The influence of cannabis and alcohol on driving

Prepared for Road Safety Division, Department for Transport

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CONTENTS

Executive Summary

The second phase of a two-phase study into the impairment effects of cannabis on driving is reported here. This phase concerns the effects of cannabis taken in conjunction with alcohol. The first phase, into the effects of cannabis taken alone, has already been reported.

Introduction

The most recent of TRL's major studies investigating the incidence of alcohol and drugs in road accident fatalities has shown a large increase in the incidence of drugs present in fatal casualties (drivers, riders, passengers and pedestrians). Among all road users illicit drugs were present in 18% of fatalities. These figures represent a six-fold increase in the detected incidence of illicit drugs present in fatalities since the previous, similar, study 12 years earlier. In the most recent research cannabis constituted around two thirds of the illegal drugs found in fatalities. In the study of fatalities referred to above, 24% of the drivers who had consumed cannabis were also over the drink/drive limit, and a further 16% had consumed some alcohol but were below the legal limit.

Anecdotal evidence suggests that regular cannabis users often consume alcohol during a cannabis-smoking session. The amount of alcohol they consume is usually below the legal limit, and hence they may believe that their driving is unaffected by the alcohol. It is therefore important to establish the degree of impairment caused by such a dose of alcohol in combination with a typical cannabis dose. In 1999, the (now) DfT (Department for Transport), commissioned a review of the latest evidence of the impairment effects of cannabis. The report of that review provided an overview of the effects of cannabis on driving and accident risk and identified areas where current knowledge was deemed to be insufficient to guide road safety policy.

This raised important questions, which have now been addressed by a research project carried out by TRL for Road Safety Division, DfT, to investigate the degree to which cannabis impairs psychomotor and cognitive skills relevant to the driving task. The first phase (reported previously) of this first UK study had the following objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of cannabis on driving.
- To determine the duration and extent of any impairment under different degrees of intoxication (using different levels of cannabis).
- To provide an overview of attitudes and habits of cannabis users in relation to driving and explore factors which may influence the decision to drive under its influence.

The objectives were addressed using male drivers who were experienced cannabis users. These subjects carried out a variety of laboratory-based tasks and drove in the TRL simulator under four cannabis conditions: placebo; low Δ^9-THC (the main active cannabinoid of tetrahydrocannabinol); high Δ^9-THC; and cannabis resin.

The second phase, reported here, considers the influence of alcohol in combination with cannabis. This research has two objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of the combination of moderate doses of cannabis and alcohol on driving;
- To investigate whether police surgeons can readily distinguish between unimpaired individuals and those impaired by alcohol, cannabis and by a combination of the two.

Background

It is well known that cannabis is often taken in conjunction with alcohol. Previous comparative studies have generally compared the effects of high doses of alcohol with those of medium-to-low doses of the active ingredient in cannabis, Δ^9-THC. It has been well established that alcohol has severe impairing effects at high blood alcohol concentrations whilst performance decrements have been demonstrated at concentrations as low as 30mg/100ml. It has also been shown that approximately 10 mg Δ^9-THC is required to induce a close to 'normal use' level of cannabis intoxication.

Previous studies have shown that simulated and actual driving and divided-attention tasks are severely affected by alcohol. Simple vigilance tasks are not so much affected and tasks such as tracking and reaction-time tasks are only affected at relatively high blood alcohol levels. Alcohol may, therefore, be seen as first disturbing the higher cognitive processes. Such disturbances are greater than the losses in psychomotor skills and simple attentional processes. However, it is well recognised that at alcohol levels of 80mg/100ml (the UK legal limit), or more, impairment effects are significantly increased.

In contrast, previous studies with cannabis show that it first seems to affect all tasks requiring psychomotor skills and continuous attention. Thus, tracking tasks, which are very sensitive to short term changes in attention, are very sensitive to cannabis impairment. On the other hand, multi-task processes and higher cognitive functions are less time-critical: a short attention lapse can be compensated for by increased activity later.

In the case of the driving task, this may explain the frequently repeated observation that drivers under the influence of cannabis drive more slowly, presumably to lower the difficulty of the driving task and its time-critical aspects in an attempt to compensate for the impairment of psychomotor skills and losses in continuous attention.

Tests

Participants were male drivers who were experienced cannabis and alcohol users. They were recruited, medically screened and tested under conditions of a strict protocol that had local ethics committee approval. They were required to carry out laboratory-based tasks and to drive in the TRL driving simulator under two cannabis conditions.

These conditions were placebo and low dose cannabis. The low dose was herbal cannabis ('grass') containing about 10mg active ingredient (Δ^9- THC). There were also two alcohol conditions: placebo and a dose to give a blood alcohol concentration (BAC) of 50mg of alcohol per 100ml of blood.

Experimental procedures included the formal sobriety testing of participants, conducted by two experienced Police Surgeons/Forensic Medical Examiners. Participants also completed a mood questionnaire at different times during their visit.

The alcoholic drink was administered before smoking so as to allow the maximum impairment effects to occur at about the same point in time. In this way the typical low level use of these substances was replicated within the trial, so that the impairing effects could be related to 'real life' situations.

Results

The results confirm and extend those from previous studies. There was a reduction of average driving speed and an increase in the minimum time headway on simulated motorway driving when participants had had the active dose of cannabis, regardless of the alcohol dose. Participants' responses on the mood questionnaire showed that they were aware of their impairment. The results suggest that they attempted to compensate for their impairment by driving more cautiously.

The results of simulator tracking tasks, which required subjects to stay within their lane on a bend, showed that participants tended to drive less accurately when they had been given the active cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

Measurements of an adaptive tracking task (a laboratory task which measures ability to track a moving object on a computer screen) also produced statistically significant results. The adaptive tracking performance deteriorated as the dose level increased, with the tracking performance under the influence of alcohol or the combined influence of cannabis and alcohol being significantly worse than participants' tracking performance under no active dose.

The results of sobriety testing showed a correlation between the active cannabis dose received and whether impairment was judged to be present. On the basis of these observations, the general medical examination and standardised impairment testing applied by the police surgeons were judged to be effective in determining impairment. The police surgeons drew preliminary conclusions as to the number and combination of failures of impairment-test elements needed to determine that a subject was significantly 'impaired'. The sobriety test findings can only be regarded as a preliminary assessment of how people under the influence of drugs and/or alcohol experience impairment and how this impairment may be independently judged and recorded. It does however suggest, in conjunction with responses to the mood questionnaire, that individual participants are aware of their own impairment to a greater extent than is generally realised and that this impairment may be detected in sobriety or performance tests.

The results of this study confirmed those of the previous trial involving cannabis alone. It was concluded that cannabis has a measurably worsening effect on psychomotor performance, particularly tracking ability. Drivers under the influence of cannabis seem to attempt to compensate to some extent for the impairment (that they recognise) by driving more slowly, but there are some aspects of the driving task where cannabis-impaired drivers cannot compensate and where their performance deteriorates (e.g. staying in lane on a bend). Within the sample of drivers, the effect of alcohol (at a dose of just more than half of the UK legal limit) and cannabis together were slightly greater than with cannabis alone; a larger sample would be needed to determine whether this is likely to apply to the population as a whole. There was no evidence that either alcohol or cannabis offset the effect of the other: impairment levels for cannabis or cannabis with alcohol remained significantly greater than placebo.

Conclusions

This research has:

- demonstrated the practicability of assessing the effects of cannabis and alcohol on driving performance in controlled experimental clinical trials;
- confirmed the results from previous studies that drivers under the influence of cannabis are aware of their impairment, attempt to compensate for their impairment by driving more cautiously, but are unable to compensate for the loss of capability in some psychomotor skills;
- confirmed previous observations that cannabis adversely affects drivers' tracking ability;
- found that tracking performance deteriorated with increasing dose level;
- judged that the general medical examination and standardised impairment testing applied by the police surgeons were generally effective in determining impairment.

In terms of road safety the results show a clear worsening of driver capability following the ingestion of cannabis or the ingestion of cannabis and alcohol together at the doses used, in comparison with placebo (i.e. having taken neither). Within the sample of drivers, the effects of alcohol (at a dose of just more than half of the UK legal limit) and cannabis taken together were slightly greater than with cannabis alone. Given that other research has extensively shown the rapid increase in the risk of accident, particularly fatal accident, with increasing blood alcohol level, the present results show how important it is to avoid any combination of alcohol and cannabis, as well as avoiding alcohol and cannabis taken on their own, before driving or riding.

1 Introduction

1.1 Background

TRL has carried out two major studies investigating the incidence of alcohol and drugs in road accident fatalities. The most recent study has shown a large increase in the incidence of drugs in fatal road casualties (drivers, riders, passengers and pedestrians). The results show that among all road users illicit drugs were present in 18% of fatalities (Tunbridge *et al.*, 2001). These figures represent a six-fold increase in illicit drug taking since a previous, similar study (Everest *et al.*, 1989). In the most recent research cannabis constituted around two thirds of the illegal drugs found.

Despite the increase in the incidence of drugs, it is not possible to say that drugs caused these deaths. There may be an association, but presence cannot be taken as evidence of causation. Cannabis remains detectable in the body for up to four weeks after use - long after any impairment of driving, and its prevalence in drivers was not significantly different from that of passengers, who can be taken as a (albeit imperfect) measure of the prevalence in the population as a whole.

In 1999, the (now) DfT (Department for Transport) commissioned a review of the latest evidence of the impairment effects of cannabis. The resulting report provided an overview of the effects of cannabis on driving and accident risk and identified areas where current knowledge was deemed to be insufficient to guide road safety policy.

The questions raised shaped a further research project, carried out by TRL for Road Safety Division, DfT, to investigate the degree to which cannabis impairs psychomotor and cognitive skills relevant to the driving task. This study was the first such study within the UK that aimed to achieve all the following objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of cannabis and alcohol on driving.
- To investigate whether police surgeons can readily distinguish between unimpaired individuals and those impaired by alcohol, cannabis and by a combination of the two.

The project was undertaken in two phases. The first phase of work addressed the effects of cannabis alone, this first trial took place in January and February 2000 and was reported in Sexton *et al.*, 2000 (see Appendix D). The second phase, reported here, took place in November/ December 2000 and studied the combination effects of alcohol and cannabis on psychomotor and cognitive skills relevant to car driving in a controlled trial.

The research aimed to identify specific aspects of cognitive/psychomotor behaviour that are affected by the two drugs, and to determine how individual differences might moderate the effects of the drugs on performance.

1.2 Review of previous research

Previous research studies on cannabis and driving have focussed largely on the effects of cannabinoids on driving performance. These studies have been almost exclusively experimental involving laboratory tasks, driving simulator and on road 'real driving' experiments. A much smaller number of studies has attempted to gain broader sociological information about driving habits under the influence of cannabis and the factors that influence the decision to drive. The research reported here attempts to combine these two aspects with a view to assessing the degree to which there may be a problem with cannabis in relation to driving.

Such international work as has been done suggests that, for up to two hours after a dose sufficient to give a 'high', there is impairment of the same order as alcohol at around the drink-drive limit (50–80mg/100ml) (Robbe, 1994).

It is well known that cannabis is often used in conjunction with alcohol. The few studies that have been conducted combining the effects of cannabis and alcohol on driving performance have tended to use relatively high doses of alcohol i.e. doses high enough to cause severe impairment alone. Psychopharmacological studies investigating the effects of alcohol and cannabis (Δ^9-THC) on psychomotor and cognitive performance have been inconsistent in terms of methodology, making comparisons difficult. There are considerable differences in drug preparations used, drug doses administered, routes of drug administration, drug consumption and absorption times, plasma analyses (if blood is taken), times of testing post-drug administration, and performance measurements. Furthermore, some studies administer alcohol and cannabis separately and compare the effects (comparative studies), while others examine the effects of the two drugs combined (combination studies).

Previous comparative studies have generally compared the effects of high doses of alcohol with those of medium-to-low doses of Δ^9-THC. It has been well established that alcohol has severe impairing effects at high blood alcohol concentrations, and performance decrements have been demonstrated at blood concentrations as low as 30mg/100 ml (Moskowitz *et al.*, 2000). It has also been shown that approximately 10 mg Δ^9-THC is required to induce a 'close–to-normal' level of cannabis intoxication (Robbe 1994). It is therefore not surprising that alcohol significantly impaired performance on most measures, whereas low doses of Δ^9-THC had a relatively small effect.

Within previous combination studies, alcohol has always been administered prior to Δ^9-THC. This allowed for the delayed absorption of alcohol into blood compared with the rapid absorption of Δ^9-THC. Perez-Reyes *et al.*, (1988) demonstrated that peak BAC was at 40 minutes following a medium dose of alcohol (to achieve a BAC 59-69 mg/100ml), and peak Δ^9-THC plasma level was between 5 and 7 minutes. Heishman *et al.*, (1997) showed that impaired performance following alcohol peaked at 30 minutes post-dosing, which correlates with subjective ratings of impaired performance and 'high'. However, this same study found that the peak behavioural effects of Δ^9-THC occurred at 60 minutes, even though peak subjective effects were reported immediately following the high dose, and at 30 minutes following the low dose. The subjective ratings of impaired performance were dose dependent. Heishman *et al.*, found a correlation between the peak

subjective rating of impaired performance and peak impaired DSST (digit symbol substitution task) performance (at 60 minutes) following the medium Δ^9-THC dose (150 ng/ml).

Previous research suggests that the combined effects of alcohol and Δ^9-THC on performance skills related to driving tend to be additive. However, when drug doses were particularly low, no effects on performance were demonstrated. The most recent combination study of the effects of cannabis and alcohol on driving performance (Lamers and Ramaekers, 2000) used alcohol and Δ^9-THC doses similar to those reported here. Performance was assessed by using a driving proficiency test and a visual search assessment. The tests were carried out on public roads in the city of Maastricht. It was concluded that effects of cannabis or alcohol alone at these levels was minimal, but the combination of alcohol and cannabis represented a significant road safety risk.

Anecdotal evidence suggests that regular cannabis users, particularly when with friends, drink low levels of alcohol whilst smoking cannabis, and then drive. The level of alcohol consumed is normally below the legal UK limit for driving, possibly due to the widespread acceptance of the dangers of drink-driving amongst the younger population (or perhaps due to an awareness of the potential to be stopped for drink-driving). However, there appears to be little appreciation of the increased impairment to driving that may be caused by combining the two substances. It is therefore important to establish the degree of impairment caused by a low dose of alcohol in combination with cannabis.

Within this study we have attempted to take into account some of the problems encountered in previous studies. The study has used moderate doses of alcohol to avoid severe impairment from alcohol dosing alone, and has used a level of cannabis dose that produced some impairment in the previous study by the same research team (Sexton *et al.*, 2000). The alcohol and cannabis doses are used in conjunction with placebo controls and every combination of placebo and active dose has been used in a balanced design. The dose levels are thought to be fairly typical of those used by cannabis and alcohol users, and as such this study attempts to replicate dose conditions that represent typical usage when users may be driving.

2 Study design

2.1 Overview

Participants were asked to attend test sessions after consenting to the conditions outlined in an information sheet, having signed the consent form and completed a questionnaire that assessed their drug use and driving histories. Each participant was required to perform cognitive and psychomotor tasks under different conditions of drug and alcohol dose. The tests were designed to assess vigilance, selectivity of attention, working memory, as well as speed and accuracy of decision-making in response to different stimuli.

Participants were medically screened by a doctor for suitability and also completed a questionnaire about their cannabis smoking and alcohol drinking habits. Their identities were confidential during the trial and all identifying information was destroyed at the end of the trial.

Each participant attended one test session for each treatment combination (at least one week apart), plus an initial screening interview. The test sessions were conducted from early evening until late evening, because most of the participants worked during the day, and also because this was a more natural time for them to be drinking and taking cannabis. Each test session was approximately two hours long. The results for the test session were recorded in a session case report form, this was very similar to that used in the previous study (Sexton *et al.*, 2000).

2.2 Experimental design

The study was designed to be a crossover analysis of variance with planned comparisons. The design was a crossover for two treatment levels of NIDA-supplied cannabis cigarettes, plus two alcoholic drink treatment levels.

The design is shown in Table 1. Twenty participants were recruited for the trial with 5 allocated at random to each of the treatment groups. The design was fully balanced across all four periods.

Table 1 Experimental design

Group (5 participants per group)	*Period*			
	1	*2*	*3*	*4*
1	A	D	B	C
2	B	A	C	D
3	C	B	D	A
4	D	C	A	B

Dose levels: A – placebo cannabis and placebo alcohol, B - cannabis dose plus placebo alcohol, C – placebo cannabis plus alcohol dose, D – cannabis dose plus alcohol dose

2.3 Ethics committee

The experimental design and methodology were presented via a protocol document to the local area ethics committee. Ethics committee approval is required for any study that involves any risk to volunteer participants, however small the risk. The committee consists of registered medical practitioners with lay representation and meets once a month. The protocol submitted included a participant information sheet and a copy of the participant consent form, signed by all participants prior to being screened. The ethics committee approved the study.

2.4 Sample size

The sample size was determined from data on impairment in earlier studies and in particular from the study using different cannabis doses that took place in January/ February 2000, (Sexton *et al.*, 2000). The power calculation, on a reaction time pulling-out event, suggested that 20 participants should show a statistically significant effect at the 95% confidence level on a 1-sided test with 84% power when comparing the difference in performance

due to being impaired just below the legal alcohol limit. (In practice, 2-sided tests were used for significance testing because it was not always clear in what direction cannabis changed the metric being evaluated).

2.5 Participants

Participants were males at least 18 years of age who had a driving license, had been driving for more than one year, and had used cannabis and alcohol at least once per week for more than 12 months. The sample was restricted to males because this avoided any possible complications that would have had to be considered in case females were already, or became pregnant during the trial. It was thus more acceptable to the ethics committee. It is also possible that there are differences between males and females in terms of the effect on driving performance of smoking cannabis with or without alcohol, due to physiological differences and/or driving style differences. Four participants who had helped with the first cannabis trial, (Sexton *et al.*, 2000) were recruited for this trial. This was to provide a check on the consistency of results between the two trials.

2.6 Recruiting

Participants were recruited through people who were known to the project team and who knew regular cannabis users. It was found that once potential participants had been contacted then they would know other cannabis users who also would be interested in helping with the trial. This recruiting technique is often referred to as a 'snowball' sampling approach.

Participants known to the 'link' people were invited to telephone the project team. The 'link' people were given a minimal amount of information about the trial, just the fact that male drivers who were regular cannabis and alcohol users were required and that complete confidentiality was assured. When participants phoned they were asked about their cannabis and alcohol use, their availability and given some background information about the trial and the commitment being sought. If they were still interested, they were asked to attend a screening session.

2.7 Screening

Participants were given a full medical screen to ensure that they were fit and healthy especially with respect to any respiratory problems or liver problems, past or current. They attended a pre-booked session at TRL and were examined by a doctor. Prior to being examined, they were asked to read a participant information sheet that informed them about the trial, and were asked to sign a consent form. An example of the screening document, which includes the participant information sheet and the consent form, is given in Sexton *et al.*, 2000. The inclusion/ exclusion criteria are shown in Table 2.

2.7.1 Medical checks

The full range of medical checks is shown in the screening document, (Sexton *et al.*, 2000). The participant was required to supply a urine sample which was checked to see that the participant had THC metabolites in his urine, and was thus a cannabis user. The urine sample was also used to check if the participant was a current polydrug user (i.e. a user of other drugs in addition to cannabis). Participants also supplied a blood sample for a blood chemistry check and, in particular, to check liver function. Any participant who failed any of the screening checks was excluded from the trial. This final decision was made once the laboratory analysis of the blood samples had been processed.

