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11762 SENATE HEALTH,EDUCATION & SOCIAL SERVICES

CHAPTER 6 - MARIJUANA, ALCOHOL AND URBAN CITY DRIVING

INTRODUCTION

In the previous study THC doses of 200 μg/kg, and higher, produced significant impairment of road tracking, but not car following, performance. The lowest dose, 100 μg/kg, failed to produce significant effects on road tracking, but increased headway during car following. The latter observation was interpreted as the result of increased caution, since mean headway did not change following subsequent higher THC doses. It therefore seems that low doses of THC do not, or only slightly, impair driving performance. Yet normal driving is far more complex and varied than simply maintaining a safe lateral position and headway during uninterrupted travel on a highway. A THC dose having no effect on these parameters might still impair driving performance in more complex urban driving situations.

There were logical and safety reasons for restricting the THC dose in the third driving study to that which had failed to produce significant impairment in the second. Both the 200 and 300 μg/kg doses impaired performance on the highway and could be expected to do so again in the urban driving environment. There the consequences of high dose THC effects are more difficult to predict and therefore safely control. The 100 μg/kg dose had some significant effects on the highway but none that could rightfully be called dangerous. This dose might still cause impairment in more complex city driving, but the risk was judged to lie within the realm of the acceptable. For that reason it was given to a group of regular cannabis users, along with placebo in the present study.

For comparative purposes another group of regular alcohol users were treated with a modest dose of their preferred recreational drug, and again placebo, before undertaking the same test. It was hoped that this addition would not only verify the sensitivity of the test but also allow a comparison between effects of recreational drugs that Dutch society considers as illicit and licit when both are given in relatively low doses. The comparison was not designed to show that one drug is "safer" for use by drivers than the other. Surely neither are safe when consumed before driving in high doses. However if respective low dose effects are comparable then one would be justified to conclude that THC may be considered as posing a traffic safety hazard which is in some respects similar to alcohol's.

The only study that has been conducted in actual traffic before this program started was also a city driving study. Klonoff (1974) assessed the effects of two THC doses, 4.9 and 8.4 mg THC which are equivalent to 70 and 120 μg/kg for a 70 kg (154 lb) person. Aspects of subjects' driving performance were scored by a professional examiner using an abbreviated version of the British Columbia Department of Motor Vehicles' standard driver's licencing test. The results showed that subjects performed less competently when under the influence of the highest, but not the lowest, dose. In particular, they scored lower on judgment and concentration scales. Moskowitz (1985) and Smiley (1986) criticized the method of measuring driving performance on the grounds that the examiners' reliability was never determined and that the scoring instrument had never been shown to provide measures related to driving safety. Smiley questioned, for example, whether ratings of posture and irritability are relevant for good driving performance. These are sound criticisms but one has to assume that Klonoff's approach should

have been sensitive to serious driving performance impairment, related to safety, if it had in fact occurred.

Two scoring methods were employed in the present study. The first was in fact a method similar to that applied by Klonoff; i.e. the driving instructor acting as the safety controller during the tests retrospectively rated the driver's performance using a standard scale. This method has been applied previously to show the impairing effects of alcohol (De Gier, 1979) and diazepam (De Gier *et al.*, 1981) in similar situations. Jones (1978) criticized this use of driver licensing assessment procedures. She opposed the lack of precise definitions for many of the behaviors rated by examiners and the requirement for rating all of them at once. In contrast to this "molar" approach, she developed a more "molecular" one for evaluating driving proficiency. Her method was also applied in the present study. It involves the employment of specially trained observers who apply simple and strict criteria for recording when the driver makes or fails to make each in a series of observable responses at predetermined points along a chosen route.

The professional observer's global ratings are inherently less reliable than the scores obtained by the molecular rating scheme. Still the molar approach has some advantages. The professional's experience with many drivers operating in all traffic situations provides him with the ability to integrate far more information than is possible to obtain from limited performance sampling. He has internalized a broad concept of acceptable driving performance and applies more flexible criteria for judging when it is unsafe within a particular test situation. Of course the danger that a professional's biases may influence his judgments needs to be overcome by training and his adherence to structured rules which are specific for the investigation. But when this is done, he may provide a more valid estimation of the overall safety of a subject's driving performance. If this were not the case it would be difficult to explain how every developed society relies upon the professional's and not a traffic scientist's opinion of whether a particular individual should be licensed to drive.

The objective of this study would be satisfied in one way if neither observer rating method yielded a significant difference between driving performance after 100 μg/kg THC and placebo. These results would confirm those obtained in the previous study by indicating that the selected dose lies below that capable of impairing driving performance. This conclusion would only be warranted, however, if it could be shown that the tests were sensitive enough to measure significant driving performance impairment after alcohol relative to placebo. If that were not the case, test insensitivity could be judged as the factor responsible for negative results, rather than the lack of a THC effect.

The objective would be satisfied in another way if either or both rating methods showed significant impairment after THC. Such results would indicate that any dose likely to be consumed before driving should be considered hazardous, regardless of whether alcohol's effects were the same, more or less. In the event that significant impairment occurred after THC, we were prepared to determine its relationship with plasma concentrations of THC and THC-COOH measured at about the same time.

METHODS

Subjects

Two groups of sixteen new subjects apiece, equally comprised of men and women, participated in the study. The groups will be referred to by the alcohol and marijuana group. Subjects in both groups were recruited according to the same inclusion/exclusion criteria as before with one exception. Subjects in the alcohol group were regular users of alcohol but not marijuana (see below). All subjects were individually trained to perform the city driving test in a preliminary "dress rehearsal" and were familiarized with the other tests and questionnaires.

Plasma analyses after conclusion of the study showed that two males' plasma contained neither THC nor THC-COOH in any sample. It was concluded that these subjects had not inhaled smoke so their data were excluded from further analyses.

Characteristics of the remaining subjects are given in Table 6.1. Except for the reported incidence of marijuana use, there were no significant differences between any of the groups' characteristics.

Table 6.1 Mean±SD (range) of subjects' characteristics.

	Alcohol Group	Marijuana Group
N	16	14
Age (yrs)	23.7±2.7 (20-28)	22.4±3.5 (20-34)
Weight (kg)	68.1±7.9 (60.0-86.1)	67.9±8.9 (54.0-90.5)
Weight (lb)	150.1±17.4 (132.2-189.8)	149.7±19.6 (119.0-199.5)
# Alcoholic Drinks/Week	8.3±6.2 (1-21)	10.6±8.4 (1-30)
Smoking Experience (yrs)	0	3.1±2.1 (1-10)
# Joints/Month	0	2.3±2.5 (1-8)
Driving Experience (yrs)	4.8±2.6 (2-10)	4.1±3.3 (2-15)
Driving Experience (km x 1000)	35.3±28.3 (5-90)	28.6±45.7 (6-180)
Driving Experience (mi x 1000)	21.9±17.6 (3-56)	17.8±28.4 (4-112)

Design, Doses and Administration

The study was conducted according to a mixed between-groups within-subjects design, one group drinking alcohol and placebo alcohol and the other smoking marijuana and placebo marijuana.

Alcohol was administered as 99.8% ethanol mixed with orange juice and Grand Marnier essence to a volume of 250 ml. The dose was 0.43 g/kg lean body mass (On average, this resulted in a dose of 0.36 g/kg body weight in males, and 0.31 g/kg in females). Lean body mass was calculated by subtracting the percentage of fat, determined by skinfold thickness (Durnin and Womersley (1974), from total body weight. The dose was chosen to yield a Blood Alcohol Concentration (BAC) approaching 0.05 g% when the driving test commenced 45 minutes after onset of drinking. Subjects were instructed to fast 2½ hours before drinking and to ingest the dose within 5 minutes. Alcohol in the subjects' expired air was monitored using a Lion S-D3 Breath-Alcohol Analyzer to ensure that subjects would not drive with BACs that were higher than 0.05 g%, which is the legal limit in The Netherlands.

Marijuana and placebo cigarettes were obtained from the same source as before. The subjects were treated on separate occasions with THC doses of 0 and 100 μg/kg. Placebo cigarettes were prepared by ethanol extraction of THC from the plant stock. Marijuana cigarettes were prepared from batches containing 1.77% THC. Cigarettes were cut to different lengths to provide the doses appropriate for the individuals' body weights. Cigarettes appeared identical in both treatment conditions and were smoked through a plastic holder in a fashion determined by the subject but with the constraint that smoking had to be finished within five minutes. After cessation of smoking, cigarettes were retained for subsequent gravimetric estimation of THC consumed. These analyses revealed that the average (±SD) amount of consumed THC in the marijuana condition was 6.9 (±1.0) mg or 101 (±6) μg/kg.

Half of both groups received the treatments in the same order, the others, in reverse order. The driving instructor and observer who rated subjects' driving performance were blind regarding both the administered drug (active or placebo) and the subject's group membership.

Testing Procedures

Upon arrival at the laboratory, subjects were tested for the presence of alcohol in breath. Subjects in the marijuana group were further tested for the presence of cannabinoids and other drugs in urine (as described in Chapter 2). If cannabinoids were found, a blood sample was taken for later verification of the presence of THC. The schedule of further activities on test-days is shown in Table 6.2.

Table 6.2 Schedule of activities on test-days.

Alcohol Group		Marijuana Group
Relative Time (min)	Activity	Relative Time (min)
0-5	Drinking / Smoking	0-5
30-35	Hand Steadiness and Time Perception Tests	15-20
35-40	Blood Sampling and Questionnaires	20-25
45-95	City Driving Test	30-80
95-100	Blood Sampling and Questionnaires	80-85
105-110	Hand Steadiness and Time Perception Tests	90-95

Driving Test and Scoring Methods

Driving tests were conducted in daylight over a constant 17.5 km (10.9 mi) route within the city limits of Maastricht (population ca. 115,000). The route was constructed through business and residential areas on 2-lane undivided streets and included a 6 km (3.7 mi) 4-lane divided segment on a major cross-city thoroughfare (Figure 6.1). Subjects drove their placebo and active drug rides through heavy, medium and low density traffic on the same day of the week, and at the same time of day. Maneuvers included left and right turns at some intersections and driving through others, left and right lane changes, and responding to traffic control devices (i.e. stop signs and signals). There was one special maneuver, repeated twice; i.e. executing a Y-turn on a residential street. A schematic representation of the standard route is shown in Figure 6.1 and the symbols used for maneuvers and road densities are shown in Table 6.3 (the performance variables will be discussed below).

Driving tests were conducted in a dual control 2-door sedan (Volkswagen Golf) normally used for driving instruction/examination. Two persons accompanied the subject: a licensed driving instructor sitting in the front passenger's seat and an trained observer sitting in the center of the rear seat. The former had access to redundant controls and his primary responsibility were controlling safety and giving the route instructions; and, to rate the driver's performance retrospectively (below) after the ride. The observer in the rear seat scored the driver's performance "on-line" and timed the duration of the ride.

As described above, two different procedures were employed for determining a driver's proficiency from observer ratings; i.e. the molecular and the molar methods. The major difference between both methods is that performance variables are repeatedly measured on-line at different points along the route using the molecular approach; and, only once, retrospectively, in the molar approach.

The molecular approach was adopted from Jones (1978) who simplified the scoring of driving behavior so that the trained observer, sitting in the rear seat, attends to only one event at a time. The events observed at specific points along the route are only few aspects of total driving behavior. Thus, the observer is enabled to attend completely to the occurrence of each event in sequence while ignoring all other behavior which would in any case vary between tests. All aspects of a maneuver, such as a left turn, will be scored a number of times over the course of the whole route, but never more than a single aspect at a given moment.

Jones defined twelve aspects, called performance variables (Table 6.3), which were repeatedly scored, 156 times in total, at specific points along the route. The route was designed to fulfill Jones' requirements concerning maneuvers and road densities. The scoring sheet consisted of the schematic route map with symbols indicating the driver behavior to be scored at each point (reproduced in Figure 6.1 with symbology defined in Table 6.3). The observer moved his finger along the route and attended only to the behavior indicated, comparing it with a predefined standard of performance, and circled (if correct), crossed (if wrong) or underlined (if not observed) the symbol. If, for example, the observer were to score *Path* (P) at a lane change (↗) the correct response was defined as: *1.* maintains straight path while scanning, *2.* signals before the lane change, *3.* steers smoothly with gradual angular movement, *4.* straightens vehicle in new lane, and *5.* cancels signal. If the driver failed to make one or more of these responses *Path* was scored as fail, otherwise pass. A complete description of all maneuvers is included in Appendix B.

