in the effects of the two drugs on the performance measures is therefore of significance.

The main dose-dependent effects of alcohol, as indicated in Table 12, could broadly be described as a slowing of reaction times both simple and complex, a clear trend towards a slowing of reaction times in the little men test, and a significant effect in increasing the error rate in this test. The effect on the error rate occurred with very little effect on the standard deviation of responses to the incorrect items (the standard deviation is a measure of the scatter of the responses about the mean). Alcohol also exerted a significant effect on the tracking task, but had no effect on short term memory.

The main effects of marijuana were observed in the test of short term memory, choice reaction time, and on the reaction times for the items in the "Little men" test when the responses were incorrect. The standard deviation of these

responses indicated a strong effect which approached significance. This effect indicated that the response times varied considerably in a dose dependent manner. Similarly, the error rate in this test approached significance for the marijuana effect. These data indicate qualitative and quantitative differences in the effects produced by the two drugs. However as the experiment was designed specifically as an interaction study, an interpretation of these differences is more appropriately discussed after an examination of the nature of the drug interactions recorded.

9. Alcohol-marijuana interactions on the performance measures.

In view of the fact that the main drug effects exerted on the test battery were those of alcohol, and as our present understanding is that this drug is the major contributor to drug-related road fatalities, the figures 1-8 which present the results in this interactive study have been expressed in terms of the effects of marijuana superimposed on the effects produced by alcohol. The latter was calculated as the difference in responses after (T2) minus the effects before alcohol (T1). The magnitude of this difference is depicted in Figures 2 to 8 in the form of histogram bars. If we begin with the null hypothesis, that marijuana exerts no main effects on those produced by alcohol, we would expect that the size of the bars, (each with the various doses of marijuana) would remain unchanged.

A measure of the extent of the drug-induced performance measure changes on the test battery as a whole is given in the calculation of the centroid, the results of which are provided in Table 12 and depicted graphicaly in Figures 1 and 2. The calculation of the linear contrasts in Table 12 indicated that both alcohol and marijuana exerted a significant dose dependent effect on the test battery and that the effect of the drugs in combination, as indicated by the non-significance of the interaction factor, was one of addition.

As can be seen in Figure 1, which is a graphical representation of the dose-response relationship of the effects of alcohol in the presence of each of the dosage conditions of marijuana, the two higher doses of marijuana (5 and 10 mg) increased the intensity of the effects produced by alcohol. There was a trend however for the lowest dose of marijuana (2.5mg) to reduce the magnitude of the alcohol effect. Figure 2 which represents the mean of the response change to all of the alcohol doses demonstrates, perhaps more clearly, the nature of this drug effect. It is instructive therefore to examine the nature of this drug interaction in terms of the mean alcohol effect for each of the tests individually.

(a) Simple reaction time (Figure 3).

Alcohol produced a significant dose-dependent increase in simple reaction times, an effect which is worthy of mention in

view of the relatively low blood alcohol doses employed. The alcohol effect showed significance as a dose dependent increase in reaction times, both to the items presented at regular and random intervals. Similarly, when examined as effects of individual doses the reaction time measures were significantly slowed for doses of 0.5 and 0.75 g alcohol/kg. These main effects for each alcohol dose were of course values in combination with all of the various doses of marijuana. As Moskowitz and Austin (19) have pointed out in their literature review of the effects of alcohol on human skills performance, simple reaction time is generally not affected at these low doses of alcohol. The results described here therefore must be seen as an example of the additive interactive effect of marijuana with alcohol. Nevertheless, the effects of marijuana alone on simple reaction time were very slight. As can be seen in Table 13 and Figure 3 the effects exerted by marijuana on the simple reaction time measures were not significant. It is worth noting the suggestion (though not significant) for an antagonism by marijuana of the effect produced by the various doses of alcohol on the reaction times to the irregularly presented items (figure 3).

(b) Choice reaction time (Figure 4).

Both the alcohol and marijuana effects on choice reaction times for the items with high stimulus-response compatibility showed a significant linear dose-response

relationship. Although alcohol also showed a significant dose-dependent slowing of reaction times for the low compatiblity items, that for marijuana failed to reach significance (Table 12).