2.7.2 Questionnaire

A questionnaire regarding use of cannabis and other drugs had been developed by Kay Wright, (University of Birmingham), who was part of the trial-team. This questionnaire had been used to obtain a profile of the typical

Table 2 Inclusion and exclusion criteria

Criteria description	*Include if:*	*Exclude if:*
Gender	Male	Female
Age	≥18 and ≤ 60	<18 or >60
Car driver	For >12 months	< 12 months
Cannabis user	For >12 months	< 12 months
Cannabis frequency	At least weekly for 12 months	< Weekly
Alcohol use	>Weekly, and between 5 and 25 units per week	< Weekly, or <5 units per week
History of substance abuse (except nicotine)	None	Any past/current
Medication	None	Any current
Respiratory disorder	None	Any history
Medical history	Normal	Any abnormalities
Height & weight	In normal range	Outside normal range*
Physical examination	In normal range	Outside normal range*
12 lead ECG	In normal range	Outside normal range*
Blood haematology, liver function and screening tests	In normal range	Outside normal range*
Visual acuity – via Snellen test	Acceptable	Unacceptable
Ability to commit to trial	Positive	Negative
Signed consent for trial	Prepared to give	Not given

** There are established ranges defined for health purposes*

cannabis user and had been administered to a sample of 90 or so users. Participants who attended for screening were asked to complete this questionnaire. The questionnaire provided a further method of checking the suitability of potential participants. A comparison of trial participants with other cannabis users is contained in Appendix A.

2.8 Analysis of samples

Samples of blood taken for screening purposes were processed by the pathology laboratory at Frimley Park Hospital, Surrey. These were delivered to the laboratories within hours of being taken and the results were usually available within 2-3 days.

Samples of urine and saliva were analysed by Epsom Hospital Laboratories Regional Assay Service. Samples of saliva were centrifuged to extract the saliva from a salivette and stored in a freezer. They were delivered to the laboratory on a weekly basis. The urine samples were also stored in a freezer on the evening of the trial and kept frozen ready for delivery.

The urine and saliva sample results took time to process. This is because the assaying of samples for relatively small quantities of cannabis metabolites is time consuming and will often require more than one analysis of the same sample in order to check the results.

3 Cannabis and alcohol dose

Participants were given two different cannabis doses (including placebo), each one used twice. The two doses were pre-prepared 'grass' based cannabis cigarettes supplied by NIDA (National Institute on Drug Abuse), each of a different strength. The drinks were tonic water plus Angostura bitters either with or without alcohol (Vodka, 40% proof). The volume of the drinks for each individual subject was always the same and the rims of the glasses were dipped in neat Vodka to disguise the content. The drinks were pre-prepared and kept in a refrigerator until required, they were labelled for subjects and administered 5 minutes before smoking the cannabis.

Factors affecting blood alcohol concentrations include: gender, body weight, previous use of alcohol, and the presence of food in the stomach. In the present study only male participants were recruited, doses were measured in grams of alcohol per kilogram of body weight. Attempts were made to standardise prior food intake and each participant was requested not to eat for at least 4 hours prior to each session. However, in practice this turned out to be difficult to control and there was some variety both in the food consumed and when it was eaten. This may have influenced the absorption of the alcohol dose.

The alcoholic drink was designed to bring subjects to 50mg/100ml on blood alcohol, or 22 µg/100ml on breath alcohol. The dose was calculated according to the subject's body mass and was presented as a drink containing 10% by volume of alcohol. This was approximately equivalent to a triple vodka and tonic.

Table C1 in the Appendix shows peak BrACs (mean BrAC 19.82µg/100ml ± 5.96; range 7 - 34) at approximately 30 minutes post-dosing, final BrACs at approximately 70 minutes post-dosing, and prior food intake (time and content) for each session.

3.1 Cannabis supply

The NIDA cigarettes were leaf/bud/florets mixed and rolled to a tightly controlled standard. They were stored frozen and with a humidity of about 10%. This needed to be increased to at least 14% prior to smoking in order to avoid a dry-smoke, which would not only be very harsh to participants but also would not convert the THC as required. Consequently, the cigarettes were humidified for 24-36 hours prior to smoking. The NIDA cigarettes weighed about 700 milligrams and were supplied in two strengths:

- Placebo containing about 0.005% ±0.002 of THC (active THC removed with a solvent).
- Low dose containing about 1.70% ±0.14 THC.

There is some evidence that the THC concentration of cannabis available on the street is often higher than this. However, the cannabis dose was intentionally low, just as the level of alcohol used was relatively low. Sexton *et al.,* (2000) demonstrated that the dosing regime employed was capable of producing significant impairment effects even with low doses of cannabis.

3.2 Cannabis control and licensing

Cannabis is an illegal drug and so a license to hold and administer for the purposes of this research had to be obtained from the Home Office. Home Office regulations regarding the license to possess cannabis require that a dosage control book is kept, in which the source of the cannabis, the quantities used, date used and other details are recorded. The cannabis cigarettes were imported by The University of Birmingham under special license conditions, then transferred to TRL and registered in the drugs control book.

3.3 Cannabis administration

Cannabis cigarettes for the required period were removed from storage by the project manager and signed out from the drugs control book. (Only he knew the dose required, although the code-break was available if required). The cannabis cigarettes were placed in a humidifier that had been clearly marked with a code which identified the participant for whom they were intended. Prior to smoking, the cannabis cigarette was taken from the humidifier by the project manager and placed in a sealed tube. The tubes were then made available to the drug administrator who checked that the code on the sealed tube matched that of the participant, prior to giving him the cannabis cigarette.

Determining the precise dosing of Δ^9-THC through inhaled cannabis smoke is problematic. Previous studies have instructed participants to smoke cannabis cigarettes ad-lib (for example: Ohlsson *et al.,* 1980; Lindgren *et al.,* 1981; Cochetto *et al.,* 1981; Cami *et al.,* 1991; Perez-Reyes, 1991; Robbe 1998). However, individual smoking techniques during ad-lib smoking vary to such an extent that differences in delivered Δ^9-THC to, and absorption from the

lungs are inevitable. In order to control for inter- and intra-individual variations in smoking style, researchers have devised numerous standardised smoking procedures.

Typically, previous studies have standardised a combination of: i) draw-time/volume, ii) breathhold duration, iii) inter-draw interval time, and iv) number of draws (for example: Zancy and Chait, 1988; Marks and MacAvoy, 1989; Tashkin *et al.,* 1991a; Azorlosa *et al.,* 1992). However, methodologies have been inconsistent in the number and timing of controlled variables.

Controlling smoking technique variables is likely to reduce the problem of delivering a precise dose of Δ^9-THC. However, draw volume is difficult to control, and individual variation in the amount of smoke drawn during each draw, even when draw duration is timed, will ultimately affect Δ^9-THC absorption. Previous studies have shown that side-stream smoke losses, pyrolytic destruction, and inter-individual variation in Δ^9-THC absorption, distribution and metabolism also contribute to the problem of Δ^9-THC delivery (Robbe, 1994). Section 3.4 sets out the standardised smoking procedure devised as a result of this review work.

3.4 Standardised smoking procedure

Participants smoked a single cigarette according to the standardised smoking procedure detailed in Table 3. The paced smoking protocol was devised following a review of the relevant literature and a pilot study using placebo cigarettes.

Table 3 Standardised smoking protocol

Variable		*Time*
i	Draw-time	3 seconds
ii	Breathhold duration	5 seconds
iii	Inter-draw interval	30 seconds
iv	Number of draws	Various

Draw-time/draw volume

An increase in draw volume has been observed during ad-lib cannabis smoking, compared with tobacco smoking (Wu *et al.,* 1988). The effects of increased draw volume on Δ^9-THC absorption, heart rate and self-rated level of intoxication were measured in a study by Tashkin *et al.,* (1991a), and no significant effects were found. However, it is important to standardise the inhalation volume of each draw in order to control for inter and intra-individual variation in smoking techniques. It is likely that standardising draw-time may facilitate the control of draw-volume. However, differences in the volume of smoke drawn during each draw are also likely.

NIDA recommend that a 7-second draw be used. Sexton *et al.,* 2000 found this to be too severe a regime and instead used a draw time of 5 seconds, which was managed by the subjects but did cause some discomfort. However, as a result of the pilot run of the smoking procedure for this study, this was further reduced to 3 seconds to minimise any discomfort experienced by the participants.

Breathhold duration

Assessments of ad-lib cannabis smoking have found breathhold durations between 7-25 seconds (Perez-Reyes 1982; Wu *et al.,* 1988; Tashkin *et al.,* 1991a; Block *et al.,* 1997; Huestis *et al.,* 1992). In the study by Tashkin *et al.,* (1991a), prolonged breathhold time was shown to enhance the absorption of Δ^9-THC from the lungs, potentiate the subjective feeling of intoxication, and increase heart-rate. However, in conjunction with a study by Zancy and Chait (1988), Tashkin *et al.,* also found that extended breathhold (14 seconds) compared with a short breathhold (4 seconds) contributed to increased carboxyhaemoglobin boost and increased tar deposition. It is likely that a breathhold of 5 seconds would be sufficient for Δ^9-THC absorption, while reducing the detrimental effects of a more prolonged breathhold.

Inter-draw interval

The length of time between draws varies considerably during ad-lib cannabis smoking. Previous studies have reported inter-draw intervals in the range of 30-72 seconds (Zancy and Chait 1988, Tashkin *et al.,* 1991b). Extended intervals are likely to promote losses of Δ^9-THC in side-stream smoke (Huestis *et al.,* 1992), in addition to a decrease in the amount of cigarette smoked. During the pilot run, participants found 30 seconds to be comfortable.

Number of draws

It has been shown that the Δ^9-THC content of a cigarette is not differentially extracted from the plant material during the smoking procedure; i.e. similar amount of Δ^9-THC are present in both the unlit cigarette and the unsmoked portion (Huestis *et al.,* 1992). Therefore, providing that the content of each cannabis cigarette is precisely the same, and that *i, ii* and *iii* in Table 3 are held constant, controlling the number of draws per cigarette is not likely to be necessary, providing the entire cigarette is consumed. However, the whole cigarette cannot be consumed since there will always be a butt remaining.

Table 4 shows the number of draws taken from each cigarette during each condition (mean 7.51 ± 1.00). This column also shows whether each participant provided a correct (Y) or incorrect (N) report of which drugs had been administered. A verbal subjective report of how intoxicated each participant felt during each of the four sessions is also included in the table.

Post trial verbal subjective reports on drug effects were not obtained from 7 of the study volunteers. Of those who did report their experiences, the majority (30/50) were consistent with the drugs administered. However, the drug combination caused more uncertainty than in the first trial, when only cannabis was administered.

During the double placebo condition, 9 of the study volunteers felt no effect at all, and 3 felt a slight cannabis effect which wore off fairly rapidly. This was probably psychosomatic, due to the smell and taste of the placebo, which closely matched the active dose.

Table C1 shows inter- and intra-individual variation in peak BrAC levels. These differences are most likely due to

Table 4 Number of draws, and subjective reports of THC effects during the cannabis dose conditions

Subject	*Session and peak BrAC*		*No. of draws*	*Subject correct in assessment?*	*Dose administered, followed by subjective report including verbatim comments where available*
060	1	33	7	Y	*Alcohol:* felt jolly and a bit tipsy.
Rob	2		9	N	*Cannabis:* felt 'a complete vegetable, far more wrecked than would normally get.' Thought he'd had both drugs.
	3	25	9	N	*Both:* felt comfortable and good, didn't feel drunk, like normal high.
	4		7	Y	*None:* expected something but felt no effect at all.
056	1	17	7	Y	*Alcohol:* a bit merry, a bit giggly, not sure if had THC at time.
Arr	2		8	Y	*Cannabis:* close to normal high but more intense as quick hit all at once. Have driven that stoned before.
	3	23	9	Y	*Both:* felt quite high and cheerful. Would not normally drive like this.
	4		7	Y	*None:* felt no effect at all but had worked out it would be placebo pair.
051	1	12	7	N	*Alcohol:* maybe alcohol but didn't feel drunk, not stoned at all.
Mar	2		8	N	*Cannabis:* didn't feel stoned or drunk.
	3	15	8	N	*Both:* felt very stoned and giggly – close to feeling at home if drinking.
	4		7	N	*None:* felt no effect at all.
050	1	19	7	Y	*Alcohol:* minor to moderate effect. Didn't feel very drunk.
Pet	2	17	6	Y	*Cannabis:* moderately stoned. Gets much more stoned at home.
	3		7	Y	*Both:* moderate effect, not particularly high. Gets higher at home.
	4		9	Y	*None:* felt no effect at all.
055	1		7	Y	*Alcohol:* felt a bit drunk, same feeling as after a pint.
Ray	2		7	Y	*Cannabis:* intense feeling that gradually subsided to normal high.
	3	21	6	Y	*Both:* felt really high, intensely higher than usual, then calmed down.
	4	20	6	Y	*None:* a bit dizzy immediately after smoking, then no effect.
058	1		7	Y	*Cannabis:* felt high to very high, more than usual.
Lou	2	20	7	Y	*Both:* felt very drunk and stoned, higher than would usually get.
	3		8	Y	*None:* felt no effect at all.
066	1		7	N	*Alcohol:* felt a slight cannabis high, and a strong alcohol high.
Jim	2	10	9	Y	*Cannabis:* felt a strong cannabis high. Still stoned at home.
	3		9	Y	*Both:* felt a strong effect of both, higher than normal at home.
	4	20	8	N	*None:* felt a slight cannabis high.
023	1		8	Y	*Alcohol:* little bit merry, not very drunk, felt more drunk and driven before.
Dav	1		7	Y	*Cannabis:* pleasant, close to normal high, but been more caned before.
	3	19	7	Y	*Both:* completely stoned, felt 'very wrecked'.
	4	17	8	Y	*None:* no effect at all.
061	1		8	Y	Did not manage to get detailed feedback, but the participant correctly guessed each condition.
Nic	2		7	Y	
	3	22	7	Y	
	4	15	7	Y	
062	1	25	8	N	*Alcohol:* wasn't sure.
Nic	2	21	8	N	*Cannabis:* thought he had both.
	3		8	N	*Both:* thought he had had nothing.
	4		9	N	*None:* wasn't sure.
053	1	18	7	?	*Alcohol:* felt a little bit merry. *Cannabis:* very pleasantly moderately stoned.
Stu	2	15	7	?	*Both:* quite high, not higher than home but mood swings and paranoid due to the strange environment.
	3		6	?	
	4		9	?	*None:* felt no effect at all but couldn't tell from taste of drugs.
003	1		8	N	*Alcohol:* thought he may have had both but was again unsure.
Nik	2		6	N	*Cannabis:* thought he had alcohol but was unsure.
	3	20	7	N	*None:* thought he may have had cannabis but was unsure.
	4		–	–	Only did 3 sessions, 1st session 3 weeks previous, couldn't remember.
052	1		7	Y	*Alcohol:* didn't feel as drunk as week 2, but a bit drunk.
Ben	2	19	8	Y	*Cannabis:* felt very stoned, different to usual but ok.
	3		8	Y	*Both:* 'properly mashed', didn't like it, more drunk than normal.
	4	25	6	Y	*None:* felt no effect at all.

variations in food consumption in respect of the content of the meal and the time food was consumed prior to each session. This was despite subjects being asked to standardise their food intake and the time that they ate.

Approximately half of the study volunteers who reported effects of the drug combination felt extremely intoxicated, and claimed they would not normally get this high at home. However, the other half claimed that the experience was similar to their normal state of intoxication, although there was a reluctance to drive in this condition. Interestingly the group who felt extremely high in the combined condition had a slightly lower mean peak BrAC level than the group who found the experience close to their normal high (17.2 µg/100ml and 20.33µg/100ml respectively).

These subjective reports are consistent with the participant's assessment of their liking of the smoking effect as reported in section 5.2 and Appendix C from the mood questionnaire. Some commentators have criticised the use of NIDA supplied cannabis cigarettes in research of this type, on the basis that the cannabis used is of a low strength. Contrary to these reports the current research indicates that the NIDA supplied grass-based cannabis cigarettes were suitable for this trial using this smoking regime.

4 Measures

4.1 Overview

On arrival, participants were checked for alcohol consumption using a Lion SD400 Breathalyser. They then answered various questions to confirm their eligibility and proceeded with the trial.

A range of measures was obtained during the trial. The case report form (see Sexton *et al*., 2000) shows the measure and the time when it was obtained. First, participants were re-familiarised with the simulator, and this included a baseline measurement of how they drove round a 'figure of eight' course. The simulator was used later in the trial session to assess their reactions to other vehicles, how they drove round the 'figure of eight' and their response to a long delay at traffic light controlled junctions.

Participants were asked to complete a mood questionnaire at various stages of their trial session. They also underwent the sobriety tests that were administered by a Forensic Medical Examiner (FME). They were also assessed on an adaptive tracking task.

At different times during the experiment, participants gave samples of saliva and breath alcohol. The saliva samples were taken to obtain a measure of how much Δ^9 - THC was in their system and the breath alcohol samples were taken to obtain a measure of their alcohol level. The initial urine sample was checked using Dade-Behring polydrug indicator strips that showed if the participant had recently been using cannabis, cocaine, amphetamines or opiates. The previous study (Sexton *et al.*, 2000) also took blood samples at different times. This is an invasive procedure, which is also uncomfortable for the subject. The data from the earlier study provided a measure of the relationship between the THC in blood and saliva samples, and hence saliva sampling could be relied on for this study.

4.2 Simulator

A range of measures was derived for each participant when driving the simulator. These are summarised in Table 5. The measures were designed to assess different skills. The motorway driving section was designed to assess reaction times to adverse events. The 'figure of eight' measures control skills in staying within a lane on a road with a curve of constantly changing radius, while the traffic light controlled junction provided a measure of vigilance while waiting for the light to change.

4.2.1 Description

The Transport Research Laboratory (TRL) Driving Simulator is a real medium-sized saloon car (a Rover 414Sli) surrounded by three 3 metre x 4 metre screens to the front providing 210° front/side image and one rear screen providing normal rear vision using vehicle mirrors.

The 'Virtual Reality world' is generated via the MultiGen 3-D modelling package and can be any driving scenario as required. Four projectors display the image on the screens; three linked to give continuous front/side image; a fourth at the rear of the car. The images are generated in 'real-time' and refreshed 60 times per second.

'State of the art' Silicon Graphics Reality engines generate the images. A further Silicon Graphics computer

Table 5 Simulated tasks and associated measures

Scenario	*Performance measure*
Motorway section with vehicles pulling out in front of the driven car.	1. Reaction times to pulling-out events, averaged over several events 2. Minimum time headway during the event.
Motorway section with vehicles braking in front of the driven car.	1. Reaction times to braking events, averaged over several events 2. Minimum time headway during the event.
Motorway section.	Minimum, maximum and average speed.
Following left hand non-circular curve of about 1 km radius.	Standard deviation of lane position from perfect path.
Following right hand non-circular curve of about 1 km radius.	Standard deviation of lane position from perfect path.
Dual carriageway with traffic lights, the lights are triggered to red so the driven vehicle has to stop and there is varying delay for the onset of the green light.	Response time to lights changing to red/amber and the time to crossing a point 10m from the stop line, averaged over several replications with varying time delays.

provides the Simulator operator station with an interface to the experiment. The operator has a 'birds-eye' view of the road layout and the position of all vehicles in the driving scenario, also a continuous representation of the use of the vehicle controls and speed.

The system generates intelligent vehicles, the behaviour of which can relate to that of the simulator vehicle or which behave as autonomous intelligent vehicles operating collision detection and avoidance with driving styles ranging from passive through 'normal' to aggressive.

The car bodyshell is mounted on hydraulic rams (in place of the shock absorbers) which supply motion to simulate the tilt and roll experienced in normal braking, acceleration and cornering. The car is equipped with speakers providing simulated engine, road tyre, and passing traffic noises. Video cameras are mounted in the car and participants' behaviour can be recorded during their drive. However, for this study no recordings were made because of the necessity of preserving the participant's anonymity. An in-car intercom system enables the experimenter to give participants instructions.

This interactive simulator offers the advantages of providing a safe environment to study situations where the risks involved would be unacceptable in the real world. It provides control of conditions enabling repetition and reproducibility. This, combined with efficient data collection, is an ideal research tool. The TRL driving simulator has been shown to be a valuable tool for measuring impairment in drivers (Sexton, 1997).

4.2.2 Motorway drive

A section of motorway was modelled based on the M3. It was about 16.7km in length and ended by turning in to a two-lane road that was modelled on the TRL small loop. The motorway consisted of 3-lanes with a hard shoulder, there were some gentle bends, slopes and bridges and it had the appearance of a normal motorway road, see Figure 1. Two versions were created with different traffic conditions.

Figure 1 An example of the simulated motorway scenario

One version was used for screening/familiarising drivers and for their baseline drive. This consisted of traffic that behaved normally and created an impression of medium to light traffic flow. The traffic is generated by assigning behaviours to specific vehicles. If the behaviour is linked to the driven car then the traffic can be told to speed up or slow down relative to the driven car. In this way traffic speeds vary relative to that of the driven car and create an impression of far more vehicles on the road than there actually are. The simulation only needs to be concerned with what the driver sees, and hence traffic is only needed near the driven car.