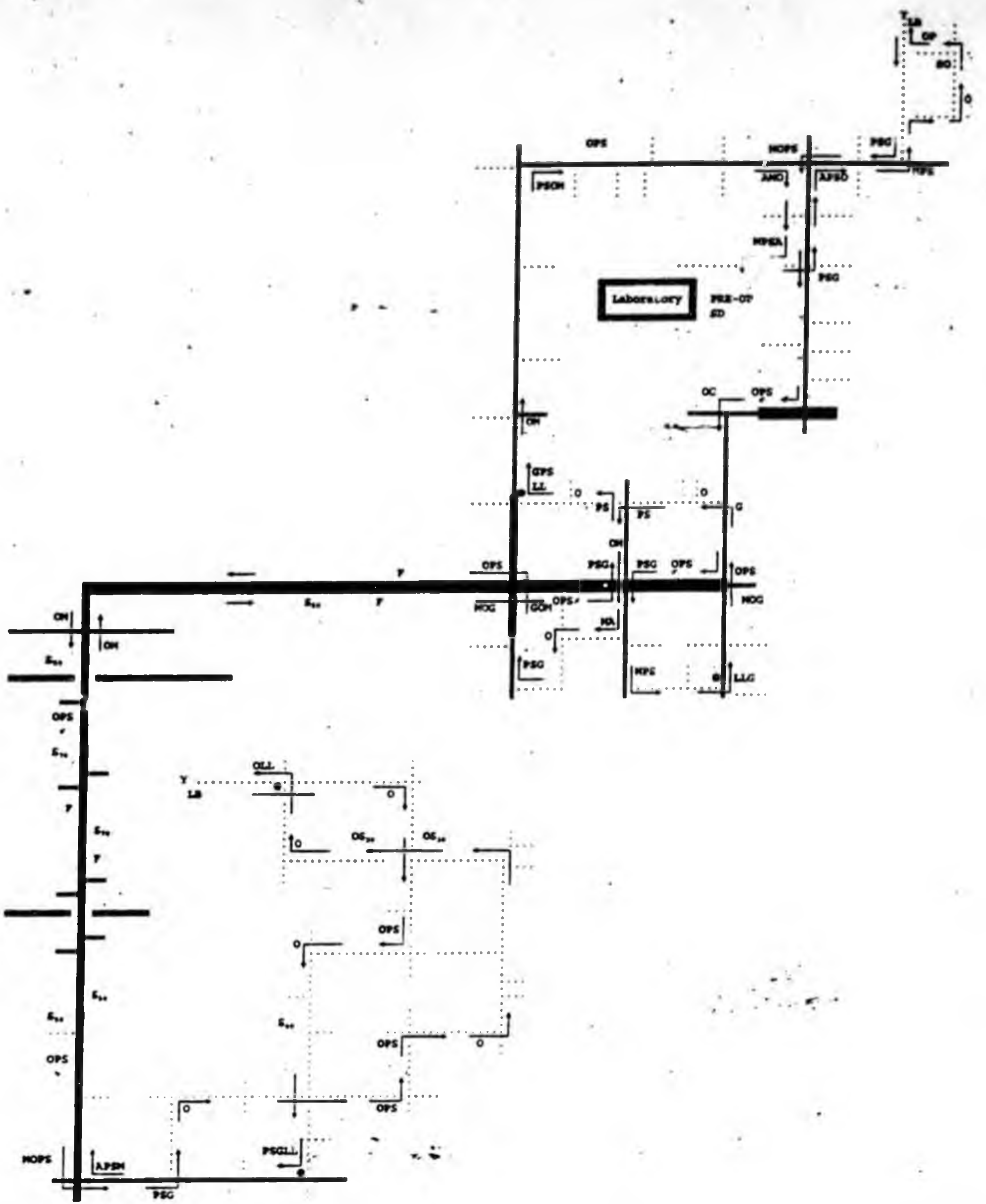

Figure 6.1 Scoring sheet for molecular approach, consisting of the schematic route map with symbols indicating the driver behavior to be scored at each point (for explanation of the symbols, see Table 6.3).

Table 6.3 Maneuvers, road densities, performance variables and their symbols.

Maneuvers:		Road Density:	
Right Turn	┌─▷	▬▬▬	Heavy Density Traffic
Left Turn	◁─┐	═══	Medium Density Traffic
Driving Through	──▷	- - - - -	Low Density Traffic
Right Lane Change	↗		
Left Lane Change	↖	Halt-Line: ●	
Y-Turn	Y		

Performance Variables:		# of times scored:
O	Observation	38
G	Gap Acceptance	14
M	Mirror Check	16
P	Path	30
S	Speed	39
A	Approach at Intersection	5
F	Following Distance	4
LL	Limit Line (stopping at halt-line)	4
L	Location at Y-Turn	2
B	Backing at Y-Turn	2
Pre-op	Pre-operations	1
SD	Shut-Down	1

At the end of the test, the *Total Score* was calculated by summing all passing items and dividing by the total number of observed items. Subscores were also calculated for *Observing*, *Car Control*, *Judgment* and *Other* (Table 6.4). Three additional scores were obtained from the driving instructor; *1. Instructor Control*, the number of times the instructor took control, either orally or physically, *2. Hazard Score*, the number of times the driver responded correctly to hazards divided by the total number of hazards encountered, and *3. Instructions*, the number of times the driving instructor had to repeat a route instruction. All scores, except *Instructor Control* and *Instructions*, were expressed as per cent correct.

The molar approach required the driving instructor to retrospectively rate the driver's performance using a shortened version of the Royal Dutch Tourist Association's (ANWB) Driving Proficiency Test (Appendix B). This instrument is normally applied for practical purposes; e.g. remedial training, driver's licensing, qualifying for a reduction in insurance premiums, etc. Items that did not apply to the driving test, e.g. those regarding railway crossing and special maneuvers like driving backwards and parking, were dropped from the normal list. In total, 108 items were dichotomously scored, as either pass or fail. Total test performance was measured by the percentage items scored as "pass". Subscores were calculated for *Vehicle Checks*, *Handling of Vehicle*, *Action in Traffic*, *Observation and Understanding of Traffic*, and *Turning* (Table 6.5).

Table 6.4 Dependent variables, and their operationalization, measured by the molecular approach.

Dependent Variable	Operationalization
Total Score	% correct of all 156 items
Observing	% correct of 68 items comprising Observation, Gap Acceptance, and Mirror Check
Car Control	% correct of 69 items comprising Path and Speed
Judgment	% correct of 13 items comprising Approach, Following Distance and Limit Line
Other	% correct of 6 items comprising Y-turn Location and Backing, Pre-Operations and Shut-Down
Hazard Score	% of correct responses to hazards encountered along the route
Instructor Control	# of times instructor took control, either orally or physically
Instructions	# of times the driving instructor had to repeat a route instruction

Table 6.5 Dependent variables, and their operationalization, measured by the molar approach.

Dependent Variable	Operationalization
Total Score	% correct of all 108 items
Vehicle Checks	% correct of 13 items regarding preparations for driving and driving away
Handling of Vehicle	% correct of 23 items regarding posture and steering, controls handling, speed adjustment and stopping, and driving through curves
Action in Traffic	% correct of 60 items regarding straight driving, behavior near and at intersections, right turns, left turns, overtaking, driving in lanes and lane changing, driving through traffic circles, and on highways
Observation and Understanding of Traffic	% correct of 8 items regarding perception and traffic insight
Turning	% correct of 4 items regarding Y-turns
Driving Time	time duration (s) of ride

Questionnaires

Questionnaires used in the previous studies were administered to the subjects in the present study. Subjective feelings of intoxication ("high" or "drunkness"), present cognitive and

emotional state, and subjects' willingness to drive were assessed before the onset and after the conclusion of the driving tests. Subjects were also asked about their perception of the administered treatment, whether it was an active or placebo. At the end of each driving test, subjects were required to retrospectively rate the effort given in performing the test and perceived driving quality. Questionnaires are enclosed in Appendix A.

Laboratory Tests

Subjects performed two laboratory tests before and after driving. The hand steadiness test was used since it had shown a significant effect of the 100 μg/kg THC dose in the previous study and confirmation of this result would indicate the equivalent sensitivities of the present and previous groups to the drug. In addition a time perception test (method of interval production; Fraisse, 1963) was used to satisfy the investigators' curiosity about an oft-reported effect of THC. The former followed the same procedures as described in Chapter 5. The latter required the subjects to stand with eyes closed and indicate when he/she thought that 30 seconds had elapsed since a starting signal. The verbal response was timed to the nearest second by stop-watch.

Blood Sampling

Blood samples were obtained by venepuncture immediately prior to and following all placebo and drug driving tests. Two aliquots containing 10 ml each were heparinized and centrifuged, and the plasma fractions were placed in frozen storage for later assays to determine [THC] and [THC-COOH], in the marijuana group; and, [EtOH], in the alcohol group. The analytical procedures regarding THC and THC-COOH assays were the same as in previous studies. As before, samples obtained in conjunction with placebo marijuana tests were only analyzed if the urine test had been positive. Plasma samples obtained from subjects in the alcohol condition were analyzed using gas-chromatography.

Data Analysis

For each variable measured on interval or ratio level, except plasma concentrations, change scores were computed by subtracting raw scores obtained in the placebo condition from those in the drug condition. In the figures, the mean change of the variable is depicted by the height of the bar and its standard error (SED) by the height of the vertical line above or below the bar. Change scores were expressed in absolute and not relative units. This means that if a performance measure fell from 80% after placebo to 70% after active drug; the change score would be 10% and not 12.5%. Mean drug-placebo changes were tested for significant departure from zero by 2-tailed t-tests, for each group separately. Differences between the groups' mean changes were tested by 2-tailed t-tests for independent samples. Willingness to drive data were again analyzed for assessing differences between drug and placebo conditions using Cochran's Q-test. Differences between the respective groups' willingness to drive after drug treatments were analyzed by Mann-Whitney's U-test. Correlations were computed by Pearson's r and tested for significant departure from zero by 2-tailed t-tests.

Preliminary analyses were executed to determine whether change scores were significantly different between subjects who received placebo in the first, and active drug in the second

condition and those who received treatments in reversed order. Significant differences were generally absent and are therefore mentioned only in the exceptional cases where these were significant.

RESULTS

Plasma Concentrations of the Drugs

Table 6.6 shows mean, median and range of [THC] and [THC-COOH] in the marijuana group and [EtOH] in the alcohol group. In the marijuana group, [THC] and [THC-COOH] were in the expected range. In the alcohol group, mean [EtOH] at t=35 was somewhat lower than expected. Furthermore, the fall in [EtOH] to t=95 was less than expected from alcohol's pharmacokinetics; a fall of .02 % per hour is commonly seen during the elimination phase in subjects who fast prior to alcohol intake. This probably means that peak [EtOH] generally occurred during the driving test and was not much higher than measurements taken before and after. This situation contrasts to that for the subjects in the marijuana group whose [THC] reached its peak before the test and fell much more rapidly during it. Average plasma concentrations were significantly different from zero in all cases ($p<.001$).

Table 6.6 Mean, median and range of [THC] and [THC-COOH] in ng/ml (N=14), and of [EtOH] in g% (N=16).

	[THC]		[THC-COOH]		[EtOH]	
	t=20	t=80	t=20	t=80	t=35	t=95
mean	10.5	2.3	7.5	5.6	.034	.028
median	7.8	1.9	6.1	4.3	.034	.028
range	4.3-31.2	1.1-4.9	2.9-18.9	1.7-15.1	.013-.050	.018-.036

Perceived "high" and "drunkness"

Mean levels of intoxication reported by both groups varied from placebo to drug conditions in a remarkable manner. Few subjects in either group reported feeling intoxicated after placebo and their average levels were about 5% of maximum personal experience. After both THC and alcohol these levels rose to about 35% when the respective groups were about to begin driving, then declined to 25% at the end of driving. Means and standard errors of differences (SED) in reported intoxication are shown in Figure 6.2.

T-tests showed that ratings of intoxication after active drugs were significantly different from zero in the marijuana and alcohol groups, both before ($T_{13}=4.36$ & $T_{15}=5.20$, respectively; $p<.001$) and after driving ($T_{13}=3.44$ & $T_{15}=5.23$, respectively; $p<.001$).

Subjects' responses to the question of whether they thought the administered drug was active or placebo showed that they were well aware of what they smoked or drunk. In the marijuana group, 93% of the subjects correctly identified the placebo cigarette when it was administered, and 79%, the active drug. In the alcohol group, 94% of the subjects correctly identified the placebo alcohol when it was administered, and 87%, the active drug.