The results depicted in figure 4 show more clearly the effect of the each dose of marijuana in combination with the various doses of alcohol. Once again, although the differences between dosage groups were not significant, there was a decided trend towards an additive effect between the two drugs at the 5 and 10 mg THC doses of marijuana. However, a trend was observed in the direction of an antagonism in the effects of the combination of alcohol with the 2.5mg THC dose of marijuana. These effects were observed in the reaction times to the high compatibility rule of choice reaction times. With the more complex rule (low compatibility), the antagonistic effects of the drugs was much less apparent.

(d) "Little men" test (Figures 5 & 6).

The results obtained with this test have provided evidence similar to that described for the other reaction time measures and also have suggested interesting qualitative differences between the two drugs. The nature of the alcohol-marijuana interactions in the responses to this test differed according to whether the response was correct or incorrect. The drug interaction for those responses which were

correct (Figure 5a and 6a) was similar to those described for simple and choice reaction time measures. The lowest marijuana dose indicated a trend, though not significant, towards a reduction in the alcohol effect on the reaction time for the correct items. The standard deviation of these responses (figure 6 a) also indicated a drug antagonism which did achieve significance ($t=1.9875, df\ 158; p<0.05$.)

It is noteworthy that the reaction times and their standard deviations for the items for which the response was incorrect indicated a drug interaction of a different nature. Increasing doses of marijuana were additive to both the alcohol related increases in reaction times and their standard deviations (fig.5b & 6b). A similar interaction is also indicated in the error rate (Fig.6c). There was a slight suggestion in the responses to these interactions for the antagonistic effects with the lowest marijuana dose as described in other tests.

Two possible interpretations for the difference in the drug interaction for the correct and incorrect responses might be offered. The first interpretation is consistent with the previously described differences in the effects of these two drugs in what might be termed a "speed-accuracy trade-off". It has been suggested that under the influence of alcohol, subjects show a greater willingness to take a risk, or the make a guess at the appropriate response. However, with marijuana, evidence suggests that subjects are less willing to do so (Casswell,1977; Dott, 1972; Ellingstad et al, 1973). The present results could be

seen in this light because with increasing doses of marijuana the reaction times to the incorrect items as well as the standard deviations were increased. This might infer the expenditure of a longer time to ponder a difficult problem when marijuana had been taken. In view of previous studies which have indicated these differences between the effects of alcohol and marijuana, a further study of the comparative effects of these two drugs on risk-taking behaviour is warranted.

The second interpretation offered is that marijuana might have produced periodic attentional deficits and it was this effect which prolonged reaction times and the standard deviation of these responses. An assumption with this interpretation is that the attentional lapses are more likely to occur during the solving of the more difficult problems which require longer solution times, and which are more likely to be accompanied with incorrect responses. This is consistent with data (not presented here) in which the performances on subsets (defined a priori in terms of difficulty of the "little men" items) were analysed separately. Here it was found that there was a significant linear dosage effect for the variability of responding (S.D.) for the most difficult items for marijuana but not for alcohol. This occurred for both the correct and incorrect responses. Another aspect of these data, consistent with the attentional lapses hypothesis, is that the change in the drug effects for increasing difficulty of items was greater for marijuana than for alcohol. This interpretation is of course tentative, but it does suggest

an area for further research.

(d) The tracking task (Figure 7)

The effect on this task was predominantly that of alcohol, there being no evidence for a linear drug dependent effect for marijuana (Table 12). The effect of the different doses of marijuana in combination with the various doses of alcohol is depicted in Figure 7. Here the apparant antagonism of alcohol by the low dose of marijuana is once again in evidence. The difference between these groups just failed to reach significance ($t = 1.7015$; when for 158df, $t = 1.9751$ at $p = 0.05$).

In a previous study in this laboratory (Chesher et al 1984;1985) marijuana was found to exert a significant dose-dependent effect on a pursuit rotor task, a task generally considered to be relatively insensitive to the effects of alcohol (Moskowitz & Austin,1979). In this study, the subjects were tested whilst standing. In this same experiment, marijuana was found to produce a significant effect on standing steadiness. The subject was required to stand upright and still whilst performing each of these tasks. In the earlier study these two tests were the most strikingly sensitive to smoked marijuana of the tests used. In the present study, subjects were seated during the performance of all tasks. In view of the effect of marijuana in producing a postural hypotension, the possibility that the effect

of marijuana on tasks requiring the subject to stand still for any period of time might be related to the postural hypotensive changes induced by the drug must be seriously considered. An investigation of this possibility is warranted.