The main version of the simulated motor traffic used a combination of vehicle behaviours. Some vehicles were programmed to slow down and speed up as in the screening/baseline version. Other vehicles were programmed to create a situation that the driver would have to react to, either by pulling out in front of the driver, or by braking for no apparent reason. The driver therefore had to modify his driving behaviour in some way, and the time taken to do this provided a measure of his response latency. A computer program was developed to automatically detect this driving behaviour change. The following order of conditions was investigated:

- Foot was on accelerator and has been removed.
- Foot was not on accelerator and the brake has been applied.
- A steering action has been made.

The minimum time headway was computed by looking for the minimum distance between the driven car and the vehicle in front (not necessarily the 'event' vehicle) during the pulling out or braking event. The minimum time was then computed from the distance and speed of the driven car.

The driving speed was continuously recorded during the motorway drive. The minimum, maximum and average speeds were calculated over the whole motorway drive, excluding the first 1000 metres and last 1500 metres and any times when the driver's speed was reduced due to an 'event'. The motorway section of the drive was about 16.7 Km in total length.

4.2.2.1 Pulling out events

Pulling out events are situations where a car pulls out in front of the driven car. The driver will normally have to take avoiding action that can be detected and thus a reaction time can be estimated. Pulling out events were triggered when the trigger vehicle was 45 metres in front of the driven car. The exact circumstances varied from event to event since they were dependent on how the driver had been driving. The events were designed such that they could not be easily anticipated, but also such that the driver had time and space to respond. There were 5 such pulling out events on the motorway drive. The average of the 5 events where a reaction could be determined was taken as a measure of the driver's reaction time. The minimum time headway to the vehicle in front in the same lane was also calculated, and proved to be a more robust and easier to determine measure. The minimum time headway was calculated from the speed and distance

to the vehicle in the same lane during a pulling-out or braking event. The minimum distance was recorded during the event, which may have been to the 'event vehicle' or to a vehicle that had come between the event vehicle and the driven vehicle. The speed at the point where the minimum distance was reached was also recorded, and the time to travel the minimum distance at this speed was calculated.

4.2.2.2 Braking events

Braking events were controlled in a similar way to pulling out events, except that the trigger vehicle braked at a distance of 50m from the driven vehicle. Again, it was not intended to be easy to spot, nor to be so dramatic an event that might cause drivers to lose control or collide with another vehicle. There were some situations where drivers did not take any detectable action. There were 3 braking events and the average of these where a reaction could be determined, was taken as a measure of the driver's reaction time. The minimum time headway to the vehicle in front in the same lane was also calculated and averaged over the three braking events.

4.2.3 Figure of eight

The 'figure of eight' loop is two 1-kilometer long loops with constantly changing radius. Participants were asked to drive between 30mph and 40mph and stay in the middle of the nearside lane. Because the curve is of a changing radius, drivers have to make almost continuous steering wheel corrections in order to stay in the centre of the road lane. The measure of success in the task was the standard deviation of their lateral position in the lane, the higher the standard deviation the more they had 'deviated' in the lane.

4.2.4 Traffic light controlled junction

The final stage of the simulator drive was a dual carriageway. There were four traffic light controlled junctions. The lights were pre-determined to be on red when the driver approached. The driver stopped and was kept waiting for a time varying between 15 and 25 seconds before the red/amber-green sequence started. Two measures of interest were analysed: the time to start from the onset of the red/amber light; and the time that it took to pass a point 10 metres into the junction. It was hypothesised that cannabis may affect drivers' responses to the changing lights. The average of the times for each of the two measures across all junctions was analysed.

4.3 Adaptive tracking

The TRL Adaptive Tracking Test is based on one used at the RAF Institute of Aviation Medicine in Farnborough and tests a subject's ability to co-ordinate eye and hand. The subject is asked to keep a 2mm dot within a 'randomly' moving circle (diameter 15mm). The circle moves according to a weighted pseudo-random sequence, which creates circle movement of a known frequency bandwidth. The subject moves the dot using a 2-degree of freedom joystick. When the dot is inside the circle there is an illusion that the circle appears to be moving more quickly than when the dot is outside. This makes the tracking task more difficult.

The test is run for 5½ minutes, during which the Tracking Speed is sampled every 300ms for a 5 minute period. The mean speed is used in the analysis, the higher it is the better tracking task ability.

4.4 Mood questionnaire

Visual analogue scales (VAS) were used to assess mood state and physical symptoms. These were derived from a variety of sources: the 'Activation-deactivation checklist' (Richardson, 1995); the 'Physical symptoms scale' (Cohen, 1994); and the 'Marijuana scale' from Stephen Heishman at NIDA.

Participants placed a mark on a 100 mm line (see Sexton *et al*., 2000) labelled with a mood state adjective (e.g. friendly, confident, muddled) from 'not at all' to 'entirely', or a physical symptom adjective (e.g. anxiety, dizziness, tiredness) labelled from 'absent' to 'severe'. To ascertain their subjective physical responses to the cannabis dose they were receiving participants placed a mark on a 100 mm line in response to statements such as: 'I have difficulty remembering'; and 'I notice that my heart is beating faster'.

In addition, an end of session questionnaire was presented requiring each participant to rate:

1 the strength of the overall drug effect on a 100mm VAS from 'I felt no effect at all' to 'I felt a very strong effect';
2 their willingness to drive on a 100mm VAS from 'I would not drive under any circumstances' to 'I would drive without any hesitation'; and
3 how much they liked the drug effect on a 100mm VAS from 'disliked a lot' to 'liked a lot'.

4.5 Sobriety tests

The sobriety tests were conducted by FMEs who were very familiar with the usual procedures followed for subjects in police custody. The FMEs used the standard sobriety test measures as recommended by Fleming and Stewart (1998). The test measures are shown in Table 6.

Table 6 Sobriety test list summary

General demeanour and behaviour:	Eyelids red or swollen?
State of clothing:	Conjunctivae?
Speech: thick, slurred, over precise etc:	Evidence of squint etc?
Condition of mouth:	Any gross visual defect – are glasses used?
Pulse: rate and character	Pupil size.
Temperature:	Pupillary reaction to direct light stimulus.
State of tongue:	Horizontal gaze nystagmus.
Breath:	Vertical gaze nystagmus.
Ears:	Convergence.
Heart:	Walk and turn test.
Blood pressure:	One leg stand.
Lungs:	Finger nose test.
Reflexes:	Romberg test: internal clock – 30 seconds estimates at.
	Writing: copying from a text.

The standardised examination form was adapted from the Fleming and Stewart report and contains space to add remarks and conclusions. The impairment testing covered pupil size and reaction to light; presence of lateral and vertical nystagmus and convergence; walk and turn test; one leg stand; finger-nose test; and Romberg's test with internal clock. A full description of these tests can be found in Appendix B with a more detailed version of the sobriety test. In addition, an example of handwriting was assessed. The physical examination included comments on the general demeanour and behaviour of the individual and examination of speech, pulse, temperature, ears, eyes, heart, lungs, blood pressure and reflexes.

Based on the participant's performance of these tests the FME concluded whether in her opinion the individual was impaired, and/or whether there was a condition that might be due to the presence of a drug. This is in accordance with standard procedures.

4.6 Biochemistry

Participants gave samples of urine and saliva prior to smoking cannabis. These were required to provide a baseline measure which facilitated checking for other drug use. A further sample of saliva was taken at 30 minutes after drinking which was 20-25 minutes after smoking. A final saliva sample was taken about 70 minutes after drinking i.e. 60-65 minutes after smoking.

The actual THC levels at peak impairment (25-30 minutes after dosing) were determined from the analysis of the saliva samples. There is good evidence (Menkes *et al.*, 1991) that subjective peak impairment correlates well with saliva THC levels and better than with plasma THC levels. This is probably because of a lag of around 15 minutes while the THC is sequestered in the buccal cavity. This is the same order of time delay between plasma THC level and THC reaching peak levels in the brain.

The saliva samples were collected by participants chewing a salivette for 5 minutes. This was centrifuged in order to extract the saliva. The samples were dispatched to Epsom Hospital Laboratories Regional Assay Service on a weekly basis having been kept frozen prior to transportation. The following substances were assayed in the analysis:

- Δ^8 THC - delta-8-tetrahydrocannabinol - a minor but psychoactive constituent of cannabis
- Δ^9 THC - delta-9-tetrahydrocannabinol - the major psychoactive constituent of cannabis
- THC-COOH - the most rapidly produced metabolite, not psychoactive
- CBD – Cannabidiol, the second main constituent of cannabis but not psychoactive, although it may interact with THC to produce effects

The main sample of interest was the quantity of Δ^9 THC in saliva, because this is the major psychoactive constituent of cannabis. However, the level of THC-COOH in the urine is an indicator of cannabis use. This is the use in terms of frequency over time as well as dose, hence high levels of THC-COOH may indicate that the subject is a frequent user, or that they used cannabis very recently.

5 Analysis and results

The experimental design required 20 participants with 5 allocated at random to each dosing order group. One person attended three sessions but, due to a family bereavement, was unable to complete the trial. Two subjects were asked to return to repeat a test session to obtain an indication of the consistency of the measures. Unfortunately one of these also missed one dose session. As a result, 18 participants completed all 4 dose combinations, two completed only 3 combinations, and two more completed 3 combinations and repeated one of them. Table 7 shows the sample of volunteers and the sample that was achieved. The achieved design is not quite balanced, but given the difficulty in booking this number of test sessions it was considered successful.

Table 7 Number of volunteers entered in the trial and sessions attended

	Number
Entered trial and completed all 4 dose combinations	18
Entered trial and completed 3 dose combinations	2
Entered trial and repeated a combination of doses	2

The data from the case report forms were entered into an SPSS (Statistical Package for the Social Sciences) file. The data from the simulator was processed on the SGI (Silicon Graphics) computers and a file suitable for input to SPSS was generated. The average response times for pulling-in and braking events were based on just those events where a reaction could be determined. The minimum time headway measures were based on just those events where a time could be determined. (In a small number of cases the subject steered around the lead vehicle before the vehicle braked. Consequently, in these cases there was no other vehicle in the same lane and so the time headway could not be calculated).

The analysis considered cannabis and alcohol as factors each with 2 levels (placebo dose and active dose).

5.1 Statistical model

The study design was a crossover experiment where participants attended four trial sessions. At each session they smoked either a placebo or active dose of cannabis and were given either a placebo or active alcoholic drink. The order of dosing was designed to be balanced such that the same number of participants took each dose level on each visit. Neither the participants nor the drug administrator knew what dose was being smoked or drunk, i.e. the administration was a 'double-blind' design.

The allocation of participant to order of dosing was randomised. The participant was treated as his own control. For most of the analyses, a hierarchic analysis of variance model was used with participant as the first level factor. The visit number (or period effect) was the next factor followed by the treatment factors (i.e. doses received). The analyses found carry-over effects for the maximum speed measure and the reaction time to braking

event. However there was no significant treatment effect for the braking reaction and although the maximum speed effect is significant with treatment, it has a similar effect as the average speed which does not have a carry-over effect. The analysis only found significant period effects for the adaptive tracking task. Only the significant probability levels have been reported. Treatments were compared using the Tukey multiple range test option, (this controls for the maximum experiment-wise error rate when comparing a number of mean values).

The analysis of the simulator and adaptive tracking measures used the SAS/GLM package module, (Statistical Analysis System/General Linear Model). The mood questionnaire had measures over time as well as between trial sessions and was analysed using SPSS (Statistical Package for Social Sciences).

5.2 Mood questionnaire

Factor analysis

A factor analysis was conducted on the mood checklist variables. Factor analysis is a statistical technique used to identify sets of variables that are measuring some underlying trait. It is used to reduce a number of correlated variables to a smaller set of factors. Examination of the variables in the three-factor solution suggested that they also went together in a logical sense and each factor was given a label, as shown in Table 8. The factor solution given in Table 8 is that as derived in the previous cannabis study, the basic structure was confirmed by an analysis of the cannabis and alcohol data albeit with some differences. The factors previously derived have been used for reporting of mood changes in this study in order to provide consistency across the two studies.

Table 8 Factors extracted from maximum likelihood factor analysis

Feelings/ signs of anxiety	*Feelings/ signs of listlessness*	*Feelings/ signs of wellbeing*
Increased heart rate	Dizziness	Clear
Shaking	Irritability	Alert
Bodily awareness	Sickness	Drowsy*
Palpitations	Difficulty concentrating	Calm
Anxiety	Slow	Cheerful
Loss of appetite	Tired	Difficulty remembering*
Sweating		
Tenseness		

**Variable coded in reverse direction*

A factor analysis was also conducted using maximum likelihood as the method of extraction, and three similar factors were extracted. The variables 'dry mouth' and 'confidence' did not correlate with the three factors in either of the analyses, and have been analysed separately.

The direction of the scale for the factors

A high score on the anxiety factor reflects a high level of some or all of the following: increased heart rate, shaking, bodily awareness, palpitations, anxiety, and loss of appetite, sweating and tenseness. A high score on the listlessness factor reflects a high level of dizziness, irritability, sickness, difficulty concentrating, slowness and tiredness. A high score on the wellbeing factor reflects a high level of feeling clear, alert, calm and cheerful, and a low level of feeling drowsy and having difficulty remembering.

Analysis and results

A repeated measure ANOVA (Analysis of Variance) and a one-way ANOVA were used to analyse the data. A range of post-hoc testing was carried out by assuming that participants in the different dosing conditions were different people. The SPSS package was used for the analysis. The results of all the mood questionnaire analyses are more fully reported in Board *et al.*, (2002). In general the participants were more anxious and listless and experienced reduced feelings of well being after dosing. This was particularly the case when they had been dosed with cannabis or both cannabis and alcohol. However, their feelings of anxiety and listlessness were generally low, while their well being was generally high.

They were generally more unwilling to drive, for any reason, post-dosing, and particularly when they had been dosed with either cannabis or both cannabis and alcohol.

The strength of the dose was felt to be most strong at 20 minutes post-dosing, reducing in perceived strength by 100 minutes post-dosing. The participants were clearly aware of when a placebo dose had been given in terms of the strength of the effect felt, and liked the stronger effect more.

They felt more stoned at 20 minutes post-dosing, and this feeling was heightened when they received both cannabis and alcohol. However they did not feel any more drunk at 20 or 100 minutes post-dosing, although their feeling of drunkenness was heightened when they had both cannabis and alcohol. Neither did they feel any more impaired at 20 minutes post-dosing compared to 100 minutes post-dosing, although their feelings of impairment were clearly heightened for all the doses compared with the placebo and particularly when they had received both cannabis and alcohol.

5.3 Simulator tasks

The data from the simulator were pre-processed on the simulator computers in order to compute the reaction times on the motorway drive, to estimate the minimum, maximum and average speed on the motorway as well as calculate the standard deviation of the lateral lane position on the 'figure of eight'. The last simulator task was moving off from a traffic light controlled junction, and the computer calculated the time to move once the lights changed to red/amber. The time taken to cross a point 10m from the stop line was also calculated. The data were transferred to an Excel spreadsheet for input to SPSS and to SAS for statistical analysis.

5.3.1 Motorway drive

Table 9 shows the mean speeds while driving the motorway section. The speed data excludes the first 1000 metres and last 1500 metres and any parts of the drive

where the participant was slowed, or stopped, because of the pulling-out or braking event. These speeds thus represent the typical speeds while driving.

Table 9 Minimum, maximum and average speeds on the motorway drive

Speed (mph)	*Cannabis*	*Alcohol*	*Sample size*	*Mean (mph)*	*Std. error*	*95% confidence interval for mean*	
						Lower bound	*Upper bound*
Min	No	No	21	30.77	2.47	24.79	36.75
	Yes	No	20	28.25	1.28	25.13	31.36
	No	Yes	19	29.20	2.75	22.47	35.93
	Yes	Yes	20	30.86	1.88	26.28	35.44
Max	No	No	21	94.27	1.45	90.75	97.78
	Yes	No	20	89.41	1.50	85.77	93.05
	No	Yes	19	97.54	3.06	90.06	105.02
	Yes	Yes	20	89.78	2.40	83.95	95.61
Ave	No	No	21	72.49	1.60	68.61	76.37
	Yes	No	20	67.41	1.63	63.45	71.37
	No	Yes	19	72.45	2.51	66.32	78.58
	Yes	Yes	20	65.87	1.94	61.16	70.58

Figures 2 and 3 show the maximum and average speeds by dose with the associated 95% confidence intervals. There were no statistically significant results from the analysis of the minimum speed data. The analysis for the maximum speed found a just significant carry-over effect, which suggests that the previous dose influenced the response and so the crossover design cannot be analysed.

The analysis of variance for the average speed showed that there was no statistically significant carry-over effect, but there was a significant subject effect ($F_{19,57}$=3.33, p<0.001), and a significant dose effect ($F_{3,57}$=4.70, p<0.01). The subject effect was to be expected because different subjects cope with this task at different tracking speed levels. The most important effect (having allowed for subject effects) was that there are statistically significant differences between the means in each dose group. The mean values suggest that subjects drive slower when they have smoked cannabis, and this effect was not off-set by drinking alcohol. The results from the Tukey multiple comparison analysis show that the cannabis & alcohol v no dose comparison and the cannabis & alcohol v alcohol comparison are significant (p<0.05). Comparison of the adjusted (for driver) means found that there were significant differences between no active dose and cannabis (p=0.023)

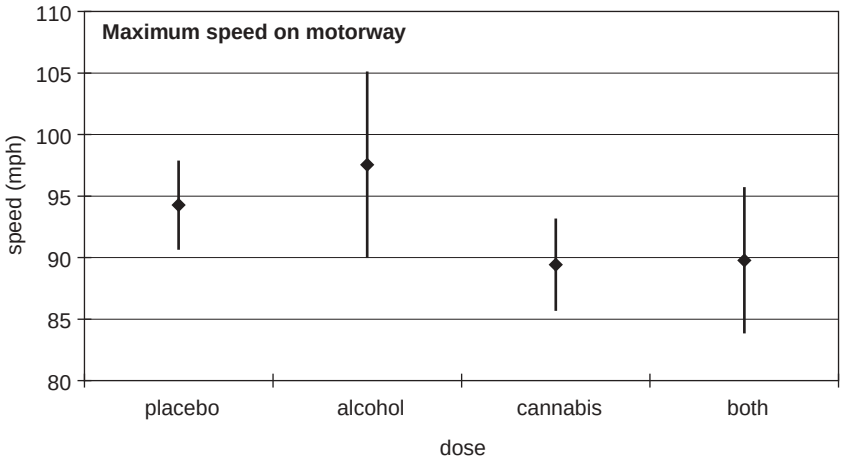

Figure 2 Maximum speed averaged for participants within each dose level

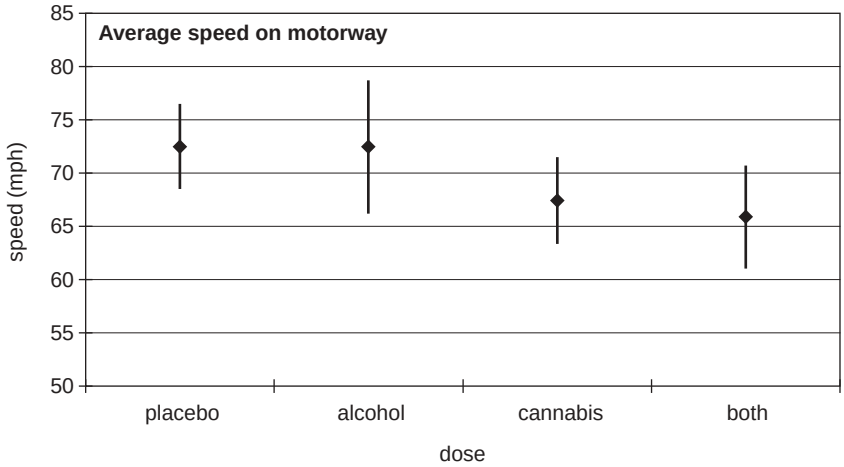

Figure 3 Average speed for participants within each dose level

and between no active dose v cannabis & alcohol (p=0.005). There were also significant differences between the alcohol dose and cannabis (p=0.025) and between alcohol v cannabis & alcohol (p=0.005).