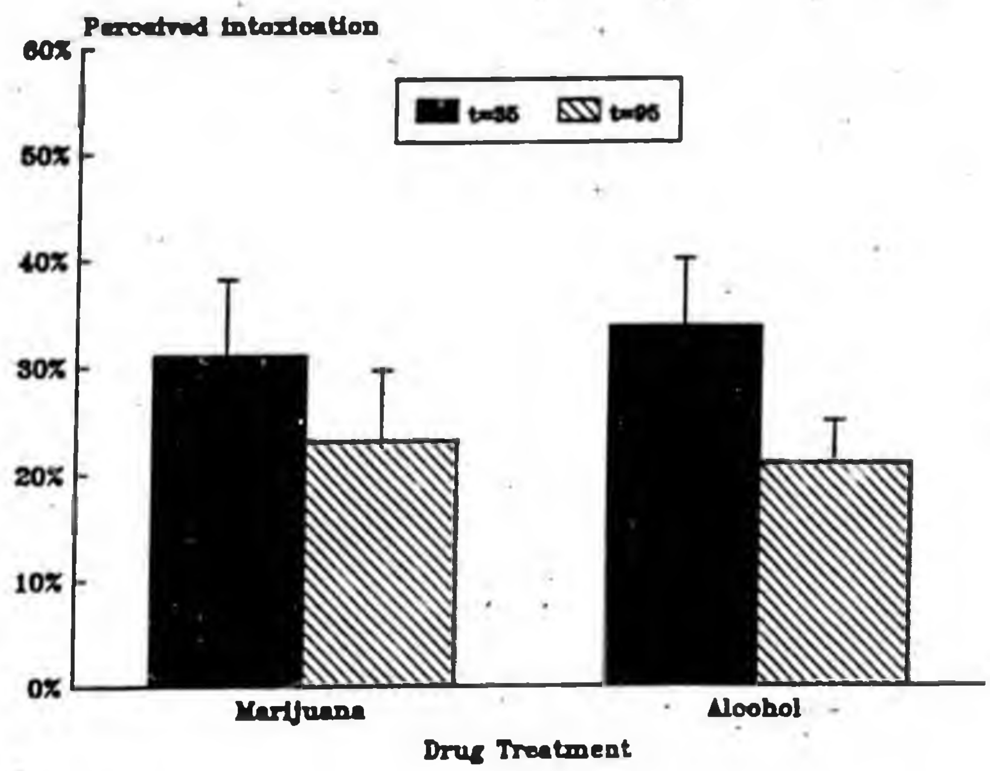

Figure 6.2 Mean (+SED) changes in perceived intoxication by *Drug* and *Time*, relative to placebo. Raw scores were expressed as percentage of maximum personal experience.

Driving Performance Measured by the Molecular Approach

Though some of the changes were positive, indicating better performance after drug and some were negative, showing the opposite, no mean change was significant (Table 6.7). Differences between the two groups' changes were also not significant, although one came close: the difference between improvement shown by the marijuana group and impairment shown by the alcohol group in *Car Control* approached significance ($p < .059$). In general, the effects of both drugs on driving performance, as measured by the molecular approach were very small or absent.

Driving Performance Measured by the Molar Approach

Mean *Total Score* obtained using the molar approach varied between 82.8% and 89.5% over the conditions of the study. Groups' mean change scores on all dependent variables are given in Table 6.8. It is apparent that THC did not significantly affect *Total Score* or any of the component scores. On the other hand, alcohol significantly diminished the *Total Score* as well as two components, *Handling of Vehicle* and *Action in Traffic*. Mean *Driving Time* was, within two seconds, the same for both groups following placebo, namely about 41½ minutes. Subjects drove 46 s slower after THC and 42 s faster after alcohol, but neither change was statistically significant.

Table 6.7 Mean (±SED) changes in driving performance scores measured by the molecular approach for the marijuana (N=14) and alcohol group (N=16); and, the significance of each change and difference between changes.

Dependent Variable	Marijuana Group		Alcohol Group		Marijuana *vs* Alcohol
	Δ	*p*<	Δ	*p*<	*p*<
Total Score	1.6 (±1.7)	ns	-1.5 (±1.7)	ns	ns
Observing	2.4 (±3.1)	ns	-0.3 (±2.8)	ns	ns
Car Control	2.7 (±2.1)	ns	-2.6 (±1.8)	ns	059
Judgment	-8.3 (±4.8)	ns	-2.2 (±4.0)	ns	ns
Other	-3.6 (±4.3)	ns	1.3 (±4.4)	ns	ns
Hazard Score	6.3 (±17.6)	ns	14.6 (±9.4)	ns	ns
Instructor Control	0.5 (±0.4)	ns	0.4 (±0.5)	ns	ns
Instructions	0.1 (±0.6)	ns	0.8 (±0.6)	ns	ns

Table 6.8 Mean (±SED) changes in driving performance scores measured by the molar approach for the marijuana (N=14) and alcohol group (N=16); and, the significance of each change and difference between changes.

Dependent Variable	Marijuana Group		Alcohol Group		Marijuana *vs* Alcohol
	Δ	*p*<	Δ	*p*<	*p*<
Total Score	-0.7 (±2.7)	ns	-6.8 (±1.8)	.002	.065
Vehicle Checks	-0.6 (±1.5)	ns	0.5 (±1.3)	ns	ns
Handling of Vehicle	3.7 (±2.8)	ns	-8.4 (±2.2)	.002	.002
Action in Traffic	-2.7 (±3.1)	ns	-8.4 (±2.3)	.003	ns
Observation and Understanding of Traffic	1.8 (±8.7)	ns	-6.3 (±7.0)	ns	ns
Turning	-1.8 (±4.9)	ns	3.1 (±7.5)	ns	ns
Driving Time	45.6 (±51.8)	ns	-42.0 (±32.4)	ns	ns

Differences between the groups' mean change scores were also significant or nearly so. The greater drop in *Total Score* caused by alcohol was almost significantly different from that caused by THC ($p < .065$). The difference between groups' changes in *Handling of Vehicle*, a component score, was significant ($p < .002$): whereas the marijuana group's performance improved slightly, that of the alcohol group deteriorated under the influence of their respective drugs. In particular, 6 items checked under the category of *Handling of Vehicle* discriminated between the groups' reactions to the drugs. These all pertained to how well the driver handled the vehicle through curves. Whereas THC had little effect on this ability, alcohol seemed to affect it

strongly. This more than any other factor was responsible for the difference between the instructor's ratings of how the two groups were affected by the respective drugs.

Perceived Driving Quality and Effort to Accomplish the Test

Both groups rated their driving performance following placebo as somewhat better than "normal". Following the active drug, ratings were about 35% lower in the marijuana group, but only 5% lower in the alcohol group (Figure 6.3). This striking mean difference was substantiated by the statistical analysis. Mean change of driving quality ratings was significantly lower in the marijuana (T_{13}=-3.05; $p<.009$), but not in the alcohol group. The difference between the groups' mean changes approached significance (T_{28}=-1.97; $p<.058$).

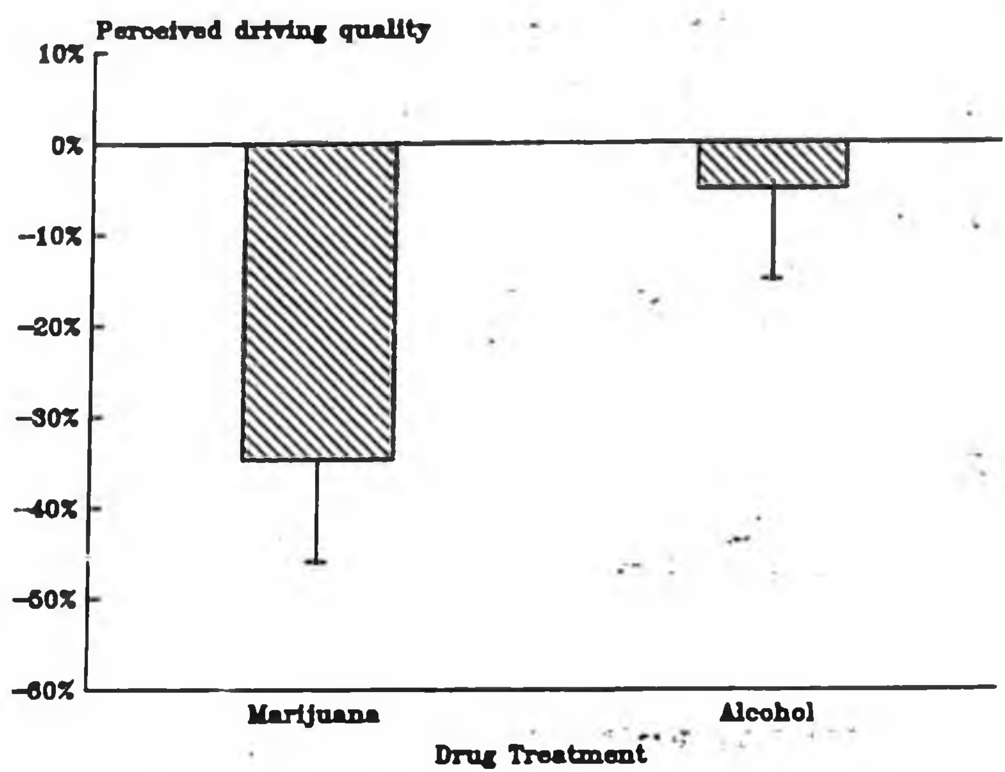

Figure 6.3 Mean (+SED) changes in perceived driving quality by *Drug*, relative to placebo. Raw scores were expressed as percentage of "normal".

Perceived effort to accomplish the driving test was about the same in both groups following placebo. Following the active drug, a greater increase in perceived effort was reported by the marijuana group than the alcohol group (Figure 6.4). Statistical analysis showed that increased effort ratings following the drug were only significant in the marijuana group (T_{13}=2.39; $p<.033$). No significant difference between the groups' mean changes was found.

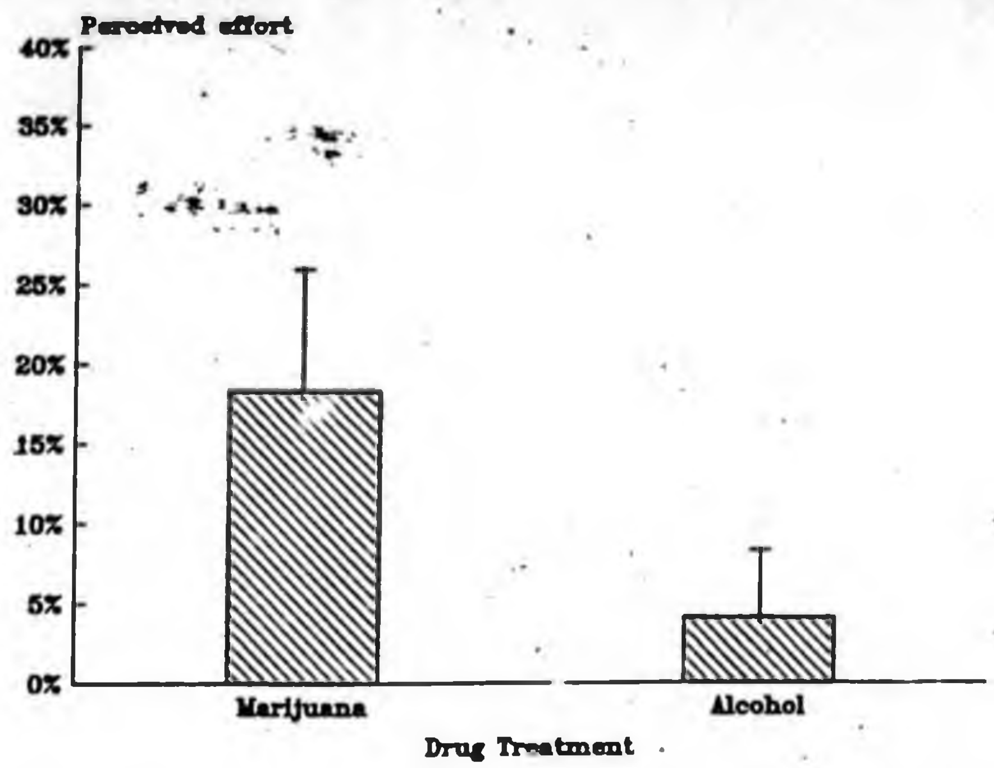

Figure 6.4 Mean (+SED) changes in perceived effort to accomplish the driving test b, *Drug*, relative to placebo. Raw scores were expressed as percentage of maximum of scale.

Willingness to Drive

Table 6.9 presents the percentage of subjects willing to drive under specified conditions of different urgencies (*A*. unimportant though gratifying; *B*. important but avoidable; and *C*. urgent). The more urgent the reason for driving, the more subjects declared that they would be willing to drive.

Table 6.9 Percentages of subjects willing to drive under circumstances *A*, *B* & *C* (see text) by treatment condition and sampling time; and, the significance of each difference between placebo and active drug condition, tested by Cochran's Q-test.

		Alcohol Group			Marijuana Group		
		placebo	alcohol	$p<$	placebo	marijuana	$p<$
A	$t=50$	100	38	.006	86	50	.044
	$t=175$	100	50	.012	93	57	.044
B	$t=50$	100	44	.008	93	57	.044
	$t=175$	100	75	.07	100	57	.03
C	$t=50$	100	94	ns	100	93	ns
	$t=175$	100	94	ns	100	100	ns

Cochran's Q-test showed that the numbers of subjects who would have driven for an unimportant reason following the active drug were significantly less than after placebo, in both groups. The same held true for the somewhat more important reason. In contrast, nearly all subjects indicated that they would have driven for an urgent reason, irrespective of the administered drug. Mann-Whitney's U-test failed to reveal any significant difference between the groups' percentages following the active drug.