(e) Short term memory (Figure 8)

The drug effect on the forward digit span task was a highly significant linear effect for marijuana. The effect of alcohol, although not significant on the overall mean of responses did show a trend toward a decrement in this task. The effect of the various doses of marijuana in the presence of alcohol, as depicted in Figure 8 show that the dominant effect is one of addition between the two drugs. An examination of figure 8 indicates once again a suggestion for an antagonism between the lowest dose of marijuana and alcohol.

10. The apparent antagonism between alcohol and marijuana.

Whilst the major actions on the performance measures in the test battery of alcohol and marijuana when taken in combination was to produce effects in the same direction, there was a consistent trend throughout for an apparent antagonism of the alcohol effect with the lowest dose of marijuana. Evidence for such a drug antagonism has been presented in earlier studies in this laboratory (Chesher et al 1977) and others (McEvoy and

Marks,1975; Stein et al 1983). The mechanism for this apparent antagonism cannot be sought in an effect by marijuana on the metabolism or distribution of alcohol because it has been clearly demonstrated in the present study and in others (Chesher et al 1976;1977; Bird et al 1980; Kalant & LeBlanc 1974; Siemens & Khanna, 1977) that marijuana had no effect on the blood alcohol concentration. The impressive nature of the evidence for this antagonism is that it was observed in all of the tests of the battery. Although the phenomenon achieved statistical significance in only one case its consistent presence in all tests is sufficient confirmation that such a drug interaction exists. Further evidence for antagonistic effects of the two drugs was described in the results of the mood scales where the drug induced changes were in opposite directions for all but one mood dimension.

11. Implications regarding the comparative effects of alcohol and marijuana.

It is quite clear that the main drug effects on human performance skills which were recorded on the test battery were those of alcohol. Although marijuana did show evidence for performance decrements, these were of a lesser severity within the doses employed. As the doses employed were considered to be of equivalent social relevance it seems that alcohol remains the drug of major concern for its role in performance impairment. The

performance measure which exhibited the greatest sensitivity to marijuana in the present study was that of short term memory. This is consistent with earlier reports of the effects of marijuana and does have relevance to the driving task as has been pointed out by Rumar (1982).

However, as has been so elegantly discussed by Naatanen and Summala (1976) impairment alone is not necessarily the sole determinant of the danger of a drug to the driver of a motor vehicle. "The demands of the driver's task are more a function of the driver's choice than of the characteristics of the task itself". The attitude and motivation of the driver, and their self-assessment of the status of their own driving skills on any given driving occasion will influences the manner (ie carefully or with risk-taking) in which they will drive. The possibility that drugs can influence these motivations and decisions of drivers has only recently been addressed in research studies. The effects of drugs on the self-awareness of drug intoxication is also of obvious importance. Of interest in this regard is the present finding that the effects of the two drugs on the mood scales were so different. Worthy of mention in the driving context are the findings on the mood scale of "Anxiety". In this scale, alcohol showed a tendency to increase those feelings described as "assertive, brave, confident and self-assured" whereas marijuana decreased this mood dimension and increased feelings described as "worried, jittery, afraid, no confidence". This self-assessment is consistent with the

interpretation placed on the performance measures which suggested a "speed-accuracy trade-off" with alcohol but not with marijuana. Alcohol increased the willingness of the subject to take a risk, marijuana may have decreased this willingness. Results from other investigators have also reported similar findings, particularly in a simulated overtaking task on a driving simulator. Studies with driving simulators as well as those using a real vehicle have consistently reported that under the influence of marijuana, drivers tend to drive more slowly and are less willing to take a risk. Under the influence of alcohol, subjects show an increased willingness to take a risk. Further studies of the effects of drugs on human moods and motivations and of the effects on behaviours involving risk-taking are recommended.