The reaction times to pulling-out and braking events are shown in Table 10. There were no statistically significant results between dose levels on either of these measures. The algorithm discussed in section 4.2.2 was only able to find 64% valid values for the pulling-out event reactions and only 48% valid braking event reactions. It is thought that drivers were sometimes easing their accelerator to reduce speed and this was difficult to determine via an automatic algorithm, hence the high number of undetected reactions.

Table 10 Reaction times (seconds) on the motorway drive

Reaction time (secs)	*Cannabis*	*Alcohol*	*Sample (secs)*	*Mean (mph)*	*Std. error*	*95% confidence interval for mean*	
						Lower bound	*Upper bound*
Pulling-out	No	No	21	0.71	0.069	0.55	0.88
	Yes	No	20	0.73	0.068	0.56	0.90
	No	Yes	18	0.54	0.034	0.45	0.62
	Yes	Yes	19	0.77	0.059	0.62	0.91
Braking	No	No	17	0.65	0.072	0.47	0.83
	Yes	No	16	0.80	0.161	0.40	1.20
	No	Yes	15	0.62	0.071	0.45	0.80
	Yes	Yes	15	0.72	0.101	0.46	0.97

The time headway mean values to pulling-out and braking events are shown in Table 11. The data in Table 11 are plotted in Figures 4 and 5, which suggest that there is an increase in average headway times when cannabis (or cannabis & alcohol) are compared to doses with no cannabis. The analysis confirmed this and the time headways to pulling-out events are significantly different ($p<0.05$) for no active dose v cannabis & alcohol. One advantage of using minimum time headway was that 94% of headway times were valid for the pulling-out events and 84% of the braking events were valid. The missing values were either because of a crash or because the driver had

Table 11 Time headway (secs) on the motorway drive

Time (secs)	*Cannabis*	*Alcohol*	*Sample (secs)*	*Mean (mph)*	*Std. error*	*95% confidence interval for mean*	
						Lower bound	*Upper bound*
Pulling-out	No	No	21	0.55	0.049	0.43	0.67
	Yes	No	20	0.78	0.087	0.57	1.00
	No	Yes	19	0.65	0.068	0.48	0.82
	Yes	Yes	20	0.80	0.102	0.55	1.05
Braking	No	No	21	0.68	0.052	0.56	0.81
	Yes	No	20	1.02	0.113	0.74	1.30
	No	Yes	18	0.73	0.068	0.57	0.90
	Yes	Yes	20	1.00	0.080	0.81	1.20

changed lanes and so there was no other vehicle close within the same lane.

For the time headways to braking events there is a significant difference ($p<0.05$) between no active dose and cannabis dose, between no active dose v cannabis & alcohol, between the alcohol dose and cannabis, and between alcohol v cannabis & alcohol. The time headway increases when subjects have been given cannabis, which suggests that they are driving at a safer distance from the vehicle in front.

The braking and pulling out events provide a useful means of checking whether some doses caused drivers to crash more than others. Crashes were identified by a zero headway time. There was also the possibility that subjects were not so concerned about crashing on their later visits. These were checked and the results are shown below in Table 12. This table shows that there was little difference between the various dose conditions in the number of crashes, but overall there were more crashes in the final visit. Statistical analysis of these results revealed that there were no significant differences between the dose conditions. However, when the proportion of crashes occurring in different visits is compared there is a statistically significant difference ($t=2.42$, $p<0.02$) between visit 2 (3.1% crashes) and visit 4 (9.9% crashes). There are no other significant differences.

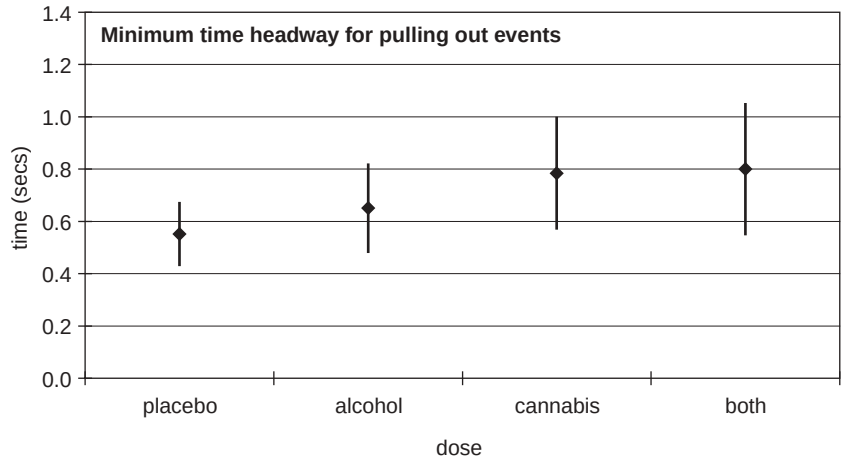

Figure 4 Minimum time head-way for pulling-out events

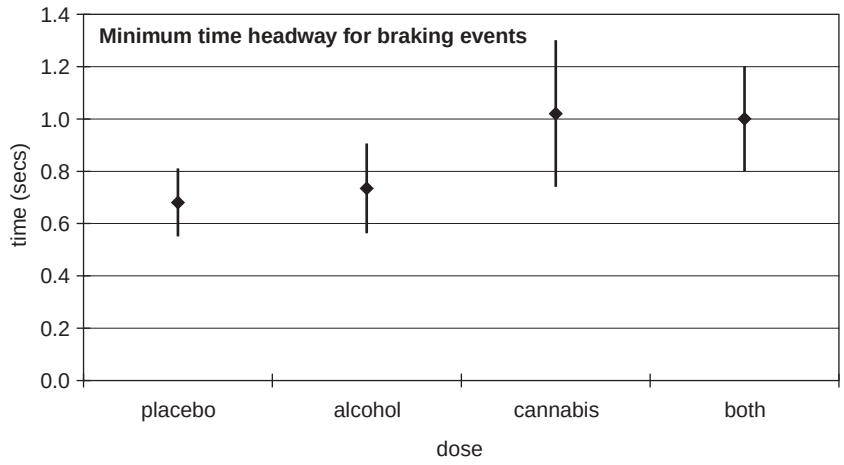

Figure 5 Minimum time head-way for braking events

Table 12 Crashes during simulator run, based on 8 interaction events per run

		Visit				
Dose		*1*	*2*	*3*	*4*	*Total*
A-Placebo	Crashes	2	0	3	5	10 (6%)
	Events	40	40	40	48	168
B-Cannabis	Crashes	3	1	1	4	9 (6%)
	Events	40	48	32	32	152
C-Alcohol	Crashes	0	1	0	4	5 (3%)
	Events	40	40	40	32	152
D-C&A	Crashes	3	3	4	2	12 (7%)
	Events	40	32	48	40	160
Total	Crashes	8 (5%)	5 (3%)	8 (5%)	15 (10%)	36 (5.7%)
		160	160	160	152	632

This finding is interesting in that one might have expected subjects' performance to be at a peak on the final visit, due to familiarity with the equipment and the task requirements. However, the finding supports the view that subjects were perhaps becoming complacent by this stage and consequently were less diligent in their driving. It is also interesting to note that the largest number of crashes for the fourth visit was the placebo condition, not – as might be expected – one of the drug or alcohol conditions.

5.3.2 Figure of eight

The measure of interest when participants are driving round the 'figure of eight' was the SDLP (Standard Deviation of Lateral Position), in the road lane. This was measured by the variability in the lateral lane position and the standard deviation of the lateral position was used as a metric. The mean values of the SDLP are given in Table 13. They show that when participants have doses of the cannabis there is a little more variation in their lateral position on the right-hand curve. Analysis of the SDLP data from the left-hand curve did not find any statistically significant differences.

Table 13 Average standard deviation of lateral position on figure of eight drive

						95% confidence interval for mean	
SD of deviation (metres)	*Cannabis*	*Alcohol*	*Sample size*	*Mean (metres)*	*Std. error*	*Lower bound*	*Upper bound*
Left curve	No	No	21	0.23	0.015	0.19	0.26
	Yes	No	19	0.22	0.016	0.18	0.26
	No	Yes	19	0.22	0.014	0.19	0.26
	Yes	Yes	19	0.23	0.017	0.19	0.27
Right curve	No	No	21	0.21	0.011	0.18	0.24
	Yes	No	20	0.24	0.016	0.21	0.28
	No	Yes	19	0.21	0.014	0.18	0.25
	Yes	Yes	20	0.25	0.013	0.22	0.28

Table 13 shows the mean SDLP from driving the left and right-handed curves. The data for the right-hand curve are plotted in Figure 6. However, the analysis of the right-hand curve data showed that the probability of no dose effect was p=0.052, which is strictly not statistically significant at the usual accepted 5% level.

The Tukey comparisons did not find any significant differences but directly comparing the adjusted (by driver) means found a significant difference between the no active dose v cannabis only (p=0.027) and a significant difference between the no active dose v cannabis & alcohol (p=0.023). Thus cannabis has a small effect on the subject's ability to steer on a right-hand curve, but this effect is not apparent on a left-hand curve.

5.3.3 Traffic light controlled junction

The average time for the participant to move from the traffic light controlled junction when the lights went to red/amber, and the time to cross a point 10 metres after the junction stop line are shown in Table 14.

Analyses of the data in Table 14 did not find any statistically significant differences between the four dose group means. The mean values suggest that the effect of cannabis may slow the time to go and to cross a point 10m after the junction, but the differences are very small especially

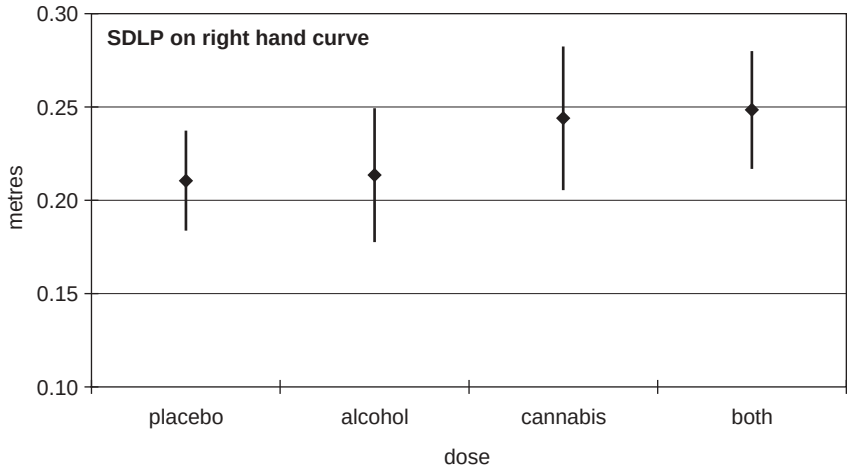

Figure 6 Average SDLP on right-hand curve

Table 14 Average time to start and to cross 10m point after traffic lights change to amber

						95% confidence interval for mean	
Time in seconds	*Cannabis*	*Alcohol*	*Sample size*	*Mean (secs)*	*Std. error*	*Lower bound*	*Upper bound*
To react to traffic lights	No	No	21	2.72	0.13	2.40	3.05
	Yes	No	20	2.74	0.18	2.30	3.18
	No	Yes	19	2.64	0.21	2.14	3.14
	Yes	Yes	20	2.77	0.19	2.32	3.22
To point 10m after traffic lights	No	No	21	4.89	0.18	4.45	5.33
	Yes	No	20	4.94	0.21	4.42	5.45
	No	Yes	19	4.76	0.24	4.17	5.36
	Yes	Yes	20	5.10	0.22	4.57	5.62

when compared with the associated standard errors. The response times are quite variable. This was also found in the previous study (Sexton *et al.*, 2000), where it looked as if high doses of cannabis may actually improve the response time. The most likely explanation is that the data are very 'noisy' and so it is difficult to obtain consistent results.

5.4 Adaptive tracking

The adaptive tracking task measured the participant's eye/hand co-ordination. The average tracking speed over a 5-minute period provides the measure, the higher the value the better the eye/hand co-ordination. Table 15 shows the mean values for each of the different dose conditions.

Table 15 Adaptive tracking results by dose

						95% confidence interval for mean	
	Cannabis	*Alcohol*	*Sample size*	*Mean*	*Std. error*	*Lower bound*	*Upper bound*
Tracking speed m/sec	No	No	21	29.40	0.99	27.42	31.38
	Yes	No	20	28.21	0.88	26.45	29.98
	No	Yes	19	27.14	1.02	25.10	29.18
	Yes	Yes	21	26.14	1.03	24.06	28.21

The analysis of variance showed that there was no statistically significant carryover effect, but there was a significant subject effect ($F_{19,53}$=9.60, p<0.001), a significant visit effect ($F_{4,53}$=4.12, p<0.01) and a significant dose effect ($F_{3,53}$=4.02, p<0.02). The subject effect was to be expected because different subjects cope with this task at different tracking speed levels. It is not surprising that there was a learning effect with the repeated number of visits. However, the most important effect (having allowed for subject and visit effects) was that there are statistically significant differences between the means in each dose group. The mean values suggest that the cannabis and alcohol impair more than just alcohol which impairs more than just cannabis. The results from the Tukey multiple comparison analysis shows that the alcohol v no dose comparison approaches statistical significance (p=0.07), and the cannabis & alcohol v no dose comparison is statistically significant (p=0.002). Figure 7 illustrates the data in Table 15 and clearly shows the decrease in the mean tracking measure with cannabis, alcohol and cannabis & alcohol doses.

The adaptive tracking task has been shown to be sensitive to impairment through alcohol (Sexton, 1997). Within this trial it suggests an increased impairment for the dose order of: placebo→cannabis→alcohol→alcohol+cannabis. This is different from the order observed on simulator based measures, where low levels of alcohol were not found to be as impairing as low levels of cannabis.

5.5 Sobriety tests

The sobriety tests were administered to participants by the Forensic Medical Examiner (FME) who then reached a conclusion about the impairment of the participant, and whether their condition was likely to be due to a drug and/or alcohol. The decision reached was subjective, but one based on the results from the tests together with the FME's experience. Table 16 shows the decision reached. A Chi-squared test shows that there is a relationship between the rows and columns, i.e. the decision made does depend upon the dose received. This suggests that the sobriety

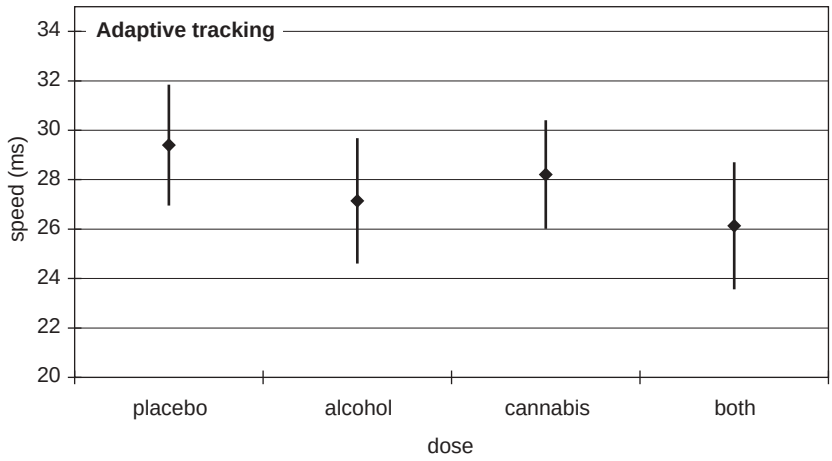

Figure 7 Adaptive tracking speed (m/sec) by dose

Table 16 Decision on impairment

		Impaired?		
Dose		*Yes*	*No*	*Total*
No cannabis, no alcohol	Count	–	21	21
	Row %		100%	
Cannabis and no alcohol	Count	–	19	19
	Row %		100%	
No cannabis and alcohol	Count	2	17	19
	Row %	10.5%	89.5%	
Cannabis and alcohol	Count	4	15	19
	Row %	21.1%	78.9%	
Total	Count	6	72	78
	Row %	7.7%	92.3%	

Chi-squared test = 8.32, df=3, p<0.05

Table 17 Condition due to a drug

		Condition due to drug?		
Dose		*Yes*	*No*	*Total*
No cannabis, no alcohol	Count	3	18	21
	Row %	14.3%	85.7%	
Cannabis and no alcohol	Count	7	12	19
	Row %	36.8%	63.2%	
No cannabis and alcohol	Count	7	12	19
	Row %	36.8%	63.2%	
Cannabis and alcohol	Count	14	6	20
	Row %	70.0%	30.0%	
Total	Count	31	48	79
	Row %	39.2%	60.8%	

Chi-squared test = 13.5, df=3, p<0.01

tests are of value in deciding whether a participant is impaired in FME terms, applied when assessing someone who may have been placed in police custody. The table indicates that the FME decision was related to the dose received. However, it should also be noted that the table shows that, when under the influence of cannabis, none of the 19 subjects were considered by the FME to be impaired. Only 2 of those under the influence of alcohol were impaired, while when under the influence of both cannabis and alcohol only 4 were considered impaired.

Table 17 shows whether the condition was judged to be due to a drug and Table 18 if the condition was thought to be due to alcohol. A Chi-squared test on Table 17 shows that there is relationship between the rows and columns, i.e. the decision made does depend upon the dose received. This suggests that the tests have validity in helping the FME to decide whether a participant has a condition due to a drug. The Chi-squared test on Table 18, for if the condition was thought due to alcohol, was not significant at the 5% level, and so the sobriety tests do not seem so useful for detecting impairment due to small doses of alcohol.

Table 18 Condition due to alcohol

		Condition due to alcohol?		
Dose		*Yes*	*No*	*Total*
No cannabis, no alcohol	Count	3	10	13
	Row %	23.1%	76.9%	
Cannabis and no alcohol	Count	7	6	13
	Row %	53.8%	46.2%	
No cannabis and alcohol	Count	5	6	11
	Row %	45.5%	54.5%	
Cannabis and alcohol	Count	11	4	15
	Row %	73.3%	26.7%	
Total	Count	26	26	52
	Row %	50%	50%	

Chi-squared test = 7.2, df=3, p<0.10

The analysis of the sobriety tests showed that there is some validation evidence in this test battery. A more complete report of this part of the trial can be found in Appendix B.

The measures obtained in the simulator were analysed to compare the performance of participants who were judged by the FME to be impaired with the performance of those judged not to be impaired. Table 19 shows the mean values for each measure for these two groups and tests if the mean values are different. It should first be noted that the group sizes are very different, which makes obtaining statistically significant results difficult. Table 19 shows that there were very few significant differences between the performances of the two groups. However, there is some evidence that the decision on impairment is substantiated by the subject's driving on the 'figure of eight'. It is not immediately clear why the right loop should present more difficulties than the left loop. It has been suggested that these results might be in some way related to the side of the road on which we drive, but this has yet to be verified.

5.5.1 Comparison of subjective ratings and FME's decisions regarding impairment

As a further means of evaluating the effectiveness of the sobriety tests the FME's decisions regarding impairment were correlated with the participants' subjective ratings of impairment which formed part of the mood questionnaire.

Table 20 shows the mean self assessment ratings (range 1-100) of those subjects who were considered impaired compared with those who were considered not impaired.

Table 20 shows that subjects considered impaired by the FME rated themselves as more impaired at 30 minutes than those considered not impaired by the FME (in both cases the FME's decision was not known by the subjects). This was the only statistically significant result. It is likely that the wide variation in subject's ratings and the variation in group sizes accounts for the lack of significance. These results are interesting for two reasons. First, they offer some support for the validity of the FME's decisions. Second, they offer further support for the view that, under the influence of cannabis, users are aware of their impairment and may modify their behaviour.