Perceived Alertness, Contentedness and Calmness

Changes in subjective feelings of alertness, contentedness and calmness are shown in Table 6.10. Feelings of alertness were significantly diminished in both groups and at both time points following the active drug relative to placebo. Subjects felt also less content and calm following the active drugs, but the effects were smaller. Statistical tests revealed only one significant effect: alcohol producing significantly diminished feelings of contentedness measured after termination of the driving test.

Table 6.10 Mean (±SED) changes in subjective feelings of alertness, contentedness and calmness (raw scores being expressed as percentages of maximum) for the marijuana (N=14) and alcohol group (N=16); and, the significance of each change and difference between changes.

Dependent Variable		Marijuana Group		Alcohol Group		Marijuana vs Alcohol
		Δ	*p*<	Δ	*p*<	*p*<
Alertness	*t*=35	-15.4 (±4.2)	.003	-18.9 (±3.6)	.001	ns
	t=95	-15.1 (±5.3)	.014	-20.1 (±3.0)	.001	ns
Contentedness	*t*=35	-6.2 (±4.0)	ns	-5.8 (±4.3)	ns	ns
	t=95	-5.7 (±3.6)	ns	-8.9 (±2.3)	.002	ns
Calmness	*t*=35	-7.5 (±4.4)	ns	-1.2 (±4.2)	ns	ns
	t=95	-10.0 (±5.2)	.077	-7.3 (±5.3)	ns	ns

Hand Steadiness Test

Mean square root of total number of side contacts were about the same in the placebo conditions for both groups. The active drugs, however, affected hand steadiness differently; the number of side contacts increased after THC whereas the opposite occurred after alcohol (Figure 6.5). Statistical analysis showed that the impairment following THC was highly significant, both shortly after smoking and more than one hour later (T_{13}=3.96 & 3.40; $p<.002$ & .005, respectively), whereas the improvement following alcohol was only significant shortly after drinking (T_{15}=-2.29; $p<.037$). The differences between the groups' mean changes were significant both before and after the driving test (T_{28}=4.71 & 3.35; $p<.001$ & .002, respectively).

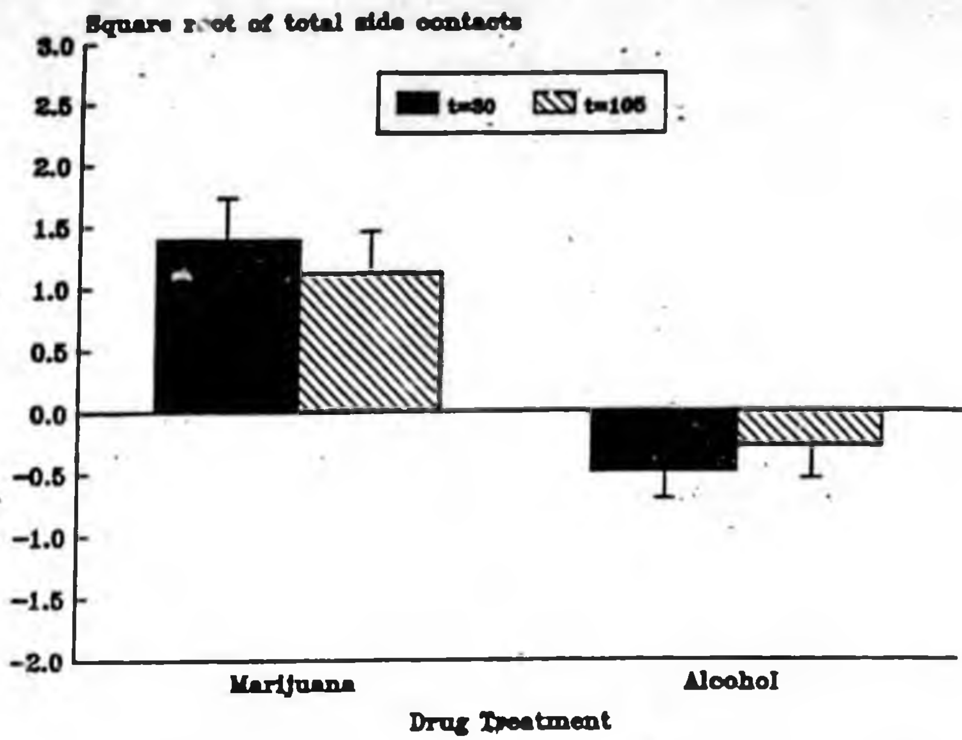

Figure 6.5 Mean (+SED) changes in the square root of total number of side contacts in the hand steadiness test by *Drug*, relative to placebo.

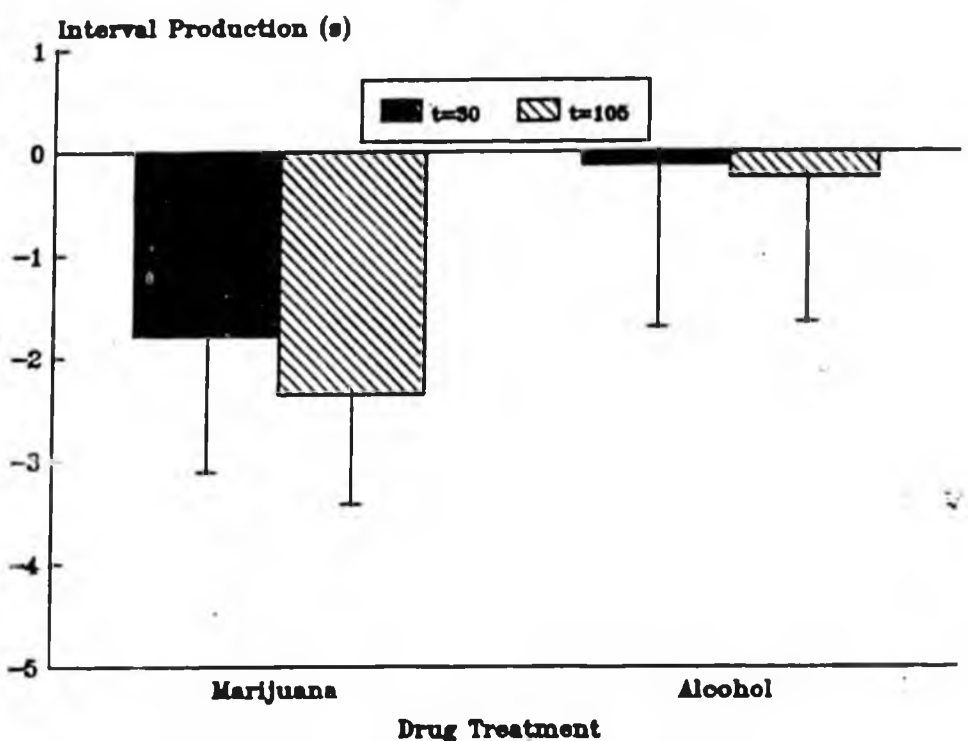

Figure 6.6 Mean (+SED) changes in attempted production of a 30-second interval by *Drug*, relative to placebo.

Time Perception Test
Mean attempted production of a 30-second interval was close to the target for the alcohol group, both after placebo and active drug yielding very small, and non-significant, changes (Figure 6.6). Subjects in the marijuana group produced a foreshortened interval in both conditions, but foreshortening was greater following THC. The change in interval production was, however, only significant after, and not before, the driving test (T_{13}=-2.36; $p<.045$).

Inter-Subject Relations between Variables
Relationship between Plasma Concentrations and Driving Performance. Correlational analyses were performed to determine whether driving performance was related to plasma concentrations of the drugs, measured both before and after the driving tests. The first step involved correlational analysis between raw variables; the second step, between changes in driving performance and plasma concentrations. Neither analysis yielded significant results.
Relationship between the Molecular and Molar Approach. Correlations were also computed between the raw *Total Scores* obtained by both the molecular and molar approach. These correlations were computed in each condition separately. For the marijuana group, the correlation between the Total Scores were 0.71 ($p<.005$; 2-tailed) and 0.54 ($p<.044$) in the placebo and active drug condition, respectively. For the alcohol group, the corresponding correlations were 0.71 ($p<.002$) and 0.79 ($p<.001$), respectively. Differences between these correlations were not significant. The second step involved correlational analysis of change scores. This analysis revealed that changes in *Total Scores* of both methods were not significantly correlated, neither in the marijuana (r=0.05) nor in the alcohol group (r=0.08).
Relationship between Driving Performance and Driving Experience. Correlations were also computed between driving experience on one hand, and driving performance and changes in driving performance following the active drug on the other. Neither analysis revealed significant correlations. This means that driving experience of the subjects in the present study could neither predict driving performance per se nor changes following the active drug.
Relationship between Plasma Concentrations and Perceived Intoxication. Correlations of perceived "high" following THC with [THC] were 0.65 ($p<.013$) shortly after smoking and 0.47 ($p<.093$) following termination of the driving test. Correlations with [THC-COOH] were 0.74 ($p<.002$) and 0.62 ($p<.018$), respectively. Correlations of perceived intoxication following alcohol and [EtOH] were not significant (r=0.27 & 0.39, respectively). Correlations of plasma concentrations with changes in perceived intoxication were nearly the same as those with the raw scores, because intoxication ratings were generally zero following placebo.

DISCUSSION

The present study showed that alcohol, administered in a dose of 0.43 g ethanol per kg of lean body mass yielding an average plasma alcohol concentration of about 0.04 g%, produced a significant impairment in city driving as measured by the molar approach, relative to placebo. Significant impairment was shown by changes in *Total Score*, and subscores describing *Handling of Vehicle* and *Action in Traffic*. Marijuana, administered in a dose of 100 μg THC per kg of whole body weight, on the other hand, did not significantly change mean driving performance

as measured by this approach. Neither alcohol nor marijuana significantly affected driving performance measures obtained by the molecular approach.

The first conclusion one might draw is that the methods applied for measuring driving performance did not yield exactly the same results. Yet both methods similarly measured individual differences in driving proficiency. Correlations between the total scores in all four conditions were between 0.54 and 0.79, and as such, highly significant. Obviously both methods were able to discriminate the relatively large pre-existing differences in the subjects' respective abilities to operate the vehicle in urban traffic. Change scores were, however, not correlated; i.e. r=0.05 & 0.08 in the marijuana and alcohol group, respectively. Since the molar, and not the molecular, approach was sensitive to alcohol's adverse effects, it is tempting to conclude that the latter may fail to measure some important driving deficits. That is, the molecular approach seems relatively insensitive to drug-induced changes.

The second conclusion one might draw is that the molar method, having proven its sensitivity by detecting impairment associated with a low BAC, should be sensitive to any similar impairment occurring after a correspondingly low THC dose. That it failed to show any significant change in the marijuana group's driving performance leads to the third and most important conclusion:

The 100 μg/kg THC dose these subjects received shortly before the test did not impair their city driving performance.

The different effects of alcohol and marijuana on driving performance can not be explained by the subjects' reported driving experience. Although subjects in the alcohol group were somewhat more experienced drivers than those in the marijuana group, the difference was not significant. Furthermore, correlational analysis showed that neither driving performance nor driving impairment was significantly related to previous driving experience. The different effects of alcohol and marijuana on driving performance can also not be explained by differences in the groups' subjective feelings. There was a remarkable correspondence between the two groups' feelings of intoxication, i.e. "high" or "drunkness". Prior to the driving test, both groups reported intoxication levels of about 35% of the highest ever experienced, and 25%, after its termination. THC's significant impairing effect on hand steadiness also showed that the subjects in the marijuana group were sensitive to THC's effects.

The difference between the drugs' effects on driving may be explained, however, by compensational mechanisms, such as increased effort. Both groups reported about the same amount of effort in accomplishing the driving test following placebo. Yet only subjects in the marijuana group reported significantly higher levels of invested effort following the active drug. Previous on-road driving studies indicate that subjects may compensate for THC's adverse effects by slowing down (Hansteen *et al.*, 1976; Casswell, 1979; Peck *et al.*, 1986). Results of the present study were in the same direction: it took the marijuana group an average of 46 s longer to complete the circuit after THC than following placebo. That this difference was not significant was probably due to the real-life character of the test: unforseen obstructions and variable traffic density probably increased the error variance of this measure over what it would have been on a closed course. Thus, there was evidence that subjects in the marijuana group were not only aware of their intoxicated condition but were also attempting to compensate for it.

There were other striking differences between the groups' reactions to their respective drugs. As stated, subjects in the marijuana group invested more effort in the test while driving under the influence of THC. The alcohol group apparently made no greater effort after the drug than placebo. Yet for all of their effort, the marijuana group rated their driving performance as being significantly worse after THC than placebo. The alcohol group who invested no special effort after the drug, not surprisingly, thought they had driven as well as following placebo. They were nonetheless driving in a deficient manner according to the instructor's ratings. These seem to be important findings. They support both the common belief that drivers become overconfident after drinking alcohol and investigators' suspicions that they become more cautious and self-critical after consuming low THC doses by smoking marijuana.