12. Potency comparisons of alcohol and marijuana

When the effects of two drugs have been examined on the same test battery it is tempting to make a direct comparison of the potency of the drugs in producing a decrement in performance on the tests. Such a comparison was made with data generated in this laboratory (Chesher et al 1984;1985). The data from this study provided no indication that there were qualitative differences in the effects produced by the two drugs. It was considered valid therefore to make an estimate of the potency ratio of the drug effects. A tentative estimate (though not valid because the dose-response curves were not parallel) was

made of the comparative potency of alcohol and marijuana on the test battery. The calculation suggested that a dose of 1 to 2 mg THC smoked produced an equivalent performance decrement on the test battery used as that produced by alcohol when the peak BAC was 0.05 g%.

However, as the findings of the present study indicate that the two drugs are producing effects which are qualitatively different, the validity of making comparisons of a quantitative nature between alcohol and marijuana by examining the composite measure of performance on the battery as a whole, is questionable. Because of this and in view of the striking difference in the extent of the performance decrements produced by alcohol and marijuana in the present study, the potency ratio of the two drugs determined in the 1984 study was more carefully examined. As has been mentioned above, the tests in which the marijuana dose-dependent effects were most striking were standing steadiness and the pursuit rotor. These tests were the only tests in the battery which required the subjects to stand still. All other tests were completed with the subject seated. It is quite possible therefore that the effects of marijuana in producing a postural hypotension and presyncope or syncope (ie dizziness or fainting) (Benowitz & Jones1975; Weiss et al 1972;) could have significantly influenced the results. This possibility has been further investigated in our laboratory. In preliminary studies we have recorded a dose-dependent marijuana induced postural hypotension and have evidence to suggest that this effect is

reproducible for at least fifteen minutes in some subjects (unpublished data). Quite clearly, these findings must be more carefully and extensively studied. In the mean time however, one might speculate that an implication of these findings is that some domestic or industrial accidents might occur to marijuana smokers if the occupation requires the worker to stand still for any length of time, such as operating a lathe or similar machinery or standing on a ladder.

13. Speculative proposal for alcohol/marijuana differences.

The different directions of change, both qualitative and quantitative, produced by the two drugs, both in mood and performance measures, are findings which point strongly to the directions of research which might reveal more information about the mode of action of each of these drugs. Indeed, the data presented in this study and others provide the authors with the luxury of some speculation.

Although the mechanism for the apparent antagonistic effects of marijuana and alcohol under some conditions is at present unknown it provides further evidence to that discussed earlier that the two drugs, alcohol and marijuana are exerting their effects by different mechanisms. The effect of marijuana appeared in this study to be more discrete or subtle than that of alcohol in both the subjective and performance measures. It is tempting, in the light of present evidence, to speculate about

the possible modes of action of these two drugs. It has been proposed that the active cannabinoid, THC, may be acting upon a specific binding site. One might speculate that the proposed binding site (if or when found) might not be homogeneously distributed within the nervous system, and that the more selective nature of the drug's action could be explained by a proposal that it is acting on specific nerve pathways involving only those nerve cells which bear the proposed binding site. This speculation is also consistent with the proposal that marijuana's effects might be sought more closely by examining the effect of the drug on more selective mechanisms such as attention.

Alcohol, on the other hand appears to produce effects which are less discrete and possibly involve a mechanism which does not depend upon a specific binding site and more generalized in its actions. The mode of action of alcohol is still unknown, but the drug is known to produce changes in the structure and function of the nerve cell membrane. Such effects would be more widespread within the central nervous system and the selectivity of the nerve cells upon which the drug acts could be more dependent on drug distribution and to physical factors than to the presence of specific binding sites.

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APPENDIX 1.
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1. Eysenck Personality Questionnaire (E.P.Q.)
Hodder and Stoughton Educational,
(a Division of Hodder and Stoughton Ltd.,)
Dunton Green, Sevenoaks, Kent TN13 2YD,
Great Britain.

CONSENT FORM

TELEPHONE: 692 3431 Beach Building
692 2408 Blackburn Building

The University of Sydney
Department of Pharmacology
N.S.W. 2006

IN REPLY PLEASE QUOTE:

I,.....of.....
.....having attained the age of eighteen years freely volunteer to take part in the project outlined below, on the understanding that all reasonable care will be exercised by the University of Sydney and others engaged in the project.