Table 20 Comparison between subjective ratings of impairment with FME's decision

	FME's decision		
	Impaired (n=6)	*Not impaired (n=72)*	
Measure	*Mean subjective rating and (standard error)*		*Prob. of difference in mean rating*
Impairment rating at 30 mins	58.0 (14.1)	32.5 (3.2)	P<0.05
Impairment rating overall	53.0 (11.0)	35.0 (3.2)	ns
'Stoned' rating at 30 mins	45.3 (15.8)	35.9 (3.7)	ns
'Stoned' rating overall	48.7 (15.6)	36.7 (4.0)	ns
'Drunk' rating at 30 mins	25.7 (7.8)	23.0 (2.8)	ns
'Drunk' rating overall	28.2 (10.8)	23.7 (2.9)	ns

5.6 Cannabis and alcohol doses

Participants smoked a pre-prepared NIDA cannabis cigarette and had a drink that may have contained alcohol (about a triple Vodka; 3 units). The alcoholic drink was designed to bring subjects to a blood alcohol concentration of 50 mg/100ml or 22µg/100ml on breath alcohol at 30 minutes post dosing. The dose was calculated according to the subject's body mass and was presented as a drink containing 10% by volume of alcohol. Subjects were asked not to eat for 2 hours before coming to the trial, nor take any caffeine or alcohol. However, in practice their food intake prior to coming in for the trial varied considerably and this affected the uptake of the alcohol. On average the 22µg/100ml was not quite achieved and there was some variation between subjects, as is shown in Table 21.

Analysis of the saliva samples provided measures of the cannabinoids in the participant at 30 minutes and at 70 minutes post dosing. The main active compound is Δ^9 THC and this has been taken as the potentially impairing substance in the main analysis. The level of Δ^9 THC depends upon the dose given and the way the dose was smoked. If participants did not inhale or only took few small draws then they would not have received as large a dose as someone taking long draws and inhaling deeply. This is unlikely because the smoking regime was closely monitored and controlled by the drug administrator, who observed and recorded the smoking style of each individual.

Table 19 Mean values for whether impaired or otherwise according to the conclusion reached by the FME conducting the sobriety test

Impaired		*Max. speed*	*Ave. speed*	*Min time headway to pulling-out event*	*Min time headway to braking event*	*Traffic light response to 'amber'*	*Left loop SDLP*	*Right loop SDLP*
Yes	Mean	90.4	67.7	0.842	0.814	3.19	0.278	0.297
	se	4.22	5.20	0.083	0.214	0.519	0.034	0.031
	Sample	6	6	6	6	6	6	6
No	Mean	92.9	69.7	0.700	0.854	2.68	0.221	0.224
	se	1.17	1.01	0.043	0.047	0.084	0.008	0.007
	Sample	74	74	74	73	74	72	74
	F-test	0.35	0.29	0.18	0.24	2.47	4.30	8.74
	Prob*	ns	ns	Ns	ns	ns	**<0.05**	**<0.01**

** The probability of the simulator measure mean values being the same*

Table 21 Alcohol (BrAC mg/100ml) and cannabis (ng/ml) levels by dose

			At 30 minutes		*At 70 minutes*	
Cannabis	*Alcohol*	*Sample size*	*Mean*	*Std. deviation*	*Mean*	*Std. deviation*
THC						
No	No	21	–	–	–	–
Yes	No	20	95	113	–	–
No	Yes	19	–	–	–	–
Yes	Yes	21	149.9	140	–	–
Breath alcohol						
No	No	21	–	–	–	–
Yes	No	20	–	–	–	–
No	Yes	19	21.6	5.81	16.2	3.60
Yes	Yes	21	18.2	4.82	15.2	3.94

Figure 8 shows the relationship between Δ^9 THC at 30 minutes and at 70 minutes after smoking commenced for those subjects who had smoked an active cannabis dose. It shows a fairly strong relationship over time as might be expected. One subject had very high values, which were fairly consistent but have been omitted from the figure. These high values may be due to oral contamination from the cannabis cigarette. This may be caused by bits of leaf getting into the mouth and contaminating the saliva. Alternatively, given that his THC-COOH values were not high he may have been a more naive user whose smoking technique gave him a large dose.

Figure 9 shows the THC-COOH level (ng/ml) in the urine sample as supplied on arrival for each test session, plotted against the Δ^9 THC (ng/ml) at 30 minutes for subjects who were given an active cannabis dose. The data on THC-COOH are an indication of the level and pattern of cannabis use. The higher the level the more frequent and/or more recent the subjects' use. It does appear from the analysis of the urine that there are 6 subjects who have

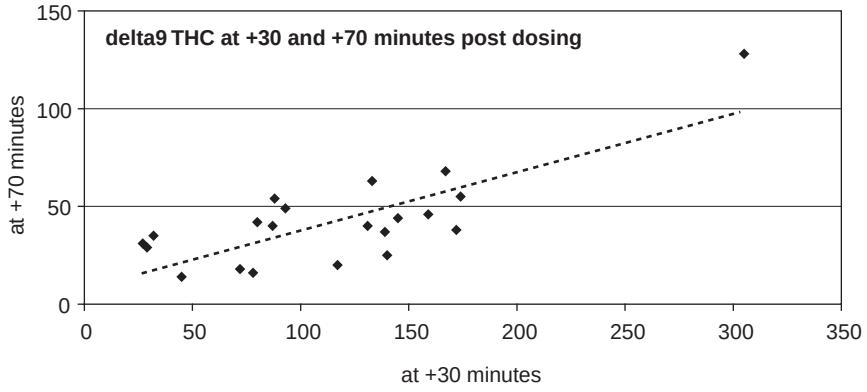

Figure 8 THC levels (ng/ml) at 30 minutes and 70 minutes post smoking

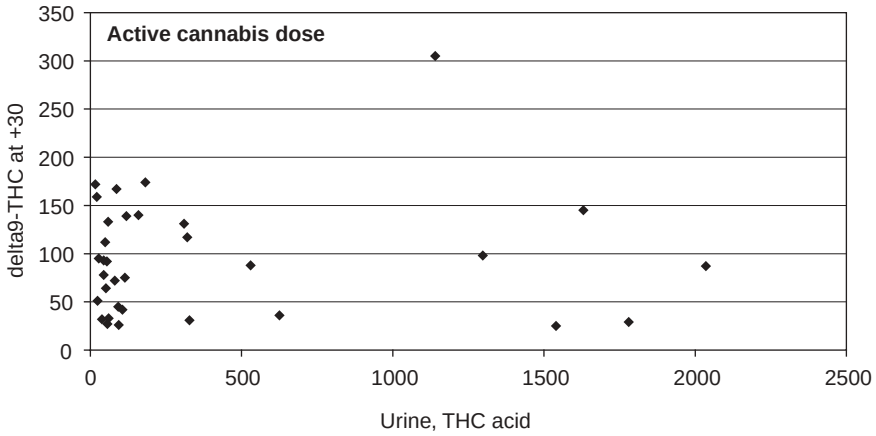

Figure 9 Saliva THC levels (ng/ml) at 30 minutes and urine THC-COOH level (ng/ml)

higher THC-COOH values than the others. However, Figure 9 does not suggest that previous usage influences the active Δ^9 THC level at 30 minutes.

Comparing the six subjects with the higher urine THC-COOH levels with the other 14 subjects across the simulator measures gave some interesting results. The average values from all the measures for those with high THC-COOH levels were all worse than those with lower values. By worse it is meant that their reaction times were slightly longer, their time headways were slightly less, their average speed was higher, or they 'wobbled' a bit more on the 'figure of eight'. However, only one of these was statistically significant which was the headway time to pulling out events while driving on the motorway. Unfortunately, it is not possible to say whether the high levels of THC-COOH in this group are due to recency or frequency of use. If the latter, the finding that this group performed poorer on the various measures would appear to be consistent with previous work that has shown that long term cannabis use has a detrimental effect on cognitive function (Solowij *et al.*, 1998). This would appear to be an interesting finding, worthy of further exploration.

As stated above, high levels of THC-COOH may be due to recency of use or frequent usage and high doses will tend to produce high THC-COOH levels. Table 3 shows the number of hours since subjects last smoked cannabis. On arrival they supplied a urine sample, the THC-COOH level in the urine provides an indication of usage. The six subjects analysed as being heavier users were identified from the THC-COOH levels, and did seem to be a bit different in terms of performance. In order to explain further the above finding the time since last smoking cannabis was plotted against THC-COOH levels in urine. This data is shown in Figure 10, which suggests that nearly 20% of the variation in THC-COOH levels can be explained by the time last smoked.

There is some evidence that subjects who smoked within 12 hours of being tested had higher THC-COOH levels. These may have been atypical because of their usage and this is reflected in their performance as seen above.

5.7 Comparison between the cannabis trial and the cannabis & alcohol trial

The cannabis trial that took place in early 2000 (Sexton *et al.*, 2000) used the same simulation task as the current cannabis & alcohol trial. As such it is interesting to compare average results from these two trials. The subjects were recruited in similar ways, but those helping with the cannabis and alcohol trial were probably heavier users and none of them were much over 30 years of age, whereas in the cannabis trial there was a group of 4-5 subjects in their late 30s or early 40s.

Results from the cannabis trial and from the cannabis & alcohol trial have been plotted together in Figures 11 and 12. Respectively, they show the mean values with 95% confidence interval for the average speed on the motorway section of the simulated drive and the SDLP measure on the right-hand loop. The suffixes 1 or 2 refer to either the cannabis trial or the cannabis & alcohol trial. The figures show that a low dose of cannabis (i.e. 10mg) or more produces a change in these measures and this is consistent between the two studies. The replicate values for the placebo condition and the low dose of cannabis condition are also very similar between the two studies.

These results are encouraging for two reasons. Firstly, being able to replicate results across studies increases the confidence in the research. The sample subjects were different (apart from 4 subjects who took part in both), the average ages were different by >2 years and there is some evidence that one group had a sub-set of heavy cannabis users – and yet the findings were very similar. Secondly, plotting these 8 values together provides a useful indication of the relative effects from different impairing substances and at different dose levels (in the case of cannabis). For example, it can be seen that the performance on the placebo doses, the alcohol alone and the very low resin dose are similar, whereas a dose of cannabis >10mg THC with or without alcohol are also similar.

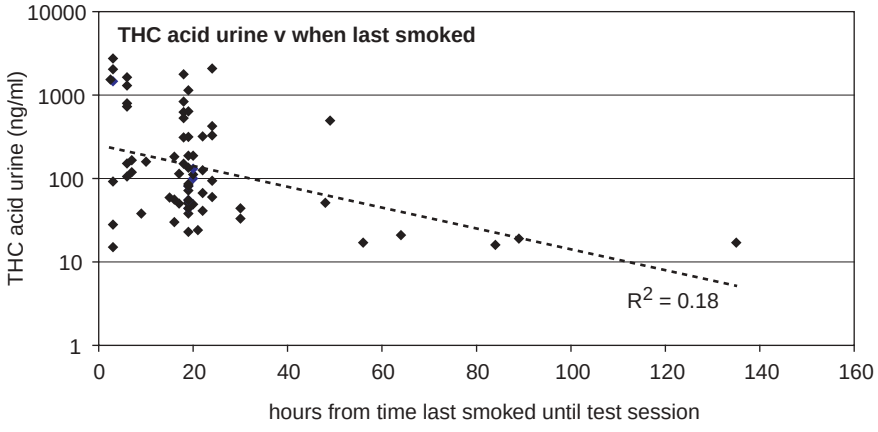

Figure 10 Urine THC-COOH levels (ng/ml) on arrival vs. time last smoked

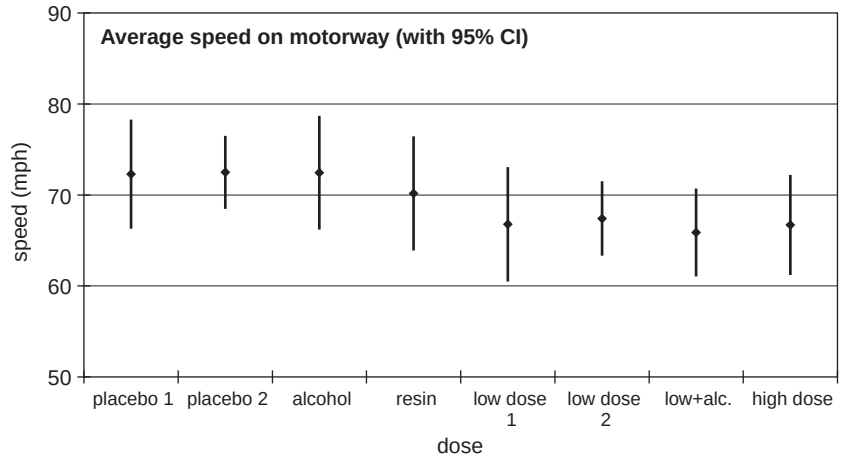

Figure 11 Average speed on motorway

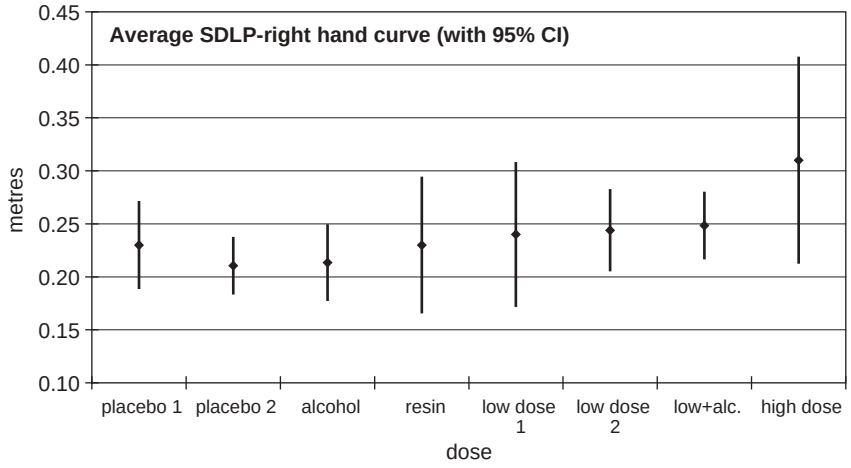

Figure 12 Average SDLP on right-hand curve

6 Summary of main results and discussion

6.1 Summary of main results

The results of statistical analyses of the observations on driving performance tasks and driving-related laboratory tests are summarised in Table 22. There was a reduction in average speed on the motorway when participants had the active doses of cannabis. This confirms the results from many previous studies. It strongly suggests that the participants, as drivers, are aware of their impairment, but attempt to compensate for this impairment by driving more cautiously. A post trial survey of participants showed that they were very good at guessing what dose combination they had received.

In the simulator trials where specific events involving other traffic were assessed, then participants tended to have a bigger minimum time headway to pulling-out events and to braking events when they had taken the active dose of cannabis regardless of the alcohol dose. This suggests a compensatory action for the effects of cannabis impairment.

When considering the simulator tracking tasks, participants tended to drive less accurately on the right loops of the 'figure of eight' when they had been on the active cannabis dose. This suggests that they were unable to control their steering as well when under the influence of a cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

The mean tracking speed on the adaptive tracking task decreased with increasing level of dose, i.e. from no active dose, to cannabis, to alcohol to cannabis & alcohol. Tracking was more accurate under the double placebo condition than under either of the doses with alcohol involved.

There were no statistically significant differences between the mean values of either of the response time measures from the traffic light controlled junctions. This is probably because of the variability in subject's responses. The responses from the previous study (Sexton *et al.*, 2000) suggested that there may have been quicker responses from high doses of cannabis, however it is now considered that this was an aberrant result. It is thought unlikely that data from traffic light responses is providing useful measures in the context of the dose levels and fluctuations in subject's responses.

Table 22 Summary of significant results (from comparison of adjusted means)

No active dose vs. cannabis	*No active dose vs. alcohol*	*No active dose vs. cannabis & alcohol*	*Alcohol vs. cannabis*	*Alcohol vs. cannabis & alcohol*
Maximum speed on m'way (lower speed with cannabis)*				
p=0.046	ns	ns	p=0.001	p=0.002
Average speed on m'way (lower speed with cannabis)				
p=0.023	ns	p=0.005	p=0.025	p=0.005
Minimum time headway to pulling-out events (longer headway with cannabis)				
p=0.024	ns	p=0.016	ns	ns
Minimum time headway to braking events (longer headway with cannabis)				
p=0.001	ns	p=0.002	p=0.003	p=0.006
SDLP on right loop (more 'wobbly' with cannabis)				
p=0.027	ns	p=0.023	ns	ns
Adaptive tracking task (poorer performance with alcohol & worse with cannabis+alcohol)				
ns	p=0.028	p=0.002	ns	ns

** Only probabilities less than 5% have been reported, i.e. 'ns' means that the probability of rejecting the null-hypothesis is greater than 0.05, i.e. there is at least a 5% chance that there is no difference between the two dose levels being compared.*

It was interesting to compare the mean results from the previous study (placebo, low cannabis, high cannabis and resin dose), with the mean results from this current study. Many of the measures used were the same across both studies, and in particular the results from average speed on the motorway and the SDLP right-hand curve suggest an ordering of the performance measures. The ordering being: placebo / alcohol / resin / low-cannabis / low-cannabis & alcohol / high-cannabis; although the analysis found two main groupings (placebo, alcohol, resin) v (low cannabis, low cannabis & alcohol, high cannabis). Similar results were also found when looking at the mood questionnaire data, e.g. for willingness to drive for various reasons, feelings of wellbeing, feelings of anxiety.

Overall, the results of this study show a broad consistency with the effects of cannabis and low doses of alcohol on driver performance observed by previous researchers. The study itself has demonstrated an ability to conduct trials investigating the impact on driving skills and related tasks of potentially impairing substances. It has demonstrated the usefulness of the TRL simulator for such studies and has proved a model for experimentation of this type. The involvement of local doctors and the liaison with the local area ethics committee and the Home Office has been necessary to conduct such trials in a safe and responsible way using subjects who are known cannabis users, in itself no trivial task. Most importantly, the study has addressed and sought to eliminate criticisms of previous trials of a similar nature and for the first time conducted them within the UK.

6.2 Discussion of results

In reviewing the results of this research it is important to consider previous studies, particularly in relation to four key issues identified in the review by Ward and Dye (1999) These were exposure, biological response, acute psychomotor response and driving response.

i Exposure

Care was taken to ensure that, as far as possible, participants were experienced cannabis and alcohol users, (defined as using cannabis and alcohol at least once a week for the past 12 months or more). Conformity with the cannabis criterion was checked by testing participant's urine samples during medical screening.

Prior to this research, few studies have attempted to gain broader sociological information about driving under the influence of cannabis. A comparison between the participants in the current study and a group of regular cannabis and alcohol users in the West Midlands (Appendix A) showed the trial group to be fairly typical. Both groups showed a reluctance to drive after consuming more than 4 units of alcohol, believing their driving to be significantly impaired. The majority of both groups thought that cannabis impaired their driving, but only to a slight degree.

ii Biological response

In considering the results of the present study, the biological response of the participants to the consumption of cannabis is of fundamental importance. Saliva and breath alcohol measurements were taken immediately prior to dosing and at 30- and 70-minute intervals post-dosing.

It is important to make any assessment of the impairing effects of cannabis relatively soon after dosing as the acute effects of cannabis intoxication are known to wear off quite quickly, certainly within 2 hours.

The subjective feelings of the 'highs' experienced were also closely correlated with the participants' 'liking' of the smoking effect as stated in the mood questionnaire. Making allowance for the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

iii Acute psychomotor response and tests of impairment

It is important to try to relate the observations derived from this experimental study to the situations likely to be encountered in real life drug-driving cases. Part of the experimental procedures therefore included the formal sobriety testing of participants. Two experienced FMEs examined the participants and carried out a comprehensive physical examination to see whether the suggested standard 'impairment' tests currently used (Tunbridge *et al.,* 2000) were effective in detecting impairment due to cannabis and/ or due to alcohol. The results of the sobriety testing show a correlation between cannabis and alcohol dose received and whether impairment was judged to be present.

Sobriety testing was carried out under the same conditions as previously applied in the trials using cannabis only (Sexton *et al.,* 2000). In that study 'preliminary'

criteria for judging impairment were suggested, based on examinations on the previous 15 participants. These were related to the failure of a specific number of parts of the standard sobriety tests. At that stage it was recognised that these criteria were very much a 'first calibration' based on a small number of subjects and would be subject to further revision and assessment.

As the current study proceeded it was recognised that the strict criteria of impairment suggested in the last trial needed to be relaxed and some revision was applied in the assessments made. On further reviewing those with a condition due to a drug or alcohol it was clear that those who failed *any* component of *three* separate impairment tests, rather than three components of three tests appeared to be impaired. Application of these revised criteria would have given rise to a further 8 cases of impairment. However, it is possible that such a relaxation of the criteria might also give rise to a greater number of false positives, i.e. cases where an individual not impaired due to drugs is deemed impaired because of their inability to perform the tests.