These impressions were seemingly contradicted by the similarity in the groups' responses indicating their willingness to drive after the respective drugs. About 50% of both groups said they would have been unwilling to drive for less than very urgent reasons. This profession of caution seems a bit odd for the alcohol group who knew that they could not be given a dose which would produce BACs over the legal limit during the test. The "contradiction" in this case seems to be a reflection of the group's desire to give "socially desirable" answers to the questionnaire, whether the same was true for the marijuana group in the present and preceding studies is a moot point.

The laboratory performance tests also discriminated between the drugs' effects. Hand steadiness was impaired following THC and improved following alcohol, relative to placebo. The difference between the drugs' effects was significant, both before and after the driving test. Impairment after THC was about as much as that produced by the same dose in the previous study, indicating equivalent sensitivities of the present and previous groups. Production of time intervals was not affected by alcohol, but THC significantly shortened interval production, relative to placebo. This confirms the common finding that THC affects time estimation (Hollister and Gillespie, 1970; Bech *et al.*, 1973). As usual, THC accelerated the subjects' perception of time passing. They arrived at a foreshortened production of 30 s and would have estimated the duration of the actual interval as longer that it actually was. Changes in driving performance were not correlated with changes in performance in either laboratory test. Nevertheless, both tests should be seriously considered for inclusion in any test battery for measuring these drugs' effects, mainly because of the different pattern of results they produced.

Plasma concentrations of THC and THC-COOH were comparable to those obtained in the previous studies. Plasma concentrations of ethanol were somewhat lower than predicted, and the fall in plasma concentration during the driving test was less than expected. This probably means that peak plasma concentrations generally occurred during the driving test. If so, it probably was about 0.04 g%. Ratings of "high" were significantly related to plasma concentrations of THC and THC-COOH but those of "drunkness" were not significantly related to plasma concentrations of ethanol. Drug plasma concentrations were neither related to absolute driving performance scores nor to the changes that occurred from placebo to drug conditions. With respect to THC, these results confirm the findings in previous studies. They are somewhat surprising for alcohol but may be due to the restricted range of ethanol concentrations in the plasma of different subjects.

How do the present results relate to those reported by Klonoff (1974)? He also assessed the effects of relatively low THC doses on aspects of subjects' driving performance in a city driving test using a similar molar approach. His subjects commenced driving immediately after cessation of smoking. They scored lower on judgment and concentration scales when under the influence

of the highest, but not the lowest, dose. Behaviors that were more directly related to driving performance, e.g. lane changing, compliance with traffic signals and posted speed advisories, were not affected by the drug. Subjects in the present study commenced driving 30 minutes after initiation of smoking. The molar method applied in the present study did not include ratings of judgment or concentration. With the exception of these two items, neither study indicated significant effects of THC on driving performance and are, therefore, in complete agreement.

CHAPTER 7 - GENERAL DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

INTRODUCTION

It is commonly assumed that marijuana smoking in real-life social situations delivers THC doses that seriously degrade the ability to safely operate motor vehicles; and, that the drug's users frequently drive shortly after smoking. If these premises are correct, it would follow that marijuana users are, while intoxicated, at increased risk of traffic accident involvement and constitute a safety hazard for other road users. However, the foremost impression one gains from reviewing the literature is that no clear relationship has ever been demonstrated between marijuana smoking and either seriously impaired driving performance or traffic safety. The epidemiological evidence, as limited as it is, shows that the combination of THC and alcohol is over-represented in injured and dead drivers and more so in those who actually caused the accidents. Yet there is little if any evidence to indicate that drivers who have used marijuana alone are any more likely to cause serious accidents than drug free drivers. To a large extent, the results from driving simulator and closed-course tests corroborate the epidemiological findings by indicating that THC in single inhaled doses up to about 250 $\mu g/kg$ has relatively minor effects on driving performance, certainly less than BACs in the range 0.08-0.10 g%.

But how well do these findings relate to the actual driving performance of regular marijuana users? If previous experience is any guide, little of crucial importance will emerge from experimental research until it is conducted in a more realistic manner. Therefore, a series of studies were conducted to determine the dose-response relationship between THC and objectively and subjectively measured aspects of real world driving. A variety of driving tasks were employed, including maintenance of a constant speed and steady lateral position during uninterrupted highway travel, adjusting velocity to the movements of a leading car on a highway, and city driving. The purpose of applying different tests was to determine whether similar changes in performance under the influence of THC occurs in all thereby indicating a general drug effect on driving safety.

However real these tests might appear, the circumstances in which the subjects smoked the drug and drove the car were still somewhat artificial. First, the subjects consumed the drug in a neutral setting, alone or in the presence of a stranger. This was of course different from the situation wherein they normally smoke marijuana, i.e. in the company of friends who might reinforce a certain type of behavior not normally considered as conservative or prudent. Marks and Pow (1989) found that marijuana smokers derived slightly greater pleasure from THC in the company of friends than strangers from which one might infer a social amplification of the pharmacological effect. However, neither they nor any other investigators ever indicated that social amplification outlasts the situation which gives rise to it. In the absence of such evidence, we tend to discount the possibility that the unusual setting for drug administration had any effect upon subsequent driving performance. Social amplification of THC's adverse effects on driving performance might well occur if the driver were accompanied by similarly intoxicated passengers. We must therefore restrict generalizations from the studies' results to those situations

where the intoxicated driver is doing his best to perform efficiently and is uninfluenced by friends or any other factor which might amplify the drug's adverse effects.

Secondly, subjects were aware of the fact that their driving behavior was being observed and that the accompanying driving instructor would intervene if necessary. The former is hardly avoidable in experimental studies but possibly provoked the subjects to do their utmost; the latter is a prerequisite for ensuring safety in actual driving studies and may or may not have produced nonchalance on the subjects' part resulting in poorer than normal performance. Yet according to what the subjects declared, they drove normally after placebo indicating that the experimental situation had not seriously altered their performance. Whether they drove in the test as they normally would after smoking marijuana remains open to question. The correspondence between experimental and epidemiological studies regarding THC's effects on driving performance suggests that this artificiality is also of minor concern.

The present series of studies are about the best simulation of real world driving one can reasonably achieve and have gone further toward defining the effects of marijuana smoking on actual driving performance than any of its predecessors. The results found in the successive studies were discussed at full length in the respective chapters. In this chapter, results of the separate studies will be integrated to provide answers to some important questions concerning marijuana's influence on driving performance. First however, the implications of the pilot study's major result will be discussed, i.e. the THC dose that marijuana users prefer to achieve their desired "high". In the following section, the driving tests will be discussed in terms of the kinds of mental operations they require. Some further remarks provided in that section concern the relevance of the driving tests for traffic safety. The major part of this chapter will be addressed to the most important issue, i.e. what the results indicate as the real effects of marijuana smoking on driving performance. Finally, attention will focus on the relationship between plasma drug concentrations and drug-induced driving impairments. This chapter will end with a list of conclusions and recommendations.

THC DOSES

To avoid arbitrarily selecting an unrealistic maximum THC dose for the driving studies, it was necessary to establish the dose which marijuana users actually prefer for achieving their desired "high". A pilot study met this requirement. The study showed that marijuana users prefer higher THC doses than those previously administered in experimental studies. Previous THC doses were generally between 100 and 200 $\mu g/kg$, including the remaining butt, whereas the subjects in the pilot study preferred an average dose of 300 $\mu g/kg$, excluding the butt. This either means that today's marijuana users prefer higher doses than in the past or that investigators failed to administer realistic doses in previous studies, or both.

Ohlsson *et al.* (1980) compared THC's effects after three different routes of drug administration. In the smoking condition, subjects were allowed to smoke a marijuana cigarette containing 19 mg THC in their own manner such as to obtain the maximum desired "high". Comparing the weight of the remaining butt with the unlit cigarette revealed that the eleven males participating in the study had smoked 13.0 mg THC on the average. Ohlsson *et al.* failed to report the subjects' mean weight but, assuming that it was 70 kg (154 lb) on average, this would equal to a THC dose of nearly 200 $\mu g/kg$. Perez-Reyes *et al.* (1982) compared THC's effects after smoking marijuana cigarettes of three different potencies. Three males and three

females participated in that study and the same procedures were applied to determine the amount of THC consumed as in Ohlsson's study. It appeared that the amount of THC consumed was proportional to the THC content, or potency, of the cigarette. The subjects consumed 9.7, 12.8 and 16.9 mg THC when smoking cigarettes containing 1.32%, 1.97% and 2.54% THC, respectively. Perez-Reyes *et al.* also failed to report the subjects' mean weight but, for a 70 kg (154 lb) person, the weight calibrated amount of THC consumed would have been 140, 180 and 240 μg/kg, respectively. These results indicate that the potency of the marijuana cigarette is a major contributor to the preferred dose. Ohlsson failed to mention the potency of the marijuana cigarettes they used which makes a comparison with the data of Perez-Reyes impossible. The potency of the cigarettes used in the present pilot study was 2.57%, nearly the same as the highest in Perez-Reyes' study, and our subjects smoked on the average a THC dose of 20.8 mg, or 308 μg/kg. This might be an indication that users presently prefer higher doses than in the early eighties. However, there is one important distinction between these earlier studies and the present one that may account for the increase. Our subjects were allowed to smoke a second, and even a third, cigarette to achieve their desired "high". Subjects in previous studies were given only one cigarette, maybe out of ignorance but probably because it was not the investigators' primary objective to determine the subjects' preferred dose. Consequently, the preferred dose of subjects who smoked one cigarette completely but not yet achieved their desired "high" was under-estimated. Thus, whether current users indeed prefer higher doses than ten years ago is hard to say. What is clear from the pilot study's results, is that higher THC doses than those usually administered in previous studies should be included in future ones.

The relation between preferred dose and the potency of the drug found by Perez-Reyes *et al.* (1982) raises two questions that might have implications for interpreting the present studies' results. The first question is, how do people regulate their THC consumption? Apparently they do not titrate brain THC concentrations to within a narrow range as tobacco smokers reliably do with nicotine (Jaffe, 1990). It's also doubtful that marijuana smokers integrate their THC concentrations over time to cease consumption when the cumulative effect approaches a certain threshold. In the earlier study the subjects may have simply ceased smoking after consuming the same volume of cigarettes, regardless of the delivered dose. But this could not have occurred in the pilot study for the present series since our subjects smoked ad lib. The probable explanation is that our subjects were somewhat aware of both the momentary brain concentration and its rate of increase and ceased smoking before the expected rise would shortly exceed the preferred effect. This procedure was accurate enough to limit the drug's effects to below what they had previously experienced as an unpleasant maximum. It was not accurate enough to attain homogeneity in the subjects' achievement of the preferred "high" in relation to the maximum (coefficient of variation: 25%). In real life, marijuana users are usually more aware of the potency of the material they smoke, from prior experience, upon the advice of other users or even from its "street" price. The material presented to the subjects in the pilot study was definitely unfamiliar and they may have suddenly become prudent smokers. Confirmation of this supposition came from the same subjects' consumption of THC in the subsequent driving study. Though treated with the same average dose they had preferred in the pilot study, their plasma drug concentrations were now higher. This difference was interpreted as the result of increased smoking efficiency due to familiarization with the potency of the material containing the drug.

If familiarization plays a major role in smoking efficiency and, consequently THC plasma concentrations, THC's adverse effects on performance may also be dependent on this factor. That being the case, the second and third driving studies' results would under-estimate THC's

adverse effects on driving performance since new groups of subjects were recruited in both. However, the remarkable resemblance between effects of every THC dose on SDLP in the first and second driving studies indicates that familiarization is not a very important factor. Nevertheless, we recommend that subjects in future studies be familiarized with the potency of the drug before the beginning of performance testing.

The second question raised by the apparent relationship between the drug's potency and the preferred dose is, what the latter would have been if marijuana of much higher potency were smoked. This is an important question since potencies of marijuana are increasing rapidly. At present, potencies of marijuana cultivated in The Netherlands may contain 5-20% THC, and, in exceptional cases, 30%. It is hard to imagine that subjects would consume as much of a cigarette containing a very high THC concentration as one containing a very low one. Future research determining marijuana users' preferred dose should also include marijuana with much higher potencies. It may then appear that Perez-Reyes *et al.*'s findings were attributable to their subjects' inability to discriminate among potencies spanning a narrow range. A broader range of cigarette potencies would probably allow regular marijuana users to discriminate well enough to alter their consumption and thereby come closer to administering the same preferred dose after every one.