The project:

I understand that the purpose of this project is to look at the effects of alcohol and marihuana on performance skills.

The agreement:

I agree to remain in the laboratories of the Department of Pharmacology, Rozelle Hospital, until the effects of the drug have worn off and I have been released by a member of the staff.

I have not knowingly witheld from any person or persons responsible for the project, any information regarding my state of health or current medications.

I agree that if the University of Sydney and others associated with the project exercise all reasonable care, I will in no way hold the University of Sydney or others involved liable in respect of any consequences that might arise from my participation in the project outlined above.

Signed..... Date.....

Witness..... Date.....

DRUG-TAKING QUESTIONNAIRE

SUBJECT NO..... NAME.....

AGE..... SEX..... DATE.....

DRINKING HISTORY

(1) On how many days last week did you drink alcohol?

(i) None
(ii) One or two days
(iii) Three or four days
(iv) Five or six days
(v) Every day

(2) On a day when you have a drink, how many drinks would you usually have?

(i) One or two drinks
(ii) Three to five drinks
(iii) Five to eight drinks
(iv) Nine to twelve drinks
(v) More than twelve drinks

(3) How long have you been drinking at this level?

Weeks..... Months..... Years..... How many years?.....

SMOKING HISTORY

(4) On how many days last week did you smoke marihuana?

(i) None
(ii) One or two days
(iii) Three or four days
(iv) Five or six days
(v) Every day

(5) On a day when you smoke marihuana, how many sessions would you have?

(i) One
(ii) Two or three
(iii) Four
(iv) More than four

(6) How long have you been smoking at this level?

Weeks..... Months..... Years..... How many years?.....

MEDICINES

(1) If you have taken any medicines in the last 24 hours, give details (ie name of medicine or the condition for which it was used).....

(2) In the last 24 hours have you taken any of the following?

alcohol [ ]	barbs [ ]
marihuana [ ]	narcotics [ ]
cigarettes [ ]	amyl [ ]
trips [ ]	speed [ ]
cocaine [ ]	anything else? [ ]

(3) If you have had any alcohol in the last 24 hours, give the time of your last drink.....

(4) Have you got a hangover?

If yes, is it mild [ ] moderate [ ] awful [ ]

(5) If you have had any marihuana in the last 24 hours give the time of your last smoke.....

YOUR ATTITUDE

Tick one statement in each of the groups below that most clearly expresses your attitude at the moment:

Marihuana

(a) Marihuana is a safe drug
(b) I think marihuana is a safe drug for most people
(c) I think that marihuana is bad for most people in the long run
(d) Marihuana is harmful to the health of all who use it

Marihuana Laws

(a) Penalties for marihuana use should be increased
(b) The laws on marihuana use are OK as they are
(c) Marihuana users should not be penalised but pushers should
(d) Marihuana should be made legal but all advertising of it prohibited

Alcohol

(a) Alcohol is a safe drug
(b) I think alcohol is a safe drug for most people
(c) I think alcohol is bad for most people in the long run
(d) Alcohol is harmful to the health of all who use it

BEFORE DRUG

RIGHT NOW, how good do you feel?

Down in the dumps ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! Really great
average

Please rate yourself on each of the scales below according to how you feel RIGHT NOW. Before starting please read the scale definitions.

1. TENSION

relaxed
calm
patient
at ease
tolerant

! ! ! ! ! ! ! ! ! ! ! ! ! ! !
average

tense
impatient
on edge
restless
keyed up

2. ALERTNESS

lethargic
slow
muddled
bored
dopey

! ! ! ! ! ! ! ! ! ! ! ! ! ! !
average

alert
clear-headed
attentive
bright

3. DEPRESSION

happy
elated
hopeful
optimistic
joyful

! ! ! ! ! ! ! ! ! ! ! ! ! ! !
average

sad
unhappy
pessimistic
weepy

4. DETACHMENT

sociable
involved
concerned
talkative

! ! ! ! ! ! ! ! ! ! ! ! ! ! !
average

detached
uninvolved
impersonal
quiet

5. ANXIETY

assertive
brave
confident
self assured

! ! ! ! ! ! ! ! ! ! ! ! ! ! !
average

worried
jittery
afraid
no confidence

IMMEDIATELY AFTER COMPLETING DRUG CONSUMPTION

Please rate yourself on each of the scales below according to how you feel RIGHT NOW. Before starting please read the scale definitions.