In order to strengthen and clarify these findings a blind review of the results by an independent experienced FME was conducted. This process is analogous to the situation where an expert is asked to review the recorded evidence prior to court proceedings.

This produced some interesting results. The independent FME agreed with the original conclusions that the 6 participants in Table 15 were impaired. However they felt that a further 12 participants originally classified with a condition were impaired and, with regard to the participants originally classified as normal, a further 2 were impaired and 23 had a condition, the remaining 24 as normal. Although this independent evaluation appears to be a substantial relaxation of the original criteria for 'defining' impairment, it is very instructive to compare this assessment with the participant's own view of how intoxicated or impaired they felt 'overall' on each particular session (Table 4).

This latter data is only available for 13 of the 20 subjects, because 7 were not surveyed. For these 13 participants, however, self-reporting of impairment was available for 50 sessions (Table 4). Analysis of these 50 sessions shows that in 33 cases the self assessment agrees with both the original and independent FME's assessment, in 2 cases there was an over assessment by the FMEs. But in the remaining 15 cases the participants felt that they were *more* impaired than assessed by the FMEs. In 12 of the 15 cases this was true both for the original and independent assessment.

As with the cannabis-only study these findings can only be regarded as a preliminary assessment of how impairment is felt by those under the influence of drugs and/or alcohol and how this impairment may be independently judged and recorded. However, it does suggest that individual participants are aware of their own impairment to a greater extent than is generally realised and that may be readily detected in sobriety or performance tests.

Such knowledge, if vindicated with a larger trial and sample, suggests that there may be considerable value in an awareness or education programme on the impairing effects of drugs, be they illicit or medicinal.

iv Driving response

The results of this study with respect to the final key issue relate to the effects of cannabis on driving response. A meta-analysis of cannabis and alcohol studies shows that actual driving, coding and divided attention tasks, which all require integrative mental processes, are severely affected by alcohol. Simple attention/vigilance tasks are not so much affected and psychomotor skills - especially tracking - and simple reaction time tasks are only affected at relatively high blood alcohol levels. Thus, the effect of alcohol may be seen as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psychomotor skills and simple attentional processes are much smaller.

In contrast, cannabis first seems to affect tasks requiring psychomotor skills and continuous attention. Thus, tracking as a fast feedback loop between continuous visual inspection and spontaneous motor reaction to changes is very sensitive to short term distortions in attention. On the other hand, integration processes and higher cognitive functions are not as time critical as motor reactions. A short attention lapse can be compensated for by increased activity afterwards.

In the case of the integrative task of driving, the negative effects of these short-term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the often-reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

7 Conclusions

This research has demonstrated the practicability of assessing the influence of cannabis and alcohol on driving performance in a controlled clinical trials experimental situation. Participants were recruited, medically screened and tested under conditions of a strict protocol that had local ethics committee approval.

The subjective reports of smokers on the effects of smoking the cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarette.

The feelings of the 'highs' experienced were also closely correlated with the participant's positive reactions to a mood questionnaire. Given the controlled conditions of the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

Previous studies have shown that simulated and actual driving and divided attention tasks, which all require integrative mental processes, are severely affected by alcohol. Simple attention / vigilance tasks are not so much affected and psychomotor skills, especially tracking, and simple reaction time tasks are only affected at relatively high blood alcohol levels. Alcohol may, therefore, be seen

as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psychomotor skills and simple attentional processes are much smaller.

In contrast, previous studies with cannabis show that it first seems to affect all tasks requiring psychomotor skills and continuous attention. Thus, tracking tasks, which are very sensitive to short term changes in attention, are very sensitive to cannabis impairment. On the other hand, integration processes and higher cognitive functions are not as time critical. A short attention lapse can be compensated for by increased activity later.

In the case of the overall driving task, it seems that the negative effects of these short-term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the frequently reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

Results using the TRL driving simulator confirm the results from these previous studies. There was a reduction of average speed and an increase in minimum time headway on simulated motorway driving when participants had the active dose of cannabis, regardless of the alcohol dose. This strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate for their impairment by driving more cautiously.

The results of the simulator tracking tasks showed that participants tended to drive less accurately on the right loops of the 'figure of eight' when they had smoked the active cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

The results of the adaptive tracking task (a laboratory task which measures ability to track a moving object on a computer screen) also produced statistically significant results. Tracking performance deteriorated with dose level, i.e. from placebo, to cannabis, to alcohol, to cannabis & alcohol. Tracking performance under the influence of alcohol or the combined influence of cannabis and alcohol is statistically significantly worse than performance under no active dose.

The experimental procedures included the formal sobriety testing of participants, carried out by two experienced Police Surgeons/Forensic Medical Examiners (FMEs). The results of this sobriety testing show a correlation between active cannabis dose received and whether impairment was judged to be present. On the basis of these observations, the general medical examination and standardised impairment testing applied by the police surgeons were judged to be effective in determining impairment. The police surgeons drew preliminary conclusions on the number and combination of impairment test failures that would allow a conclusion that the driver was 'impaired'. The FME's assessment was compared with the participant's own view (given in Table 4) of how intoxicated or impaired they felt 'overall' on each particular session.

In two thirds of cases these assessments were in agreement, but interestingly in the majority of the remainder the participants felt that they were *more* impaired than assessed by the FMEs.

These findings can only be regarded as a preliminary assessment of how impairment is felt by those under the influence of drugs and/or alcohol and how this impairment may be independently judged and recorded. However, it does suggest that individual participants are aware of their own impairment to a greater extent than is generally realised and that may be readily detected in sobriety or performance tests.

The results of this study confirmed those of the previous trial involving cannabis alone. It was concluded that cannabis has a measurably worsening effect on psychomotor performance, particularly tracking ability. Drivers under the influence of cannabis seem to attempt to compensate to some extent for the impairment (that they recognise) by driving more slowly, but there are some aspects of the driving task where cannabis-impaired drivers cannot compensate and where their performance deteriorates (e.g. staying in lane on a bend). Within the sample of drivers, the effect of alcohol (at a dose of just more than half of the UK legal limit) and cannabis together were slightly greater than with cannabis alone; a larger sample would be needed to determine whether this is likely to apply to the population as a whole. There was no evidence that either alcohol or cannabis offset the effect of the other: impairment levels for cannabis or cannabis with alcohol remained significantly greater than placebo.

In summary

This research has:

- demonstrated the practicability of assessing the effects of cannabis and alcohol on driving performance in controlled experimental clinical trials;
- confirmed the results from previous studies that drivers under the influence of cannabis are aware of their impairment, attempt to compensate for their impairment by driving more cautiously, but are unable to compensate for the loss of capability in some psychomotor skills;
- confirmed previous observations that cannabis adversely affects drivers' tracking ability;
- found that tracking performance deteriorated with increasing dose level;
- judged that the general medical examination and standardised impairment testing applied by the police surgeons were generally effective in determining impairment.

In terms of road safety the results show a clear worsening of driver capability following the ingestion of cannabis or the ingestion of cannabis and alcohol together at the doses used, in comparison with placebo (i.e. having taken neither). Within the sample of drivers, the effects of alcohol (at a dose of just more than half of the UK legal limit) and cannabis taken together were slightly greater than with cannabis alone. Given that other research has extensively shown the rapid increase in the risk of accident, particularly fatal accident, with increasing blood alcohol level, the present results show how important it is to avoid any combination of alcohol and cannabis, as well as avoiding alcohol and cannabis taken on their own, before driving or riding.

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10 Glossary

ATT	Adaptive Tracking Test
BAC	Blood Alcohol Concentration
BrAC	Breath Alcohol Concentration
CBD	Cannabidiol (the second main constituent of cannabis, but not psychoactive)
DSST	Digit symbol substitution task
FME	Forensic Medical Examiner (Police Surgeon)
GLM	General Linear Model
NIDA	National Institute on Drug Abuse
Salivette	Saliva collection system, which uses a cotton wool swab
SAS	Statistical Analysis System
SDLP	Standard Deviation of Lateral Position
SGI	Silicon Graphics
SPSS	Statistical Package for the Social Sciences
Δ^9 THC	Delta-9-tetrahydrocannabinol (THC) (the major psychoactive constituent of cannabis)
Δ^8 THC	Delta-8-tetrahydrocannabinol (a minor but psychoactive constituent of cannabis)
THC-COOH	9-carboxy-THC (the most rapidly produced metabolite of Δ^9 THC, not psychoactive)
VAS	Visual analogue scale

Appendix A: Comparison of sample with other cannabis users

In order to investigate how typical the cannabis trial study volunteers were of general regular cannabis users, the group were compared with a sample of regular users from the West Midlands. A questionnaire regarding use of cannabis and other drugs had been developed by Kay Wright who used this to obtain a profile of the typical cannabis user and had been administered to a sample of 90 or so users. Participants who attended for screening were asked to complete this questionnaire, which was contained within the screening document. Data on drug-use history, and attitudes and behaviour towards drink/drug-driving were collected from both groups using the same questionnaire. The questionnaire provided a further method of checking the suitability of potential participants.

Table A1 shows that the trial participants were younger than the regular cannabis users, and had therefore driven for fewer months. Differences in other drug use can be explained by the fact that trial participants were only recruited if they were not current polydrug users (see Table A2). As a consequence the sample was likely to be biased. Similarities between groups are shown in alcohol use, and the age that cannabis was first used.

Table A1 Characteristics of volunteers

Mean ±SD	*Regular cannabis users Sample=29*	*Trial participants Sample=20*
Age	29.6±6.64	24.9±3.51
Alcohol drinkers	96.6%	100%
Units of alcohol per week	24.4 ±13.61	24.5 ±19.22
Age started using cannabis	16.6 ±2.66	15.5 ±1.32
Drivers	29 (100%)	20 (100%)
Months driving	115.9 ±83.8	92.4 ±40.1
Use other drugs	82.7%	40%

Table A2 Percentage of volunteers who have used other illicit drugs

Mean ±SD	*Regular cannabis users Sample=29*	*Trial participants Sample=20*
Ecstasy	58%	30%
Amphetamine	62%	15%
Cocaine	19%	25%
Hallucinogens	21%	0%

History of cannabis and alcohol use

Similarities in cannabis use were found between groups. All trial participants smoked cannabis on at least a weekly basis compared with 75.8% of the regular cannabis users. The majority of both groups had smoked at this frequency for 12 months or over (regular cannabis users 82.8%, trial participants 100%). A similar pattern was found in the number of cannabis cigarettes smoked, with the majority smoking three or more per occasion (regular cannabis users 51.7%, trial participants 60%).

Patterns of alcohol use, alone and combined with cannabis were also similar between groups. All of the regular cannabis users who drank alcohol, and all of the trial participants, drank on at least a weekly basis. All trial participants combined alcohol with cannabis, compared with 93.1% of the regular cannabis users. 75% of the trial participants combined the two drugs on a least a weekly basis, compared with 60.8% of the regular cannabis users.

Drink/drug-driving behaviour

Table A3 shows a higher percentage of trial participants drive after consuming cannabis and low levels of alcohol compared with regular cannabis users. However, one of the inclusion criteria for the trial was that they must have experience of driving whilst under the influence of cannabis. The study sample is therefore biased in relation to these criteria. Fewer trial participants drive after consuming a quantity of alcohol above the legal limit for safe driving (4+ units). However, overall differences were small, and a similar pattern of driving behaviour is apparent (see Figures A1 and A2). A slightly higher number of trial participants (80%) drive after combined use of cannabis and alcohol (25% weekly, 15% monthly) compared with 62.1% of the regular cannabis users (13.8% weekly, 10.3% monthly).

Table A3 Percentage of volunteers who report driving under the influence of alcohol and cannabis

Group	*Alcohol ≥ 4 units*	*Alcohol <4 units*	*Cannabis*
Regular cannabis users	24.5%	63.3%	81.3%
Trial participants	15%	85%	100%

Drink/drug-driving attitudes

The majority of respondents from each sample consider their driving to be either very much impaired (31.0% regular cannabis users, 60% trial participants) or slightly impaired (62.1% regular cannabis users, 40% trial participants) by 4+ units of alcohol. However, one regular cannabis user believed driving was improved. Similarities between groups in attitudes towards driving after consuming cannabis and related driving behaviour were also found. Seventy nine per cent of the regular cannabis users and 85% of the trial participants believed cannabis impaired driving. However, the majority thought their driving was only slightly impaired (65.5% regular cannabis users, 80% trial participants).

Despite these attitudes towards drink and drug driving, incidences of this behaviour (particularly after the consumption of cannabis) are high, and the pattern is similar between groups (see Table A4). Drug driving in Table A4 refers to the situation when the driver had been taking drugs and was stopped by the Police, however they were not charged. This contrasts to the similar situation

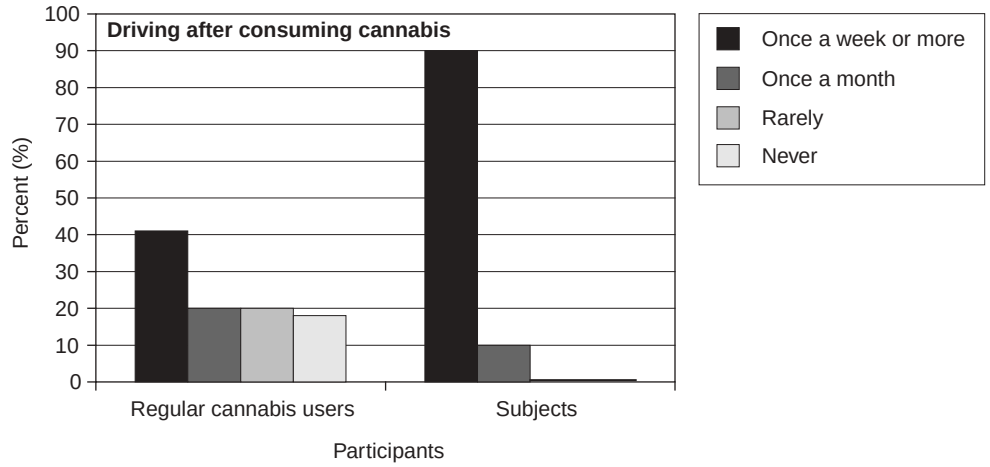

Figure A1 Percentage of volunteers who report driving under the influence of alcohol and cannabis

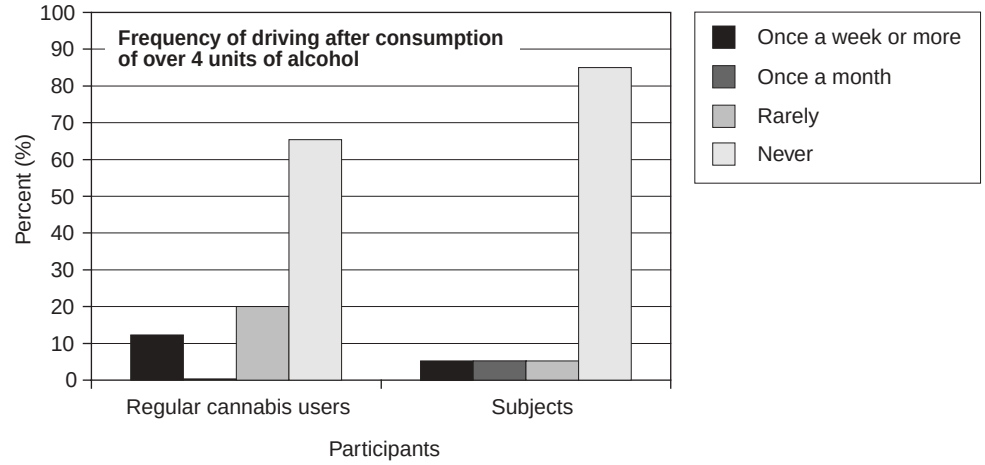

Figure A2 Frequency of driving after drinking alcohol

Table A4 Number of volunteers (and %) stopped/ charged after having consumed drugs/alcohol and deterred from drink/drug-driving

	Regular cannabis users (n=29)		*Trial participants (n=20)*	
	Drink-driving	*Drug-driving*	*Drink-driving*	*Drug-driving*
Stopped	11 (38%)	12 (41%)	10 (50%)	15 (75%)
Charged	4 (14%)	0 (0%)	2 (10%)	0 (0%)
Deterred	5 (17%)	2 (7%)	7 (35%)	0 (0%)
Others	9 (31%)	15 (52%)	1 (5%)	5 (25%)

when they had been drinking alcohol and were stopped and were often charged. This is presumable because detecting alcohol, from the smell or via a breath test, is far easier than detecting drug use.

Drink/drug-driving incidences

The number of respondents stopped and/or charged for, and deterred from, drink/drug-driving was similar between groups, although a higher number of trial participants were deterred from drink driving than regular cannabis users.

Table A4 clearly shows that, although a greater number of respondents have been stopped for drug driving, or at least stopped whilst under the influence of cannabis, none were charged, and only 2 regular cannabis users were deterred from repeating the behaviour. In comparison 4 of 6 regular cannabis users and 2 of 10 trial participants were charged for drink driving. Furthermore, being stopped for drink-driving deterred 5 of the regular cannabis users and 7 of the trial participants.

In conclusion, the results show that the trial participant group used for this trial study was fairly typical of a more general population of regular cannabis users in their history of alcohol and cannabis use, as well as their attitudes and behaviour towards drink-drug-driving.

Appendix B: Report on the sobriety tests

Introduction

This project looked at the effects of cannabis and alcohol, alone and in combination, on an individual's fitness to drive.

A police officer may arrest a person if he has reasonable grounds to suspect that the person has been driving or attempting to drive whilst unfit through drugs (Section 4 (1) of the Road Traffic Act 1988 as amended by the Road Traffic Act 1991 (RTA)). Being unfit is defined in Section 4(5) of the Road Traffic Act 1988 '*…a person shall be taken to be unfit to drive if his ability to drive properly is for the time being impaired.*' At the police station following such an arrest a doctor (registered medical practitioner – forensic physician) will be called to examine the person.

Two registered Forensic Medical Examiners examined the participants recruited for this study and carried out a comprehensive physical examination to see whether any of the suggested standard 'impairment' tests currently used to assess fitness to drive were of value in assessing an individual's ability to drive a motor vehicle whilst under the influence of cannabis and/or alcohol. Details of the examination performed and guidelines to the interpretation of the results have previously been reported (Sexton *et al.*, 2000) (Medical Examination Form Table B1). The physical signs of alcohol use are summarised in Table B2.

The doctors were asked to conclude whether in their opinion at the time of the examination the individual was 'impaired' or whether there was 'a condition' that might be due to the presence of alcohol and/or a drug. The doctors used the following criteria, deduced from the previous study using cannabis alone, and proposed as '*preliminary standards'*:

The initial 'criteria', developed during the previous cannabis study (Sexton *et al.*, 2000) suggested that a condition due to a drug and/or alcohol may exist with at least one abnormal finding on general physical examination and two abnormalities on 'impairment tests'.

For impairment to be present these initial 'criteria' suggested that there *must* be abnormal findings on general physical examination *and* failure to perform three parts of at least *three* 'impairment tests'. These preliminary 'criteria' were reviewed and revised during the experimental sobriety testing process in the current study and were modified accordingly.

Guide to the interpretation of results

Physical examination

Although the participants had been screened and were healthy male volunteers it was important to exclude any recent or current medical problem that may have affected the interpretation of any tests used to assess fitness to drive e.g. a current ear infection which may have an affect on balance (Romberg's test). The physical examination is also important to document physical signs (physiological effects) of a drug e.g. tachycardia, conjunctival reddening. It was decided that we would not ask them specifically how they felt at the time of the exam but that any unsolicited comments would be noted. Abnormalities included a pulse rate of 90 beats per minute or over and a blood pressure with a diastolic of 90 or over, and total systolic of 100 plus their age.

The 'Impairment' Tests

In general, for each of the tests below the participant was reminded once of the instructions if they initially failed to perform the test correctly. The 'impairment' tests are reported with failures over the total number of parameters measured, e.g. in the finger nose test if the participant failed all four parameters this would be reported as 4/4.

Pupillary examination

Pupil size and equality were assessed by comparing the size of the pupils against the pupillometer on a card held up at the side of the face. The normal range for pupil size was 3.0-5.0mm given the lighting conditions (bright) of the room when compared to roadside testing. At the same time an evaluation of the pupillary reaction to a direct light stimulus was performed.