On the basis of the pilot study's results, the highest dose of THC administered in subsequent driving studies was defined as 300 μg/kg; other doses were 100 and 200 μg/kg, and placebo. Marijuana cigarettes were prepared from batches obtained from NIDA with potencies varying from 1.75% to 3.58%, the highest that were then available. If future research shows that current users of marijuana prefer much higher THC doses when they smoke very potent marijuana, the results of the current program can only serve as an indication of the minimal effects the drug may have on actual driving performance. If, on the other hand, it shows that users prefer a THC dose of about 300 μg/kg to reach their desired "high" irrespective of the potency of the drug, the results presented in this report are truly valid estimates of what may happen in daily life after smoking THC doses that induce a preferred "high".

THE DRIVING TESTS

Three different tests were applied in the experiments that progressively increased in the number of skills employed by the driver: road tracking, car following and city driving. The first is now a standardized test which, in more than 40 studies, has proven to be very sensitive to sedation produced by a variety of medicinal and social drugs, including alcohol. The car following and city driving test were developed following the recognition that parameters measured in the standard test fail to represent all abilities considered important for safe driving. This section will describe the differences between the driving tests and the relevance of each to traffic safety.

The difference between the three driving tests can be characterized in many ways. The one described here is that in terms of the type of information processing each requires. Two distinct types of human information processing can be distinguished (Shiffrin and Schneider, 1977): "automatic" and "controlled". The former is capable of accepting an enormous volume of perceptual information at a relatively high rate to mediate coordinated multi-effector responding in a normally stable input-output relationship. This process is not generally under voluntary control, proceeds in parallel with the stream of consciousness and involves no decision making. Controlled information processing is much slower but highly adaptive. It begins with the

conscious perception of a discrete event or situation. Identification of the meaning of that perception is made by comparing it with information stored in memory. A decision involving the selection and execution of a particular series of motor responses and/or the suppression of a motor routine in progress occurs next. This process can proceed in parallel with an automatic process and the integrity of both are essential for safe driving.

Aspects of both types of information processing are present in most well practiced tasks. Most would agree that skilled performance is the integrated sum of automatic and controlled information processing and that their respective weights vary constantly with the task requirements. The more controlled information processing a task requires, the more it is experienced as demanding effort. According to this concept, lateral position control in the road tracking test depends principally upon automatic information processing. The car following test requires somewhat more controlled information processing and driving in urban traffic, even more. The concept can be illustrated by the ease of having a conversation with other occupants of a vehicle while driving. It is easy to converse with them while driving on a highway in light traffic. It becomes somewhat more difficult when driving in heavy traffic and maintaining a safe headway behind cars travelling in a platoon. Conversing while driving in urban traffic is even more difficult and, at times, even impossible for most drivers. Thus, the more controlled processing involved in a particular situation, the more effort the driving task demands and the less "spare capacity" is left for having a conversation with other occupants. This concept of effort relates to task or computational demands, and often, to the allocation of attention. There exists, however, also another concept of effort which relates to brain arousal mechanisms (Kahneman, 1973; Pribram and McGuinness, 1975) or the required psychological state (Hockey, 1986). If one perceives a discrepancy between his actual state of arousal and that required to efficiently accomplish the task, he will first attempt to resolve the difference by compensatory effort, e.g. focussing attention. Failing that, he will try to reduce task demands to what can be efficiently accomplished in the deficient arousal state. The latter can be accomplished during driving by reducing speed or assuming a greater headway to compensate for slower reaction times.

It is sensible to keep the relevance of the separate driving tests for driving and traffic safety in mind while discussing THC's effects on driving performance. It is obvious that the road tracking test measures only a few aspects of driving behavior. Yet proper road tracking is a general prerequisite for safe driving. Consequently, drugs that substantially impair a driver's fundamental road tracking ability possess a real potential for adversely affecting driving safety. Whether this means that drivers under the influence of such drugs have also a greater probability of becoming involved in a traffic accident seems plausible but has yet to be determined. The same kind of reasoning applies to the car following test. It measures only a few additional aspects of driving behavior, but their impairment is also incompatible with safe driving. The city driving test measures most aspects of driving behavior and therefore comes closest to reality. Driving in urban traffic is so common in daily life that any drug-induced impairment found with this test should be considered as the most important, though not necessarily the earliest, sign that the drug possesses properties that adversely affect traffic safety.

EFFECTS OF THC ON DRIVING PERFORMANCE

One of the issues addressed by the first driving study was whether it would be safe to continue using the same approach for subsequent on-road studies in traffic. The first group complied with all instructions, even after high doses of THC. Changes in mood were often reported but changes in personality were never observed. Most importantly, the subjects were always able to complete every ride without major interventions by the driving instructors and their safety was never compromised. The same occurred in the subsequent studies showing that it is possible to safely study marijuana's effects on actual driving performance in the presence of other traffic. In this respect, the drug is no different from many others studied by the same investigators and their colleagues.

The standard test measured the subjects' ability to maintain a constant speed and a steady lateral position between the lane boundaries. Standard deviation of lateral position, SDLP, increased after marijuana smoking in a dose-related manner. The lowest dose, i.e. 100 μg/kg THC, produced a slight elevation in mean SDLP, albeit significant in the first driving study. The intermediate dose, i.e. 200 μg/kg THC, increased SDLP moderately; and, the highest, i.e. 300 μg/kg THC, substantially. It is remarkable how well the changes in SDLP following THC in the first driving study were replicated in the second, in spite of the many differences in the ways they were designed. The replication of THC's effects on SDLP substantiates the generality of these results. Other objective measures obtained by this test were much less affected by THC. Mean speed was somewhat reduced following the higher THC doses, but the effects were relatively small (max. 1.1 km/h or 0.7 mph). Standard deviations of speed and steering wheel movements were unaffected by the drug. Subjective ratings of perceived driving quality followed a similar pattern as SDLP indicating that the subjects were well aware of their diminished ability to control the vehicle after marijuana smoking.

The car following test measured the subjects' ability to follow a leading car with varying speed at a constant distance. All THC doses increased mean headway, but according to an inverse dose-response relationship. This type of relationship was unexpected and probably due to the particular design of the second driving study, i.e. the ascending dose series. It means that subjects were very cautious the first time they undertook the test under the influence of THC (i.e. after the lowest dose) and progressively less thereafter. As a consequence of this phenomenon, mean reaction time to changes in the preceding car's speed also followed an inverse dose-response relationship. Statistical adjustment for this confounding by analysis of covariance indicated that reaction times would not have increased significantly if the mean headway were constant. Coefficient of headway variation increased slightly following THC. Together, these data indicate that there is no more than a slight tendency towards impairment in car following performance after marijuana smoking. They also show that subjects try to compensate for anticipated adverse effects of the drug by increasing headway, especially when they are uncertain of what these might be. As in the standard test, subjects' ratings of driving quality corresponded to the objective changes in their performance.

The city driving study measured the subjects' ability to operate a vehicle in urban traffic. For reasons mentioned in the respective chapter the THC dose in that study was restricted to 100 μg/kg. For comparative purposes another group of subjects was treated with a modest dose of alcohol, producing a mean BAC of about 0.04 g%. Results of the study showed that the modest dose of alcohol, but not THC, produced a significant impairment in driving performance, relative to placebo. Alcohol impaired driving performance but subjects did not perceive it. THC

did not impair driving performance yet the subjects thought it had. After alcohol, there was a tendency towards faster driving and after THC, slower.

The results of these studies corroborate those of previous driving simulator and closed-course tests by indicating that THC in single inhaled doses up to 300 μg/kg has significant, yet not dramatic, dose-related impairing effects on driving performance. They contrast with results from many laboratory tests, reviewed by Moskowitz (1985), which show that even low doses of THC impair skills deemed important for driving, such as perception, coordination, tracking and vigilance. The present studies also demonstrated that marijuana can have greater effects in laboratory than driving tests. The last study, for example, showed a highly significant effect of THC on hand unsteadiness but not on driving in urban traffic.

It is a natural question why the effects of marijuana on actual driving performance appear to be so small. As in many previous investigations, subjects attempted to compensate for anticipated adverse effects of marijuana smoking. Our subjects were aware of the impairing effects of THC as shown by lower ratings of perceived driving quality. Consequently, they invested more effort to accomplish the driving tests following THC than placebo. Furthermore, in the car following test, they drove at a greater headway after marijuana smoking; and, in both road tracking and city driving tests, they slightly reduced their driving speed. Yet despite their effort, subjects were unable to fully compensate for THC's adverse effects on lateral position variability. This is because SDLP is primarily controlled by an automatic information processing system which operates outside of conscious control. The process is relatively impervious to environmental changes, as shown by the high reliability of SDLP under repeated placebo conditions, but highly vulnerable to internal factors that retard the flow of information through the system. THC and many other drugs are among these factors. When they interfere with the process that restricts SDLP, there is little the afflicted individual can do by way of compensation to restore the situation. Car following and, to a greater extent, city driving performance depend more on controlled information processing and are therefore more accessible for compensatory mechanisms that reduce the decrements or abolish them entirely.

This still leaves the question open why performance appears to be more affected by THC in laboratory than actual driving tests. Many researchers defend the primacy of laboratory performance tests for measuring drug effects on skills related to driving on the basis of superior experimental control. Certainly some control is always necessary to reduce the confounding influence of extraneous factors that would otherwise so increase measurement error as to totally obscure the drug's effects. However, only some extraneous factors are truly sources of measurement error and others either attenuate or amplify drug effects in real driving and must be considered as relevant to a test's predictive validity. Simply eliminating all of them, first, removes their normal mediating influence on the drug effect, and secondly, affects the subject's motivation to perform the test by making it appear "unreal". Controlling the test usually involves drastic simplification and restriction of response options. The desire in doing this is to isolate a particular driving skill and determine how it changes under the influence of drugs. However, drivers always apply numerous skills in parallel and series. Should one become deficient, they are often able to compensate in a number of ways to achieve a satisfactory level of proficiency. Thus the demonstration of some particular skill decrement in the laboratory in no way indicates that this would ultimately reduce driving safety in reality. Finally there are some skills that simply can not be measured in laboratory tests, at least not easily enough to make it a routine matter. The acquisition of any skill which depends upon automatic information processing requires practice over weeks or months. After learning to drive, subjects possess such skills in

abundance and one can only demonstrate how they vary with drug effects in the real task or a very close approximation thereof.

Profound drug impairment constituting an obvious traffic safety hazard could as easily be demonstrated in a laboratory performance test as anywhere else. But THC is not a profoundly impairing drug. It does affect automatic information processing, even after low doses, but not to any great extent after high doses. It apparently affects controlled information processing in a variety of laboratory tests, but not to the extent which is beyond the individual's ability to control when he is motivated and permitted to do so in real driving. In short, it would appear as if over-control in laboratory performance tests has resulted in a misimpression of THC's effect, incomplete in some respects and exaggerated in others. The actual driving tests may provide a more realistic impression of the drug's effects, albeit still incomplete and perhaps tending to minimize them with respect to more complex driving situations that come closer to "worst case".

The degree of experimental control also varied between driving tests in this series in ways affecting the subjects' motivation. This is illustrated by a comparison between the first and second driving study. The standard road tracking test was applied in both, first in the absence and then in the presence of other traffic. It was only during the former that disturbing observations of two individuals' attentional deficits caused the driving instructor to intervene. Driving in the presence of other traffic, subjects were always able to complete the rides without intervention. Lateral position control, an automatic process, did not change as a consequence of the absence or presence of other traffic. What did change was the subjects' motivation to focus attention, a controlled process. Motivation in the second study was very probably affected by recognition of the increased risk of the untoward consequences of wandering attention. This means that the intrinsic motivation produced by the reality of the test situation is an important mediator of THC's effects on performance.

Compensatory mechanisms help the driver under the influence of marijuana to maintain an effective level of performance but with an associated cost. If drivers compensate for THC's adverse effects by diminishing driving demands (e.g. by reducing speed and/or increasing headway), this will occur without a reduction in spare capacity. But if they increase effort as well (e.g. by focusing attention), it will occur at the expense of spare capacity. Less capacity would be left for simultaneously performing another task, such as conversing with passengers, using a car telephone, or handling emergency situations. The information processing capacity these situations demand may well go beyond the driver's spare capacity with the result of impaired and perhaps dangerous driving. Results of the present program show that THC increases the mental load of driving, as shown by increased effort ratings and reduced heart rate variability, and consequently reduces spare capacity. This corroborates results from previous simulator and closed-course studies that with reasonable consistency show an adverse THC effect on subsidiary task performance (Smiley, 1986). Further research is required to determine marijuana's effects on *actual* driving performance when the driver is simultaneously performing another task or suddenly confronted with a situation that requires a rapid adaptive response. The latter was occasionally encountered during the city driving test, but only after a low THC dose. The city driving test should therefore be repeated with subjects consuming higher THC doses.

Hazardous driving can also occur in situations that demand very little of the driver's information processing capacity. If the driving task is very monotonous and the demand is low, wandering attention may result in negligent monitoring with disastrous results. This is in fact what happened twice during the driving study on the closed road. After the highest THC dose,

one subject failed to shift attention from the prescribed task to an unexpected event (screwdriver on the road); another failed to anticipate a normal event (end of circuit). Though even sober experienced drivers may experience similar deficits, the fact that it happened twice after the highest THC dose, and never after a lower dose or placebo, strongly suggests that drivers under the influence of THC would be unusually susceptible to attentional deficits during prolonged and monotonous driving.