1. **TENSION**

relaxed calm patient at ease tolerant	! ! ! ! ! ! ! ! ! ! ! ! ! ! !	tense impatient on edge restless keyed up
	average	

2. **ALERTNESS**

lethargic slow muddled bored dopey	! ! ! ! ! ! ! ! ! ! ! ! ! ! !	alert clear-headed attentive bright
	average	

3. **DEPRESSION**

happy elated hopeful optimistic joyful	! ! ! ! ! ! ! ! ! ! ! ! ! ! !	sad unhappy pessimistic weepy
	average	

4. **DETACHMENT**

sociable involved concerned talkative	! ! ! ! ! ! ! ! ! ! ! ! ! ! !	detached uninvolved impersonal quiet
	average	

5. **ANXIETY**

assertive brave confident self assured	! ! ! ! ! ! ! ! ! ! ! ! ! ! !	worried jittery afraid no confid- ence
	average	

BLOOD ALCOHOL CONCENTRATION

What would you estimate your blood alcohol concentration to be NOW?.....

IMMEDIATELY AFTER COMPLETING DRUG CONSUMPTION

RIGHT NOW, how good do you feel?

Down in the dumps ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! Really great
average

RIGHT NOW, how affected OVERALL do you feel by what you have taken?

Not at all affected ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! Extremely affected
moderately affected

How do you rate this effect? (ie too out of it, just right or not enough)

Not nearly enough affected ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! Far too much affected
just right

HOW MUCH of this effect do you attribute to MARIHUANA?

None of it ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! All of it

RIGHT NOW, how stoned do you feel?

Straight Not at all stoned ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! The most stoned I've ever been

HOW MUCH of this effect do you attribute to ALCOHOL?

None of it ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! All of it

RIGHT NOW how drunk do you feel?

Sober Not at all drunk ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! The most drunk I've ever been

If you were at a party, would you RIGHT NOW like to smoke more dope?
YES [ ] NO [ ]

If you were at a party, would you RIGHT NOW like to drink more alcohol?
YES [ ] NO [ ]

As you feel RIGHT NOW, how safely could you drive a car?

Absolutely certain I COULD NOT drive safely ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! Absolutely certain I COULD drive safely
dont know

Would you drive a car as you feel right now? YES [ ] NO [ ]

APPENDIX 2.

RANDOM TABLE FOR ALLOCATION OF DOSES AND ORDER OF TESTS:
S = Subject number; D = dosage group; T = order of presentation of tests.

S	D	T	S	D	T	S	D	T
1.	8	B	2.	3	A	3.	4	D
4.	7	C	5.	4	B	6.	4	A
7.	13	E	8.	10	C	9.	14	B
10.	11	A	11.	7	D	12.	15	E
13.	2	A	14.	10	D	15.	13	B
16.	12	B	17.	2	D	18.	4	E
19.	15	A	20.	14	C	21.	3	E
22.	2	E	23.	12	A	24.	11	B
25.	11	C	26.	15	D	27.	12	C
28.	15	B	29.	3	C	30.	4	C
31.	2	C	32.	8	A	33.	3	D
34.	16	A	35.	1	B	36.	6	E
37.	14	A	38.	2	B	39.	4	A
40.	14	D	41.	4	B	42.	1	A
43.	11	D	44.	12	D	45.	7	A
46.	2	A	47.	9	A	48.	12	A
49.	10	E	50.	3	B	51.	6	C
52.	14	E	53.	14	B	54.	11	A
55.	13	D	56.	5	B	57.	11	B
58.	12	B	59.	14	C	60.	10	A
61.	10	B	62.	8	C	63.	13	C
64.	10	A	65.	11	E	66.	11	C
67.	7	B	68.	6	D	69.	1	C
70.	8	A	71.	14	D	72.	10	B
73.	12	C	74.	2	B	75.	3	E
76.	13	A	77.	13	C	78.	12	E
79.	7	D	80.	12	D	81.	16	B
82.	2	C	83.	2	D	84.	13	E
85.	14	A	86.	10	E	87.	13	D
88.	11	D	89.	10	C	90.	12	E
91.	15	E	92.	12	A	93.	12	C
94.	6	A	95.	11	B	96.	5	E
97.	3	D	98.	11	C	99.	8	E
100.	5	A	101.	12	B	102.	3	C
103.	5	C	104.	2	E	105.	7	A