Eye movements

The presence of lateral nystagmus, vertical nystagmus and convergence were sought. A stimulus is held about 12-15 inches away from the face and the participant is instructed to follow the stimulus with their eyes keeping their head still. The stimulus is moved from the centre of the nose to the right and then the left (to check for horizontal nystagmus) and up and down (to check for vertical nystagmus). The stimulus should be moved to the right or left until the white of the eye is no longer observed but not out of the person's line of site. To examine for convergence (having excluded a squint – weak eye muscles) the participant is again asked to follow the stimulus with their eyes, keeping their head still, the stimulus is brought in towards the nose. If one of the eyes drifts away or fails to converge non-convergence is present.

Walk and turn test

The participant is instructed to place his left foot on the line and then to place the right foot on the line in front of the left foot, with the heel of the right foot in contact with the toe of the left foot. The participant is then told to put his arms at his sides and take nine heel to toe steps along the line, turning around and take a further nine heel to toe steps back along the line.

Abnormalities that were looked for included whether the individual (9 parameters):

- starts too soon;
- stops walking;
- misses heel/toe;
- raises arms;
- starting balance impaired;
- turns improperly;
- steps off line;
- counts incorrect steps;
- fails to follow instructions.

Table B1 Medical examination form

General examination

General demeanour and behaviour:	Normal	Euphoric	Anxiety	Verbosity
	Sedation	Hallucination		
State of clothing:	Normal			
Speech: (ask "Have you been well over the last week?")	Normal	Slurred		
Condition of mouth:	Normal			
Pulse: rate and character		b.p.m.	Normal	Bounding
Temperature:		^{o}C		
State of tongue:	Normal			
Breath:	Normal			
Ears:	Normal	Wax	TM Red	
Heart:	Normal			
Blood pressure:				
Lungs (added sounds):	Normal	Wheeze		
Reflexes:	Normal	Increased	Decreased	
Eyelids red or swollen?	Normal			
Conjunctivae?	Normal	Injected		
Evidence of squint etc?	Normal			
Any gross visual defect?	Normal			
Glasses?	Yes	No		

Continued ....

Table B1 (Continued) Medical examination form

Impairment testing

Pupil size (using card pupillometer)		mm
Anisocoria	Absent	Present
Pupillary reaction to direct light stimulus	Normal	Sluggish
Horizontal gaze nystagmus	Absent	Present
Vertical gaze nystagmus	Absent	Present
Convergence	Present	Absent

Walk and turn test (9 steps)	Start too soon	Yes	No
	Stops walking	Yes	No
	Misses heel/toe	Yes	No
	Raises arms	Yes	No
	Starting balance	Impaired	Normal
	Turns improperly	Yes	No
	Steps off line	Yes	No
	Correct step count	Yes	No
	Fails instructions	Yes	No

		Right		Left	
One leg stand	Sways	Y	N	Y	N
	Raises arms	Y	N	Y	N
	Hops	Y	N	Y	N
	Puts foot down	Y	N	Y	N
	Fails instructions	Y	N	Y	N

Finger nose test (eyes closed) Left / Right / Left / Right / Right / Left	Touch tip of nose	Yes	No
	Correct hand	Yes	No
	Sways	Yes	No
	Fail instructions	Yes	No

Romberg test – body sway	Yes	No

Internal clock – 30 seconds estimates at		Time
(allow 10 seconds either way)	Normal	Abnormal

Writing: copy this

Remarks (include any unsolicited remarks regarding volunteer's feelings)

Conclusion

Impaired?	Yes	No
Condition might be due to a alcohol/drug?	Yes	No

Table B2 Signs of alcohol use related to physical examination

Effects	*Physical signs*	*Examination parameters*
Psychological	Euphoria.	Comment on general demeanour and behaviour.
Perception	Distortion of time sense.	Internal clock.
Sedative	Sedation, relaxation.	Conscious level.
Cognition	Impairment of short-term memory and concentration, disorientation.	Walk and turn test. One leg stand. Finger nose test.
Motor function	Dysarthria, inco-ordination, ataxia, ability to perform complex motor tasks. Balance and stability impaired.	Speech. Walk and turn test. Finger nose test. One leg stand. Romberg's test.
Cardiovascular	Bounding tachycardia. Increased blood pressure.	Pulse. Blood pressure.
Eye	Conjunctival injection. Change in pupil size. Sluggish reaction to light. Horizontal nystagmus. Vertical nystagmus. Absent of convergence.	Pupillometer. Pupil reaction to direct light stimulus. Eye movements.
Other	Flushing. Smell of alcoholic liquor.	Skin appearance. Breath.

One leg stand

The participant stands with his feet together and arms by his sides and is then asked to raise his right foot 6 - 8 inches off the ground keeping his leg straight. The toes must be pointing forward and the foot parallel to ground. The participant should keep his arms by his sides and look at the raised foot while counting 15 seconds, as 1001, 1002, 1003 etc. to 1015. The test is then repeated for the left foot.

Abnormalities that were looked for included whether the individual (5 parameters for each side):

- sways;
- raises arms;
- hops;
- puts foot down;
- fails to follow instructions.

Finger nose test (eyes closed)

The participant is instructed to stand with his feet together and arms at his sides and tilt his head back slightly. The participant should then extend both hands, palm side up, out in front and make a fist. The index finger of both hands is then extended and keeping the fingers in that position, place the hands at his sides, with the palm side forward. The examiner then says either left or right to indicate which hand should be raised directly in front and touch the tip of the nose with that index finger. The hand is then lowered until the next is indicated. The hands are called out in the following order: left, right, left, right, right, left.

Abnormalities that were looked for included whether the individual (4 parameters):

- misses tip of nose;
- uses incorrect hand;
- sways;
- fails to follow instructions.

Romberg test

This test is used to evaluate the participant's internal clock and body sway. The participant is instructed to stand up straight with his feet together and arms by his sides. The participant must tilt his head back slightly, and close his eyes while estimating to himself that 30 seconds have elapsed and then bring his head forward and say 'stop'. The test is abnormal if the body sways (Romberg's positive) and the timing is less than 20 seconds or more than 40 seconds.

Writing

Writing is a useful tool in the assessment of alcohol impairment and so it was decided to add a specimen of writing to the overall evaluation. The participants were asked to copy:

> *'A football team has bounced back to victory thanks to jelly babies.*
>
> *Players chew on the sweets every Saturday before a game.'*
>
> (Smith E. Jelly Well Played. The Sun, Monday December 13 1999, pp.3)

Writing was considered abnormal if the participant started in the wrong place and if there were mistakes in the flow of the writing.

Results

79 examinations were performed and on 6 occasions participants were found to be impaired, a further 24 were found to have a condition that could be due to a drug and/or alcohol, but were not impaired, 49 were normal. It should be noted that the presence of a condition and impairment are not mutually exclusive. Tables B3, B4 and B5 give the classifications with the abnormal examination findings and any unsolicited comments.

Discussion

As in the previous study (Sexton *et al.*, 2000) one of the main limitations in performing the examinations was time pressure due to the protocol of the main study.

From clinical examination alone it is not possible to differentiate between a condition or impairment due to alcohol or cannabis in this setting especially as the smell of alcoholic liquor was disguised.

Assessment of writing

Only when all four examples of writing were reviewed together was one considered abnormal because of poor

Table B3 Participants considered to be impaired

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
069 Nic 1 MS	C & A	Pulse 123 Conjunctivae injected	Pupils 5.0mm sluggish reaction Walk and turn 1/9 One leg stand L 2/5 R 2/5 Finger nose 2/4 Romberg's positive	Impaired
060 Rob 3 KE	C & A	Pulse 112 BP 134/95 Conjunctivae injected	Horizontal nystagmus One leg stand L 3/5 R 3/5 Finger nose 2/4	Impaired
067 Ada 4 KE	A	BP 157/83	Horizontal nystagmus One leg stand R 2/5 Finger nose 2/4 Internal clock 43 seconds	Impaired
053 Stu 1 MS	C & A	Euphoric Pulse 120 BP 150/92 Conjunctivae injected	Pupils 6.0mm sluggish reaction Walk and turn 2/9 One leg stand R 3/5 L2/5 Finger/nose 3/4	Impaired
053 Stu 2 KE	A	BP 141/102	Walk and Turn 1/9 One leg stand R 5/5 L 4/5	Impaired
053 Stu 4 KE	C & A	Laughing Pulse 101 bounding BP 144/86 Conjunctivae injected	Pupils 5.5mm sluggish reaction Walk and turn 3/9 One leg stand R 5/5 L 5/5	Impaired

Table B4 Participants considered to have a 'condition'

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
053 Stu 5 MS	C	Euphoric Pulse 124 BP 154/90	Pupils 4.0mm sluggish reaction Finger nose 1/4	Condition
067 Ada 2	C & A A	BP 154/87 Conjunctivae injected	Pupils 4.0mm sluggish reaction Finger nose 1/4	Condition
060 Rob 1 MS	A	BP 144/101 Conjunctivae injected	Pupils 5.0mm sluggish reaction Finger nose 1/4	Condition
069 Nic 4 MS	C	Pulse 108 BP 157/85 Conjunctivae injected	Pupils 3.5mm sluggish reaction Walk and turn 2/9	Condition
014 Ric 4 MS	C & A	Giggling Pulse 124 bounding BP 151/100 Conjunctivae injected	Pupils 4.0mm sluggish reaction Finger nose 1/4 Writing abnormal	Condition
056 Arr 3 KE	C & A	Pulse 93 BP 144/103 Conjunctivae injected	Horizontal nystagmus Finger nose 2/4 Internal clock 42 seconds	Impaired
070 Lee 4 MS	C	Pulse 144 bounding BP 154/82 Conjunctivae injected	Pupils 5.0mm sluggish reaction Finger nose 1/4	Condition
059 Nig 1 MS	A	BP 155/101 Romberg's positive	Finger nose 2/4	Impaired
059 Nig 4 KE	P	BP 144/106	One leg stand L 2/5	Condition
004 Jam 1 KE	A	BP 139/95 Increased reflexes	Horizontal nystagmus One leg stand L 2/5	Impaired
004 Jam 2 MS	C	BP 146/94 Conjunctivae injected	Pupils 5.5mm sluggish reaction Romberg's positive	Condition
004 Jam 3 MS	C & A	BP 153/93 Conjunctivae injected	Pupils 5.0mm sluggish reaction Walk and turn 1/9	Condition
066 Jim 2 KE	C & A	Pulse 98 bounding BP 155/94 Conjuntivae injected	Horizontal nystagmus Walk and turn 1/9 One leg stand 1/5	Impaired
066 Jim 3 MS	C	Pulse 134 bounding BP 158/90 Conjunctivae injected	Pupils 4.5mm sluggish reaction Finger nose 1/4	Condition
051 Mar 1 MS	A	BP 151/105	Convergence absent Walk and turn 2/9 Finger nose 1/4 Internal clock 45 seconds	Impaired
051 Mar 4 KE	P	BP 174/113	Horizontal nystagmus	Impaired

Continued ....

Table B4 (Continued) Participants considered to have a 'condition'

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
063 Jai 2 KE	C	Euphoric BP 160/110 Mouth pink Conjunctivae injected	Pupils 3.0mm sluggish reaction Horizontal nystagmus One leg stand R 1/5	Impaired
062 Nic 1 MS	C & A BP 151/77	Pulse 110 bounding Conjunctivae injected	Pupils 4.5mm sluggish reaction Walk and turn 1/9 One leg stand L 1/5 Internal clock 18 seconds	Impaired
061 Nic 3 MS	A	BP 140/74 Conjunctivae injected	Pupils 4.0mm sluggish reaction Horizontal nystagmus Convergence absent One leg stand L 2/5	Impaired
061 Nic 4 MS	C & A	Pulse 97 Conjunctivae injected	Pupils 4.5mm sluggish reaction Walk and turn 2/9	Condition
055 Ray 1 KE	C	Inflamed mouth BP 149/87 Increased reflexes	Walk and turn 1/9 One leg stand R 1/5 L 1/5 Tremor 'I feel a bit stoned'	Impaired
055 Ray 4 MS	C & A	Pulse 107 bounding BP 166/109 Conjunctivae injected	Pupils 5mm sluggish reaction Walk and turn 1/9 One leg stand R 1/5 Finger nose 1/4 Romberg's positive	Impaired
050 Pet 1 MS	C & A	Conjuntivae injected	Pupils 4mm sluggish reaction One leg stand L 3/5 Finger nose 2/4	Impaired
023 Dav 4 MS	C & A	Pulse 118 bounding BP 178/99 Conjuntivae injected	Pupils 4.5 sluggish reaction Walk and turn 1/9 Finger nose 1/4	Condition

Table B5 Participants considered normal (not impaired with no condition)

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
067 Ada 1 MS	P	BP 156/95 Conjunctivae injected	Pupils 5.0mm sluggish reaction	Condition
067 Ada 3 KE	C	BP 140/79		Normal
060 Rob 2 MS	C	Pulse 91 bounding BP 144/73 Conjunctivae injected	Pupils 5.5mm sluggish reaction	Condition
060 Rob 4 MS	P	BP 150/104		Normal
069 Nic 2 KE	A	Euphoric BP147/89		Normal
069 Nic 3 KE	P	BP 135/78		Normal
003 Nik 1 KE	C	BP 171/113	Finger nose 2/4	Condition
003 Nik 2 MS	P	BP 186/110	Walk and turn 1/9	Condition
003 Nik 3 MS	A	Pulse 74 bounding BP 181/99		Condition
014 Ric 1 KE	C	Pulse 90 bounding Increased reflexes Conjunctivae injected	Pupils 3.5mm sluggish reaction	Condition
014 Ric 2 MS	P	BP 148/91 Conjuntivae injected	Pupils 4.5mm sluggish reaction	Condition
014 Ric 3 KE	A	BP 137/88		Normal
056 Arr 1 MS	A	BP 141/92		Normal
056 Arr 2 MS	C	Humming/Giggling Pulse 92 bounding BP 156/95 Conjunctivae injected	Pupils 6mm 'I do feel quite stoned' '(tests) Not too difficult'	Condition
056 Arr 4 MS	P	BP 159/95	'I've had placebo stuff'	Normal
070 Lee 1 MS	C & A	Pulse 119 bounding BP 148/90 Conjunctivae injected	Pupils 5.5mm sluggish reaction	Condition

Continued ....

Table B5 (Continued) Participants considered normal (not impaired with no condition)

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
070 Lee 2 MS	A	BP 141/79 Conjunctivae injected	Pupils 4.5mm sluggish reaction	Condition
070 Lee 3 KE	P	BP 147/89	Horizontal nystagmus	Impaired
052 Ben 1 KE	P	BP 131/93		Normal
052 Ben 2 KE	C & A	BP 141/80 Increased reflexes Conjunctivae injected		Condition
052 Ben 3 KE	C	BP 140/88	Pupils 4.0mm sluggish reaction Horizontal nystagmus Internal clock 43 seconds	Impaired
052 Ben 4 MS	A	BP 147/89	Pupils 5.5mm Internal clock 50 seconds	Normal
059 Nig 2 KE	C	BP 144/97		Normal
059 Nig 3 MS	C & A	Conjunctivae injected	Walk and turn 1/9	Condition
004 Jam 4 KE	P	BP 141/94		Normal
066 Jim 1 KE	P	BP 151/86		Normal
066 Jim 4 MS	A	Pulse 119 bounding BP 162/90		Condition
051 Mar 2 MS	C	BP 157/98		Normal
051 Mar 3 MS	C & A	BP 158/104		Normal
063 Jai 1 KE	P	BP 159/102 Decreased reflexes Conjunctivae injected Inflamed mouth		Condition
063 Jai 3 KE	C & A	Pulse 94 BP 159/96 Decreased reflexes Conjunctivae injected	Tonsillitis	Condition
063 Jai 4 KE	A	Mouth inflamed BP 167/96 Conjunctivae injected	'I'm actually feeling quite stoned'	Condition

Continued ....

Table B5 (Continued) Participants considered normal (not impaired with no condition)

Ref No *Doctor*	*Dose*	*General exam*	*Impairment testing*	*Independent doctor's assessment*
062 Nic 2 KE	A	Inflamed throat BP 141/84 Increased reflexes Eyelids red and swollen Conjunctivae injected	Viral infection	Condition
062 Nic 3 MS	P	Conjunctivae injected BP 129/65	Pupils 5mm sluggish reaction One leg stand 1/5	Condition
062 Nic 4 MS	C	Pulse 112 bounding BP 149/78 Conjunctivae injected	Pupils 5.0mm sluggish reaction	Condition
061 Nic 1 MS	C	Pulse 93	Pupils 4.5 sluggish reaction Finger nose 1/4	Condition
061 Nic 2 KE	P			Normal
055 Ray 2 KE	P	BP 116/98 Throat inflamed	Finger nose 2/4	Condition
055 Ray 3 MS	A	BP 143/95	'I know I've been drinking'	Normal
050 Pet 2 MS	A			Normal
050 Pet 3 MS	P			Normal
058 Lou 1 KE	P	BP 140/98	Internal clock 45 seconds 'I don't feel impaired'	Normal
058 Lou 2 KE	C & A	BP 142/97	One leg stand L 1/5 'I do feel a little under the influence'	Normal
058 Lou 3 MS	C	BP 153/99		Normal
058 Lou 4 MS	P	BP 141/100	Walk and turn 1/9	Normal
023 Dav 1 MS	C	Pulse 95 BP 161/90 Conjunctivae injected		Condition
023 Dav 2 KE	P	BP 142/82		Normal
023 Dav 3 MS	A	Pulse 76 bounding BP 147/80 Conjunctivae injected		Normal
053 Stu 3 KE	P	BP 140/94 Increased reflexes	One leg stand R 1/5	Condition

spelling and mistakes in letter formation suggesting poor hand-eye co-ordination. The participant had alcohol and cannabis and with the benefit of hindsight would have been judged impaired. It would seem that unless grossly abnormal the examples of writing are not very useful in the medical assessment at this dose of alcohol and cannabis.

Presence of nystagmus

Interestingly the two doctors gave different classifications to participants who had the presence of horizontal nystagmus (KE 'condition'; MS 'normal'). According to the criteria, although the presence of one abnormality on impairment testing should be not be considered a 'condition' the presence of horizontal nystagmus is a significant finding where other causes have been excluded on screening (e.g. congenital nystagmus, neurological conditions) and concurrent physical examination (e.g. recent middle ear infection). Horizontal nystagmus – spontaneous rapid rhythmic eye movements in a side-to-side direction – may seriously affect driving ability.

General examination

There was one participant who had a number of abnormalities on general examination included a bounding tachycardia, hypertension and injected conjunctivae. He also had dilated pupils (a soft sign alone) but had significant behavioural abnormalities in that he was humming and giggling and admitted to feeling 'quite stoned'. Again, on the criteria proposed he would be classified as 'normal' but clearly there was ' a condition' due to a drug. In a real case in the police station there may be very crucial evidence given to the examining doctor by the arresting officer as to the manner of his driving.

Assessment of the criteria used

When the two doctors reviewed the results, some relaxation of the original 'criteria' was considered justified. It was agreed that all those considered to be impaired were so despite the fact that they did not completely fulfil the original criteria proposed but they did have abnormalities on physical examination and had failed two or three of the impairment tests by more than one parameter.

On further reviewing those with a condition it was felt, in retrospect, that a number had been incorrectly classified in that they had failed three impairment tests but not necessarily three parts of the impairment tests. Using these further revised criteria of failure of three impairment tests, which would now seem to be more appropriate, a further 8 would have been considered impaired and one originally considered normal would certainly have had 'a condition'.

Blind review of our results by an experienced forensic physician (Dr Debbi Rogers) produced interesting results. This process is analogous to the situation where an expert is asked to review the evidence prior to court proceedings.

She agreed with our conclusions that the 6 participants in Table 3 were impaired. However, she felt that a further 12 participants originally classified with a condition were impaired and, with regard to the participants we classified as normal, a further 2 were impaired and 23 had a condition, the remaining 24 as normal.

The criteria used to indicate a condition included two objective physical signs. As a condition could exist without impairment she concluded that there was no necessity to have any abnormalities on impairment testing, but for impairment to be present there needed to be three failures (single parameters) in one or more impairment tests even with normal physical exam. However, the presence of horizontal nystagmus alone would indicate impairment.