How do marijuana's effects on driving performance compare to those of alcohol? There are two sources from which one can draw to answer the question. Information can be directly obtained from studies comparing THC and alcohol effects in the same experiment; and, indirectly, from studies wherein alcohol's effects were assessed using the same methods as applied in the present THC studies. As mentioned in Chapter 1, most closed-course studies on THC also measured alcohol's effects (BACs between 0.04 and 0.10 g%). It was generally concluded that THC's effects were less than alcohol's, especially at BACs above 0.08 g%. The city driving study in the present program also compared the effects of modest doses of alcohol and THC. For doses administered in that study, alcohol produced the greater effects. Indirect evidence concerning the relative effects of THC and alcohol can be obtained from three studies. First, the alcohol calibration study by Louwerens *et al.* (1985, 1987) which resembled our first driving study in many respects. According to their empirical equation, THC's effects on SDLP were equal to or less than that of BAC=0.07 g%. More recently, studies by Riedel *et al.* (1989) and Ramaekers *et al.* (1992a) measured the effects of low doses of alcohol (BACs of 0.05 and 0.03 g% respectively) on SDLP. Both groups applied the standard test in the presence of other traffic, as in our second driving study, but on another highway. Mean SDLPs were respectively about 5.0 and 2.5 cm higher while driving after alcohol than placebo. The former elevation is greater than that produced by the highest THC dose in our study. The latter lies between the effects of 200 and 300 μg/kg doses, which were 1.8 and 2.9 cm respectively. There was some discrepancy between alcohol's effects on SDLP in the more recent studies and those predicted by the empirical equation: the former were higher than predicted. The discrepancy appears to be related to the difference between alcohol's effects on the ascending and descending phases of its pharmacokinetic profile. Louwerens measured alcohol's effects at the time when BAC was at the ascending but Riedel and Ramaekers measured them during the descending phase. Notwithstanding methodological differences among studies, both direct and indirect evidence converge on the conclusion that THC's effects after doses up to 300 μg/kg never exceed alcohol's at BACs of 0.08 g%.

How do marijuana's effects on driving performance compare to those of drugs other than alcohol? No direct comparisons have ever been made, but many studies employing the standard road tracking test were conducted for measuring other drugs' effects on SDLP during the last decade. The results from a few will be mentioned. Diazepam (Valium®) given for one week in a low therapeutic dose (5 mg, thrice daily) caused anxious patients to drive with a mean SDLP about 7 cm higher than their premedication baseline (Van Laar *et al.*, 1992). The same drug and dose given over the same period caused healthy volunteers to drive with a mean SDLP about 6 cm higher than placebo (Van Veggel and O'Hanlon, 1993). Lorazepam (Ativan®), another anxiolytic, given twice daily for one week in a 1.5 mg dose to healthy volunteers (Volkerts *et al.*, 1988) and a 2 mg dose to patients (Vermeeren *et al.*, 1993), produced an elevation of SDLP of about 10 cm in both cases. Amitriptyline (Elavil®), a widely prescribed antidepressant, given in a dose of 50 mg at night and 25 mg in the morning caused healthy volunteers to drive with a mean SDLP about 6 cm higher than placebo (Robbe *et al.*, 1989). Flurazepam (Dalmane®),

a hypnotic, was administered to insomniacs and its "hang-over" effects on SDLP were measured 10-11 hours after ingestion. A 15 mg dose of flurazepam elevated mean SDLP by about 4 cm; a 30 mg dose, 7 cm. Antihistamines also cause sedation and, consequently, impair road tracking performance. Triprolidine (Actifed®) increased SDLP by 3.5 cm after a single 5 mg dose (Riedel *et al.*, 1990); and, diphenhydramine 50 mg (Benadryl Kapseals®) increased SDLP by 4.5 cm (Ramaekers *et al.*, 1992b). This is not to say that all psychotropic drugs produce greater elevations of SDLP than THC. Many in the same and other experiments had less effect than THC did in our studies. These examples are merely cited to indicate that THC's effects as measured in the standard test were in no way unusual. In so far as its effects on SDLP are concerned, THC was just another moderately impairing drug.

The foregoing comparisons might be misleading. THC's effects differ qualitatively from many other drugs, especially alcohol. For example, subjects drive faster after drinking alcohol and slower after smoking marijuana (Hansteen *et al.*, 1976; Casswell, 1979; Peck *et al.*, 1986; Smiley *et al.*, 1987). Moreover, the simulator study by Ellingstad *et al.* (1973) showed that subjects under the influence of marijuana were less likely to engage in overtaking maneuvers, whereas those under the influence of alcohol showed the opposite tendency. Very importantly, our city driving study showed that drivers who drank alcohol over-estimated their performance quality whereas those who smoked marijuana under-estimated it. Perhaps as a consequence, the former invested no special effort for accomplishing the task whereas the latter did, and successfully. This evidence strongly suggests that alcohol encourages risky driving whereas THC encourages greater caution, at least in experiments. Another way THC seems to differ qualitatively from many other drugs is that the former's users seem better able to compensate for its adverse effects while driving under the influence. Weil *et al.* (1968) were among the earliest authors who mentioned the possibility that marijuana users can actively suppress the drug's adverse effects. They presumed that THC's effects were confined to higher cortical functions without any general stimulatory or depressive effect on lower brain centers. According to them, the relative absence of neurological, as opposed to psychiatric, symptoms in marijuana intoxication suggests this possibility. More recently, Moskowitz (1985) concluded that the variety of impairments found after marijuana smoking could not be explained by decrements in sensory or motor functions which led him to hypothesize that some important central cognitive process is impaired by THC, without saying what it is. Identification of THC's site of action would greatly enhance our understanding of the drug's psychopharmacological effects.

Epidemiological research has shown that THC is infrequently detected in the blood of fatally injured drivers as the only drug present. In most cases alcohol is also detected. The effects of the combination of THC and alcohol on actual driving performance have never been studied in the presence of other traffic. Closed-course studies have shown that the effects of both drugs, when taken in combination, are generally additive (Attwood *et al.*, 1981; Peck *et al.*, 1986). This may only be so for those behaviors that are similarly affected by both drugs given separately. Closer examination of the combined use is warranted in those driving situations where both drugs produce qualitatively different effects. It may well be so that alcohol reduces drivers' insight or motivation to the point where they would no longer attempt to compensate for the THC effect. As a result, the combined effects on drivers' performance could well be greater than the sum of either drug acting separately. There is therefore a great need for further research on marijuana and actual driving research, but now extended to the combination of marijuana and alcohol.

In summary, this program of research has shown that marijuana, when taken alone, produces a moderate degree of driving impairment which is related to the consumed THC dose. The impairment manifests itself mainly in the ability to maintain a steady lateral position on the road, but its magnitude is not exceptional in comparison with changes produced by many medicinal drugs and alcohol. Drivers under the influence of marijuana retain insight in their performance and will compensate where they can, for example, by slowing down or increasing effort. As a consequence, THC's adverse effects on driving performance appear relatively small. Still we can easily imagine situations where the influence of marijuana smoking might have an exceedingly dangerous effect; i.e., emergency situations which put high demands on the driver's information processing capacity, prolonged monotonous driving, and after THC has been taken with other drugs, especially alcohol. We therefore agree with Moskowitz' conclusion that "any situation in which safety both for self and others depends upon alertness and capability of control of man-machine interaction precludes the use of marihuana". However, the magnitude of marijuana's, relative to many other drugs', effects also justify Gieringer's (1988) conclusion that "marijuana impairment presents a real, but secondary, safety risk; and that alcohol is the leading drug-related accident risk factor". Of the many psychotropic drugs, licit and illicit, that are available and used by people who subsequently drive, marijuana may well be among the least harmful. Campaigns to discourage the use of marijuana by drivers are certainly warranted. But concentrating a campaign on marijuana alone may not be in proportion to the safety problem it causes.

DRUG PLASMA CONCENTRATIONS AND DRIVING PERFORMANCE

One of the program's objectives was to determine whether it is possible to predict driving impairment by plasma concentrations of THC and/or its metabolite, THC-COOH, in single samples. The answer is very clear: it is not. Plasma of drivers showing substantial impairment in these studies contained both high and low THC concentrations; and, drivers with high plasma concentrations showed substantial, but also no impairment, or even some improvement. The first driving study showed that impairment in the road tracking test was nearly the same in the first and second test, executed between 40-60 and 100-120 minutes after initiation of smoking, respectively. Plasma concentrations of THC and THC-COOH, however, were not the same during the tests: both were lower during the second than the first. The same pattern was found for ratings of perceived "high". It has been said that behavioral signs of intoxication, though small, outlast physiological and subjective reactions to THC (Reeve *et al.*, 1983; Yesavage *et al.*, 1985). To examine this hypothesis, future research should extend actual driving performance measurements to 4, 8, 16 and 24 hours after smoking. If driving impairment still occurs after THC disappears from plasma, it could mean that previous epidemiological research has underestimated the proportion of drivers who were driving under the influence of marijuana at the times their accidents occurred.

Mean speed was the only measure of driving performance that was even moderately related to plasma concentrations of the drug. Subjects with higher THC concentrations in plasma drove slower in the standard road tracking test (correlations varying from $r=-.18$ to $r=-.72$ between conditions). This effect might have been even more pronounced if the subjects had not been instructed to drive at a particular speed, and if they had had no feedback from the speedometer.

CONCLUSIONS

The major conclusions from the present program are summarized as follows:

- Current users of marijuana prefer THC doses of about 300 μg/kg to achieve their desired "high".

- It is possible to safely study the effects of marijuana on driving on highways or city streets in the presence of other traffic.

- Marijuana smoking impairs fundamental road tracking ability with the degree of impairment increasing as a function of the consumed THC dose.

- Marijuana smoking which delivers THC up to a 300 μg/kg dose slightly impairs the ability to maintain a constant headway while following another car.

- A low THC dose (100 μg/kg) does not impair driving ability in urban traffic to the same extent as a blood alcohol concentration (BAC) of 0.04 g%.

- Drivers under the influence of marijuana tend to over-estimate the adverse effects of the drug on their driving quality and compensate when they can; e.g. by increasing effort to accomplish the task, increasing headway or slowing down, or a combination of these.

- Drivers under the influence of alcohol tend to under-estimate the adverse effects of the drug on their driving quality and do not invest compensatory effort.

- The maximum road tracking impairment after the highest THC dose (300 μg/kg) was within a range of effects produced by many commonly used medicinal drugs and less than that associated with a blood alcohol concentration (BAC) of 0.08 g% in previous studies employing the same test.

- It is not possible to conclude anything about a driver's impairment on the basis of his/her plasma concentrations of THC and THC-COOH determined in a single sample.

RECOMMENDATIONS FOR FUTURE RESEARCH

The recommendations for future research are summarized as follows:

- Future studies on marijuana's effects on driving performance should include the THC dose that currents users of marijuana prefer to achieve their desired "high", i.e. 300 μg/kg.
- Subjects in future studies should be familiarized with the potency of the material providing THC before the beginning of tests designed to measure its effects on performance.
- Future research determining marijuana users' preferred dose should involve administering THC in different marijuana preparations that encompass a wide range of potencies.
- Further research is required for determining marijuana's effects on actual driving performance in the presence of other traffic when the driver is simultaneously performing another task or suddenly confronted with a situation that requires a rapid adaptive response.
- The city driving test should be repeated with subjects consuming THC doses over 100 μg/kg.
- Further research on marijuana and actual driving research should be extended to include combinations of marijuana and alcohol.
- Future research should extend actual driving performance measurements to 4, 8, 16 and 24 hours after smoking.