106. 12 D
107. 4 E
108. 4 D
109. 9 B
110. 4 C
111. 8 D
112. 3 B
113. 16 C
114. 9 C
115. 12 E
116. 7 B
117. 6 B
118. 9 D
119. 3 A
120. 13 A
121. 9 E
122. 9 D
123. 16 D
124. 10 D
125. 15 C
126. 1 C
127. 5 D
128. 3 A
129. 13 B
130. 14 E
131. 1 D
132. 16 E
133. 6 A
134. 1 D
135. 5 A
136. 2 A
137. 13 C
138. 15 A
139. 8 A
140. 9 C
141. 10 A
142. 9 A
143. 8 B
144. 5 B
145. 2 B
146. 7 C
147. 12 A
148. 5 C
149. 6 B
150. 6 E
151. 13 A
152. 10 C
153. 3 C
154. 9 B
155. 3 B
156. 10 D
157. 13 E
158. 8 C
159. 11 A
160. 1 B
161. 2 D
162. 14 A
163. 14 C
164. 8 D
165. 11 D
166. 2 C
167. 7 E
168. 13 B
169. 1 A
170. 14 B
171. 3 D
172. 9 E
173. 6 C
174. 13 D
175. 9 A
176. 5 D
177. 15 B
178. 9 E
179. 11 E
180. 16 A
181. 8 E
182. 7 A
183. 1 E
184. 1 E
185. 14 D
186. 14 E
187. 2 B
188. 10 E
189. 16 B
190. 15 D
191. 3 E
192. 16 C
193. 4 A
194. 8 A
195. 7 E
196. 5 E
197. 6 D
198. 9 B
199. 11 E
200. 1 A
201. 15 C
202. 3 B
203. 14 C
204. 2 E
205. 15 A
206. 10 B
207. 4 B
208. 11 A
209. 5 A
210. 11 E
211. 5 C
212. 6 D
213. 1 C
214. 11 C
215. 1 C
216. 9 D
217. 5 B
218. 14 A
219. 12 B
220. 8 E
221. 10 E
222. 15 D
223. 10 A
224. 6 A
225. 16 D
226. 7 B
227. 15 E
228. 4 C
229. 16 E
230. 5 D
231. 10 D
232. 9 C
233. 3 E
234. 4 D
235. 16 E
236. 13 C
237. 1 D
238. 15 B
239. 14 B
240. 2 E
241. 9 D
242. 8 D
243. 4 C
244. 16 D
245. 16 A
246. 10 B
247. 6 E
248. 15 C
249. 6 B
250. 5 E
251. 4 D
252. 2 C
253. 1 E
254. 4 E
255. 8 B
256. 7 C
257. 6 C

258. 16 B	259. 7 D	260. 12 E
261. 12 C	262. 16 C	263. 4 A
264. 16 D	265. 14 D	266. 16 B
267. 15 C	268. 13 A	269. 15 D
270. 1 B	271. 5 D	272. 6 A
273. 7 E	274. 1 B	275. 16 E
276. 5 C	277. 9 A	278. 7 A
279. 13 D	280. 2 D	281. 10 C
282. 9 B	283. 15 E	284. 4 B
285. 14 E	286. 9 E	287. 16 A
288. 8 C	289. 6 B	290. 1 A
291. 7 B	292. 2 A	293. 7 C
294. 5 A	295. 8 D	296. 1 E
297. 16 C	298. 4 E	299. 6 C
300. 9 C	301. 8 C	302. 5 E
303. 15 A	304. 15 B	305. 8 E
306. 3 D	307. 6 D	308. 11 B
309. 1 D	310. 7 D	311. 6 E
312. 8 B	313. 5 B	314. 3 C
315. 7 E	316. 11 D	317. 13 B
318. 12 D	319. 13 E	320. 3 A