Conclusion

In retrospect it is clear that hard and fast quantitative assessments which clearly define impairment as previously proposed are not possible on the basis of the number of subjects in these trials alone. Furthermore, although our original criteria may be considered too restrictive, if criteria are used that are too liberal in the real setting then individuals may be considered to have a condition or be impaired who have not taken any drugs. Dr Rogers classified 8 with a condition who had in fact had placebo. However, it should be born in mind that in this experimental situation participants were not told what dose they had been given so there may have been an additional factor at play due to a 'placebo effect'.

There are at least two aspects of this project that need further evaluation. It would be of interest to carry out the sobriety tests on a 'normal' population in an attempt to establish a 'normal range'. It would also be valuable to carry out a prospective survey of the results of the medical examinations performed by experienced forensic physicians in real life suspected drug driving cases in the police stations, including results of any prosecutions, in an attempt to establish 'working criteria'.

References

Sexton B R, Tunbridge R J, Brook-Carter N, Jackson P G, Wright K, Stark M M, Engelhart K (2000). *The influence of cannabis on driving*. TRL Report TRL477. Crowthorne: TRL Limited.

Glossary

Anisocoria	Unequal diameters of the pupils of the two eyes.
Ataxia	Unsteadiness, incoordination.
Conjunctival	Reddening of the conjunctivae injection.
Convergence	The simultaneous act of both eyes coming together towards the midline.
Dysarthria	Disorder of articulation, slurred speech.
Nystagmus	Spontaneous rapid rhythmic eye movements in a side-to-side (horizontal) or up-and-down (vertical) direction.
Tachycardia	Fast heart rate.

Appendix C: Report on food eaten

Table C1Alcohol level, food eaten prior to trial and when last smoked cannabis

Session/ subject	*BrAC µg/100ml*		*Food Content*	*Approximate time (hrs) since last ate*	*Number of hrs since smoked cannabis (and no. of joints)*
056arr					
1	13		cheese/quorn/mayo/roll/crisps/choc	6	20 (1)
2	3		as above	6	20 (1)
3	17		cous-cous & humous, cheese bap	6	20 (1)
4	0		cheese salad baguette, wholenut choc. bar	6	20 (1)
060rob					
1	21		cheese salad sandwich/butter	9	19 (1)
2	0		ham/cheese sandwich/butter	10	19 (1)
3	23		MacDonalds fillet of fish, fries, coke	9	19 (1)
4	0		cheese & pickle roll	7	19 (1)
051mar					
1	12	14	cheese, tomato sandwich	6	24 (1)
2	3	4	cheese, tomato roll, butter	6	6 (1)
3	15	15	cheese burger	7	6 (1)
4	0		cheese & tomato roll	6	6 (1)
050pet					
1	19		roll, butter, cheese, crisps	6	3 (1)
2	16		roll, butter, cheese, crisps	6	3 (1)
3	0		chicken sandwich	4	3 (1)
4	0		egg roll	6	2½ (1)
055ray					
1	0		cheese sandwich, crisps	7	30 (2)
2	0		chicken curry, rice	7	30 (3)
3	21	17	ham, egg & chips	7	3 (3puffs)
4	20		tomato soup, 2 slices toast	7	3 (1)
058lou					
1	0		cheese sandwich, crisps	5	48 (2)
2	20	12	salmon sandwich and pate, crisps	5	10 (2)
3	0		sausage sandwich	5	24 (5)
014ric					
1	0		beans on toast (2 pieces)	4	6 (2)
2	0		cajun rap	6	6 (6)
3	16		tomato soup & 1 slice toast	5	6 (2)
4	16		soup	5	18 (6)
066jim					
1	0		egg mayo sandwich	6	56 (3)
2	10	15	chicken sandwich	6	64 (4)
3	0		chicken, salad, mayo baguette	6	67 (3)
4	20	20	cornish pasty, Mars bar	7	30 (2)
059nig					
1	–		chicken sandwich	9	16 (10)
2	0		chargrilled chicken sandwich	7	18 (10)
3	15		1 chicken breast & salad	6	7 (2)
4	0		–	–	–
023dav					
1	0		6 slices bread, beef, tomato,	6	19 (3)
2	0		chicken pie, choc x 2, crisps	6	19 (4)
3	19	15	chicken/ham sand. M/shake	6	135 (5)
4	17	13	cheese & pickle roll, Mars bar	6	84 (5)
061nic					
1	0		crisps and mars bar (all day)	4	18 (5)
2	0		cheese sandwich (got up at 3.00pm)	3	18 (5)
3	22	13	braising steak, mash, carrots, peas	3	7 (1)
4	15	12	triple burger, cheese burger, chips	6	24 (6)

Continued ....

Table C1(Continued) Alcohol level, food eaten prior to trial and when last smoked cannabis

Session/ subject	*BrAC µg/100ml*		*Food Content*	*Approximate time (hrs) since last ate*	*Number of hrs since smoked cannabis (and no. of joints)*
062nic					
1	25	23	cheese ploughman's baguette	7	22 (1)
2	21	20	6 chicken nuggets and chips	5	22 (1)
3	0		chicken nuggets, fries, burger	5	22 (2)
4	3		chicken sandwich. 4.00pm crisps	6	24 (2)
004jam					
1	27	20	saveloy, chips - 4.00pm Maltesers	6	22 (4)
2	0		3 sausages, 2 eggs	5	21 (3)
3	24	15	chicken curry, rice	6	19 (1)
4	0		–	–	–
053stu					
1	18	16	couscous salad, cheese	5	89 (2)
2	15	15	brie & redcurrant jelly sandwich	5	116 (2)
3	0		tuna & mayo sandwich, crisps	5	–
4	0		lasagne & chips	6	–
063jai					
1	0		ham & mustard sandwich, crisps	5	20 (lots)
2	0		egg & ham baguette, crisps	5	16 (lots)
3	11	8	bacon burger	5	3 (1)
4	25	19	ham, mustard sandwich	4	19 (2)
067ada					
1	0		cheese sandwich	4	24 (3 shared)
2	15	14	salad with potatoes & beans	6	19 (1)
3	0		fish pie	3	18 (2)
4	25	15	–	?	19 (1)
003nik					
1	0		3 sausage rolls, 1 pork pie	6	16 (4)
2	0		pork pie, Pepperami	6	18 (3)
3	20	15	pork in breadcrumbs, rice	6	19 (4)
052ben					
1	0		ham sandwich, apple	6	17 (lots)
2	19	18	ham sandwich, apple	6	17 (lots)
3	0		smoked salmon bagel, apple	7	48 (lots)
4	25	22	smoked salmon bagel, apple	6	19 (lots)
070lee					
1	9	9	2 x slices of pizza	2	15 (1)
2	7	6	sweet & sour chicken, rice, chow-mein	2	19 (2)
3	0		chicken chasseur	1	19 (1)
4	0		jacket potato with low fat spread	1	48 (3)
069nic					
1	22	17	2 ham rolls	6	9 (1)
2	24	16	cheese sandwich	6	19 (1)
3	0		cheese sandwich	6	19 (2)
4	0		ham sandwich, Twix	6	19 (4)

Appendix D: Executive Summary from (Sexton *et al.*, 2000), TRL477 The influence of cannabis on driving

Introduction

Results from the study of the 'Incidence of alcohol and drugs in road accident fatalities' have consistently shown a large increase in the incidence of drugs in fatal road casualties (drivers, riders, passengers and pedestrians) since the last comparable study in the mid-1980s. The latest results show that among all road users traces of illicit drugs were present in 18% of fatalities. These figures represent a six-fold increase in presence of illicit drugs when compared with the previous study. Cannabis constitutes around two thirds of the illegal drugs found.

Despite the increase in the incidence of drugs, it is not possible to say that drugs caused these deaths. There may be an association, but presence cannot be taken as evidence of causation - there is no way of telling how much was consumed and how long before the fatal accident. So far as cannabis is concerned, the prevalence in drivers was not significantly different from that of passengers, who can be taken as a (albeit imperfect) measure of the prevalence in the population as a whole. However, cannabis remains detectable in the body for up to four weeks after use - long after any impairment of driving.

In addition, in most surveys reported in Europe cannabis is the most frequently detected illicit drug. In a range of accident involved populations cannabis is found with an incidence between 2 and 12% with a mode incidence around 5-8%. This is certainly significantly above that of any other illicit drug.

Previous research studies on cannabis and driving have focussed largely on the effects of cannabinoids on driving performance. These studies have been almost exclusively experimental, involving laboratory tasks, driving simulator and on road 'real driving' experiments. A much smaller number of studies have attempted to gain broader sociological information about driving habits under the influence of cannabis and what factors influence the decision to drive. This research attempts to combine these two aspects, certainly for the first time in the UK, with a view to assessing the degree to which there may be a problem with cannabis in relation to driving. The research has three primary objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of cannabis on driving.
- To determine the duration and extent of any impairment under different degrees of intoxication (using different levels of cannabis).
- To provide an overview of attitudes and habits of cannabis users in relation to driving and explore factors which may influence the decision to drive under its influence.

The research attempted to address these objectives using experienced cannabis users carrying out a variety of laboratory-based tasks and driving in a simulator under four cannabis conditions: placebo; low THC; high THC; and cannabis resin. The placebo, low and high dose THC conditions used herbal cannabis ('grass') cigarettes supplied by the National Institute on Drug Abuse (NIDA), while the cannabis resin condition used cannabis supplied by Customs and Excise from seized supplies.

In 1999 the DETR commissioned a review of the latest evidence of the impairment effects of cannabis. That report provided an overview of the effects of cannabis on driving and accident risk and identified key research questions for areas where current knowledge was deemed to be insufficient to guide road safety policy. These research questions have shaped and informed the current research project. In addition to the primary objectives outlined above, the research reported here sought to inform four key issues identified by the review.

These were: exposure; biological response; acute psychomotor response; and driving response:

i Exposure

Prior to this research, few studies have attempted to gain broader sociological information about driving under the influence of cannabis. A comparison between the participants in the current study and a group of regular users in the West Midlands showed the trial group to be fairly typical. Both groups showed a reluctance to drive after consuming more than 4 units of alcohol, believing their driving to be significantly impaired. The majority of both groups again thought that cannabis impaired their driving, but only to a slight degree.

ii Biological response

In considering the results of the present study, the biological response of the participants to the consumption of cannabis is of fundamental importance. Urine was screened on arrival to check for and exclude multiple drug use.

Blood and saliva measurements were taken immediately prior to dosing and at 10 and 30 minutes post dosing. The subjective reports given by the participants of the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes. The maximum amounts of THC administered were around 10mg for the low dose and 20 mg for the high and the majority of participants were able to distinguish between the effects of these doses and placebo. The subjective feelings of the 'highs' experienced were also closely correlated with the participants 'liking' of the smoking effect as stated in the mood questionnaire. Making allowance for the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

iii Acute Psychomotor Response and Tests of Impairment

It is of the utmost importance to try to relate the observations derived from this experimental study to the situations likely to be encountered in real life drug driving

cases. Part of the experimental procedures therefore included the formal sobriety testing of participants. Two registered medical practitioners (experienced Forensic Medical Examiners (FMEs)) examined the participants and carried out a comprehensive physical examination to see whether the suggested standard 'impairment' tests currently used were effective in detecting impairment due to cannabis.

The results of the sobriety testing clearly show a strong correlation between cannabis dose received and whether impairment was judged to be present. In total, 56 assessments were performed on the 15 participants at the various dose levels. In 7 cases on high dose and 3 cases on low dose impairment was judged to be present, but no cases on placebo. In assessments where a condition was judged to be due to a drug 30 had received one of the three cannabis dose levels and only 2 were placebo conditions. On the basis of these observations, the general medical examination and standardised impairment testing applied by the FMEs were judged to be effective in determining both impairment and establishing condition due to a drug. There was also a strong relation between the FME's decision regarding the participant's impairment and the participant's subjective rating, which formed part of the mood questionnaire.

These results are important for two reasons.

First, they offer strong support for the validity of the FME's decisions and for the effectiveness of the sobriety tests as detectors of impairment. Second, they offer further support for the view that, under the influence of cannabis, users are acutely aware of their impairment.

It is also interesting to note that, despite participants having smoked some form of cannabis before 42 of these examinations, on only 11 occasions did the FME consider the participant to be impaired. This finding could have implications for the number of cases that will be detected by the Field Impairment Testing recently launched in the UK by the police.

In addition to the general medical examination, pupil size was measured using a Pupillometer, supplied by Procyon Ltd. The Pupillometer showed a significant increase in pupil sizes 25-30 minutes after dosing. The difference was statistically significant for the placebo v high dose and the placebo v low dose. This suggests that this measure may be helpful in assessing if a person has recently smoked and may be impaired through cannabis, although this would require a baseline and an 'impaired condition' measure to be useful.

iv Driving response

The final key objective of the study was to consider the effects of cannabis on driving response. Statistically significant results, which have been found for the simulator-derived measures, are given in the report. There was a reduction of average speed on the motorway when participants had the high or low doses of cannabis. This confirms the results from many previous studies. It strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate by driving more cautiously. Participants did not know what strength of cannabis they had received, but knew there was a likelihood of having had something 'active' and so were perhaps being more careful. A post trial survey of participants showed that they were very good at guessing when they had taken the placebo dose and most participants even managed to correctly guess if they had the low dose or high dose.

In the simulator trials, participants reacted more slowly to a pulling-out event when they had taken the low dose of cannabis, suggesting a similar compensatory action for the effects of cannabis impairment. However, when taking the high dose this effect was not significant. This is probably due to the variability in the response data.

Similarly, there was no significant difference between braking reaction times. The mean response times increased slightly, but there was too much variability in the data for this to be statistically significant. This variability in the results when considering the impairing effects of cannabis has been observed by other researchers. The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than with other drugs.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the 'figure of eight' when they had been on the high cannabis dose. There was also a significant increase in their Standard Deviation of Lateral Position (SDLP) on the right loop when on the high dose as compared to the low dose of cannabis. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

The mean time to move from stationary at a traffic light controlled junction once the lights had turned to red/amber on the driving simulator produced an interesting result. This was significantly reduced with high cannabis dose level, the reduction was in the order of ½ second between the placebo condition and high dose condition, and slightly less from the low dose to high dose. There are a number of possible explanations for this. It may suggest that in the 'observational' conditions of the driving simulator participants were aware of missing the traffic light change and so reacted slightly more quickly. Alternatively, the effects on the participants' internal clocks might have made them feel that they had been at the lights longer than they actually had and therefore heightened their attention to the imminent change in lights. It has been suggested that cannabis, in a similar way to alcohol at low doses, can have a stimulant effect on dopamine that may account for more risky behaviour in some circumstances. Other explanations are possible, however, and further assessment of this observation will be required.

The hazard perception[1] (HP) task did not produce any statistically significant results. Although reaction times were found to increase with dose level, there was too much

[1] *The hazard perception task used in this research was quite different from the hazard perception tests being introduced for testing L-drivers.*

variability in the data for statistical significance. An increase of 0.08 seconds between the placebo and low dose and an increase of 0.14 seconds between the placebo and high dose was observed. This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant. This would also seem to confirm earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat indeterminate.

The mean tracking accuracy on the Compensatory Tracking Task (CTT) decreased with increasing level of dose. The placebo tracking accuracy was higher than either the high dose or resin tracking accuracy. Thus tracking accuracy does change with dose. The proportion of correct trials also decreased with increasing dose level. All participants were still quite accurate, but the difference from 99.5% accuracy when on placebo was statistically significantly different from the 97.0% accuracy when on the high dose. The HP and CTT results are of particular interest because the HP test was taken at least 75 minutes post smoking the cannabis, and the CTT test at least 85 minutes post dosing. Some of the acute impairment effects may well have diminished by then.

In summary, the results of this study show a broad consistency with the effects of cannabis on driver performance observed by previous researchers. In addition, the habits and attitudes of cannabis users in relation to driving have been explored for the first time in the UK.

Conclusions

The research has demonstrated the practicability of assessing the influence of cannabis on driving performance in a controlled clinical trials experimental situation. Participants were recruited, medically screened and tested under conditions of a strict protocol that had local ethics committee approval.

The maximum amounts of THC administered in the cannabis cigarettes were shown to be typical of that available with ‘street’ cannabis. Participants were generally able to distinguish between the effects of cannabis with active THC and placebo conditions. The subjective reports of smokers on the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes.

The feelings of the ‘highs’ experienced were also closely correlated with participants’ positive reactions as measured by a mood questionnaire. Given the controlled conditions of the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

Previous studies have shown that simulated and actual driving and divided attention tasks which all require integrative mental processes are severely affected by alcohol. Simple attention / vigilance tasks are not so much affected and psychomotor skills, especially tracking, and simple reaction time tasks are only affected at relatively high blood alcohol levels. Alcohol may, therefore, be seen as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psychomotor skills and simple attentional processes are much smaller. In contrast, previous studies with cannabis show that it first seems to affect all tasks requiring psychomotor skills and continuous attention. Thus, tracking tasks, which are very sensitive to short term changes in attention, are very sensitive to cannabis impairment. On the other hand, integration processes and higher cognitive functions are not as time critical. A short attention lapse can be compensated for by increased activity later.

In the case of the overall driving task, it seems that the negative effects of these short-term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the frequently reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

Results from the current study using the TRL driving simulator confirm the results from these previous studies. There was a reduction of average speed on simulated motorway driving when participants had the high or low doses of cannabis. This strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate by driving more cautiously.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the ‘figure of eight’ when they had been on the high cannabis dose. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects driver’s tracking ability.

There is variability in the results when considering the impairing effects of cannabis that has been observed by other researchers. The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than with other drugs. The failure to produce significant results on various driving performance measurements when compared to alcohol may be explained by the more variable effects of cannabis on participants.

The results of the driving related laboratory tests conducted in general did not produce statistically significant results. Although reaction times were found to increase with dose level, there was too much variability in the data for statistical significance. This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant. This again confirms earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat difficult to predict.

The general medical examination and standardised impairment testing applied by the FMEs were judged to be effective in determining both impairment and establishing condition due to a drug. Preliminary conclusions were drawn by the FMEs on the number and combination of impairment test failures which would allow a conclusion

that the driver was ‘impaired’. Further refinement and calibration of these techniques in the field, for use by both police officers and FMEs, is however desirable and is planned.

Overall, it is possible to conclude that cannabis has a measurable effect on psychomotor performance, particularly tracking ability. Its effect on higher cognitive functions, for example divided attention tasks associated with driving, appear not to be as critical. Drivers under the influence of cannabis seem aware that they are impaired, and attempt to compensate by reducing the difficulty of the driving task, for example by driving more slowly.

In terms of road safety, it cannot be concluded that driving under the influence of cannabis is not a hazard, as the effects on various aspects of driver performance are unpredictable. However, in comparison with alcohol, the severe effects of alcohol on the higher cognitive processes of driving are likely to make this more of a hazard, particularly at higher blood alcohol levels.

Abstract

The results from a study of the influence of different doses of cannabis and alcohol on driving and driving related skills are reported. Male drivers who were regular cannabis and alcohol users undertook a variety of different tasks. The participants were given cannabis to smoke in the form of a prepared grass-based cannabis cigarette and had a drink that may or may not have contained alcohol. The prepared 'grass' based cannabis cigarettes varied in active THC (tetrahydrocannabinol) content to give a placebo, and a low dose. The drinks were either a placebo or about 10% by volume of alcohol. The participants drove the TRL driving simulator in a variety of scenarios and various measures of their driving skill were assessed. They also took an adaptive tracking task. They underwent sobriety testing 10-15 minutes after dosing and completed a mood questionnaire at different times during their test session.

Related publications

TRL477 *The influence of cannabis on driving* by B F Sexton, R J Tunbridge, N Brook-Carter, P G Jackson, K Wright, M M Stark and K Englehart. 2000 (price £50, code N)

TRL464 *Recognising drug use and drug related impairment in drivers at the roadside* by R J Tunbridge, M Keigan and F J James. 2000 (price £25, code E)

TRL226 *Validation trial for testing impairment of driving due to alcohol* by B F Sexton. 1997 (price £25, code E)

RR202 *The incidence of drugs in road accident fatalities* by J T Everest, R J Tunbridge and B Widdop. 1989 (price £20, code A)

SR441 *A review of drinking and drug taking in road accidents in Great Britain* by B E Sabey. 1978 (price £20)

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