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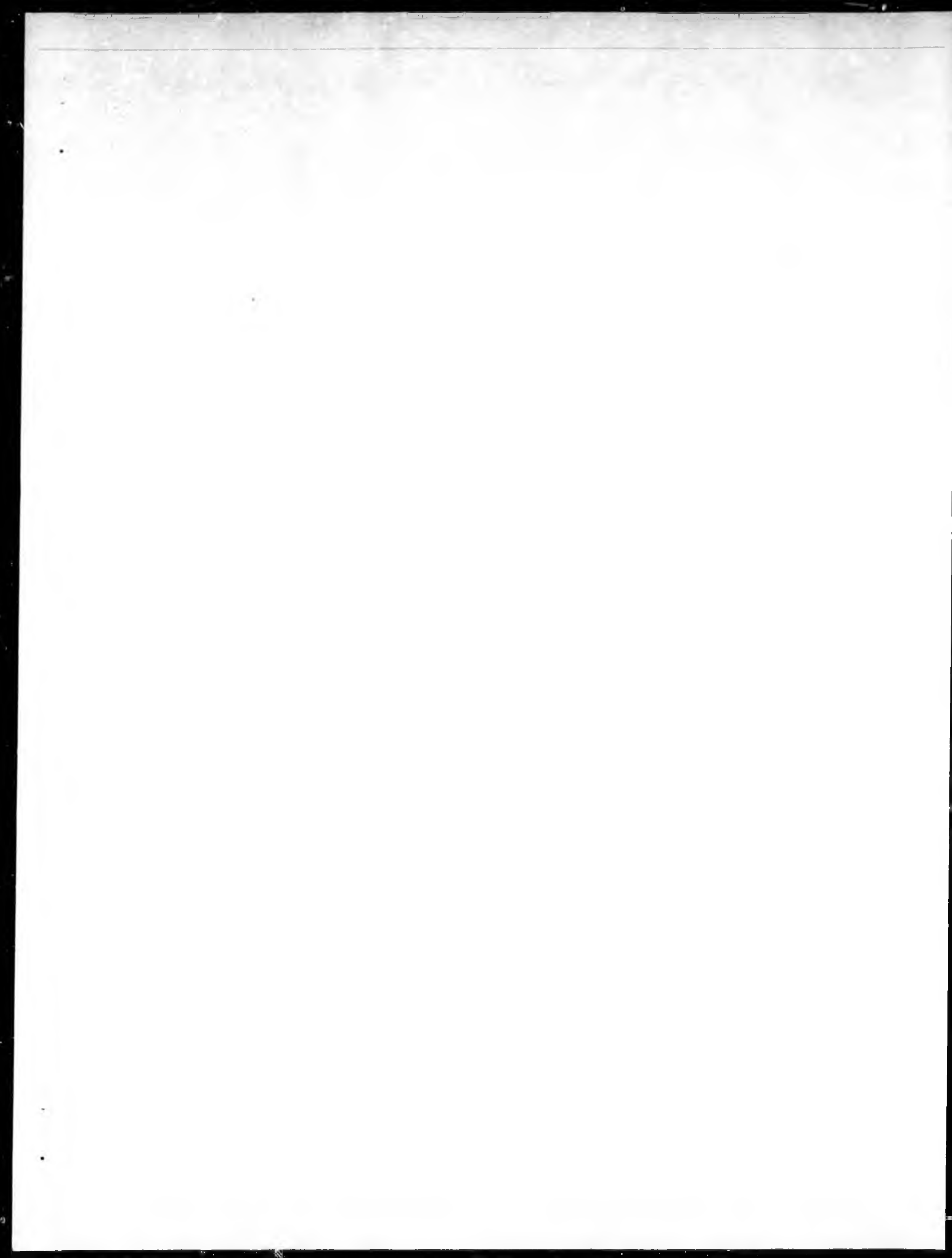
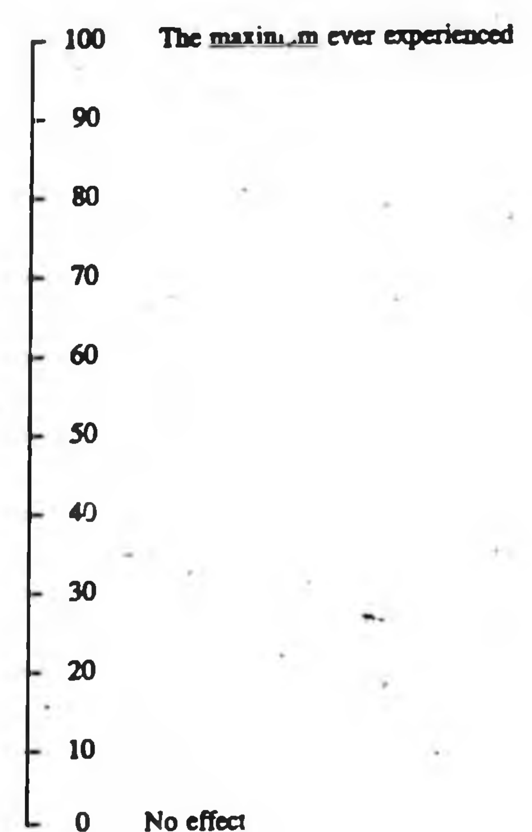


APPENDIX A

Questionnaires

Subjective Intoxication and Willingness to Drive Questionnaires

Please rate your feeling of "high" (or "drunkness" after drinking alcohol) as a percentage of the maximum ever experienced.



Would you attempt to drive for a set distance if the reasons were:

A. unimportant though gratifying, such as for transporting a friend to another party Y / N

B. important but avoidable, such as for transporting a mildly sick friend home when he would otherwise have to call a taxi Y / N

C. urgent, such as transporting a severely sick infant to the hospital Y / N

Mood Rating Scale (Bond and Lader, 1974)

This form is a mood rating scale and the intention is to measure your feelings as they are at this moment. The instructions are given below. Please read them carefully and proceed. Have you any questions?

1. Please rate the way you fee in terms of the dimensions given below.
2. Regard the line as presenting the full range of each dimension.
3. Rate your feelings as they are at the moment.
4. Mark clearly and perpendicularly across each line.

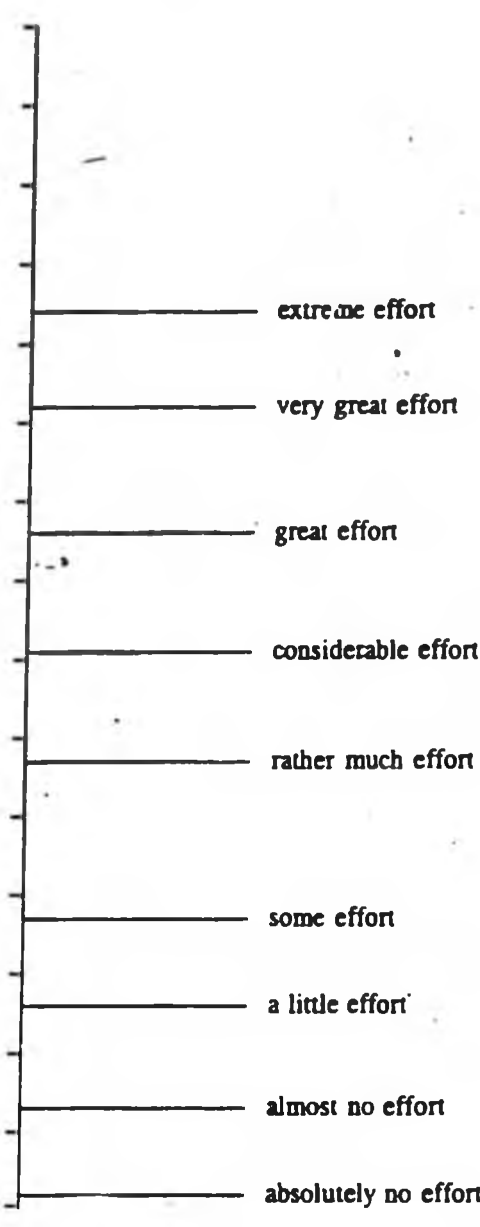
Alert	______________________________	Drowsy (1)
Calm	______________________________	Excited (2)
Strong	______________________________	Feeble (3)
Muzzy	______________________________	Clear headed (4)
Well-coordinated	______________________________	Clumsy (5)
Lethargic	______________________________	Energetic (6)
Contented	______________________________	Discontented (7)
Troubled	______________________________	Tranquil (8)
Mentally slow	______________________________	Quick witted (9)
Tense	______________________________	Relaxed (10)
Attentive	______________________________	Dreamy (11)
Incompetent	______________________________	Proficient (12)
Happy	______________________________	Sad (13)
Antagonistic	______________________________	Amicable (14)
Interested	______________________________	Bored (15)
Withdrawn	______________________________	Sociable (16)

Do you think you received placebo or active drug ? Placebo / Active

Scores on these scales were grouped to form 3 cluster scores for measuring the corresponding factors: alertness (1,3,4,5,6,9,11,12,15), contentedness (7,8,13,14,16) and calmness (2,10).

Perceived Effort Scale (Zijlstra and Van Doorn, 1985)

Please rate the effort made while performing the driving test.



Perceived Driving Quality Scale (translated from Dutch)

Please rate the quality of your driving in the test you just finished.

I drove exceptionally well

I drove normally

I drove exceptionally poorly

Translation of the Royal Dutch Tourist Association's original "Verslag Rijvaardigheidsrit".

The following categories did not apply to the driving test and were dropped from the scoring sheet: "Condition of the Car" (Category I.01), "Railway Level Crossing" (Category III.16), and several Special Maneuvers (Categories V.19 to V.26, V.28 to V.30).

I VEHICLE CHECKS

02 Preparing to drive off

02-1 Passing in front of car and observing traffic
02-2 Clear view and clean windows
02-3 Position of driver's seat
02-4 Instrument check
02-5 Starting the engine
02-6 Use of safety belt(s)
02-7 Checking mirrors
02-8 Proper use of lights

03 Driving off

03-1 Checking position of hand-brake
03-2 Looking ahead, to the side and to the rear before driving off
03-3 Selecting correct position in traffic lane
03-4 Adapting speed immediately to traffic flow
03-5 Re-checking mirrors

II HANDLING OF VEHICLE

04 Manner of sitting behind the wheel, and steering

04-1 Manner of sitting behind the wheel when driving
04-2 Position of hands on the wheel
04-3 Steering through curves
04-4 Position of head whilst talking to passengers

05 Handling of controls

05-1 Accelerator
05-2 Foot-brake
05-3 Hand-brake
05-4 Clutch-pedal
05-5 Gear-lever

06 Speed control, deceleration and stopping

06-1 Choice of speed in view of circumstances
06-2 Use of accelerator and brake
06-3 Use of mirrors before and during deceleration
06-4 Indication of deceleration in good time by use of stop-lights
06-5 Correct sequence of maneuvers for deceleration
06-6 Declutch at the correct stage and put gear-lever in neutral
06-7 Come to a stop smoothly
06-8 Clutch not depressed whilst waiting

07 Taking corners

07-1 Safe starting speed
07-2 Selecting correct gear before entering corner
07-3 Without slipping clutch or foot on the clutch-pedal
07-4 No braking in corner
07-5 No free-wheeling
07-6 Correct driving line

III ACTION IN TRAFFIC

08 Driving straight

08-1 Keeping to the right
08-2 Adapting speed to that of other similar traffic
08-3 Looking into side streets
08-4 Taking into account blind spots caused by car design and passengers
08-5 Taking into account limitation of mirrors
08-6 Keeping distance from traffic in front
08-7 Driving in offset position with regard to preceding vehicle
08-8 Pedestrian crossings
08-9 Watching for pedestrians crossing the road (at other places than at zebra crossings)

09 Behavior at or near crossroads

09-1 Judging the situation beforehand
09-2 Behavior at the approach to traffic lights
09-3 Driving in traffic lanes marked with arrows, and according to other indications on road surface
09-4 Taking position in traffic lanes marked with arrows
09-5 Bicycle and bus lanes
09-6 Consideration of other drivers
09-7 Complying with priority rules

10 Right-hand turn

10-1 Taking position in good time when filtering (selection of correct lane)
10-2 Looking behind and to the right
10-3 Switching on direction indicators
10-4 Positive filtering and in good time, adapting speed
10-5 Looking over right shoulder
10-6 Not impeding traffic that continues straight ahead
10-7 Final check
10-8 Taking corner as closely as possible

11 Left-hand turn

11-1 Taking position in good time when filtering (selection of correct lane)
11-2 Looking to the rear, rear left and left
11-3 Switching on direction indicators
11-4 Positive filtering and in good time, adapting speed
11-5 Not impeding traffic that continues straight ahead
11-6 Correct timing of wheel turning and position on wide crossings
11-7 Final check
11-8 Taking a sufficiently wide corner

12 Overtaking

12-1 Judging traffic flow correctly and in time (oncoming, behind and to the left)
12-2 Switching on direction indicators
12-3 Moving out smoothly and in good time
12-4 Canceling direction indicators
12-5 Observing vehicle that will be overtaken
12-6 Overtaking quickly and safely
12-7 Keeping well clear of overtaken cyclists
12-8 Reverting to the right
12-9 Overtaking on the right when permitted

13 Traffic lane technique

13-1 Keeping well within lane
13-2 Checking traffic before leaving lane
13-3 Changing traffic lanes one at a time
13-4 Driving straight, avoiding minor deviations
13-5 Driving in lines abreast
13-6 Overhead traffic lane control

14 Driving on roundabouts

14-1 Observation (dividing attention)
14-2 Using direction indicators during the entire maneuver
14-3 Correct positioning for turning in good time
14-4 Selecting and driving in the correct traffic lane
14-5 Weaving out of the traffic flow correctly and in good time

15 Driving on highways

15-1 Using acceleration lane, observing traffic on highway
15-2 Choice of speed and lane
15-3 Correct distance to vehicle in front
15-4 Stopping and parking in emergency stopping lane (if permitted)
15-5 Leaving emergency stopping lane
15-6 Use of lay-bys
15-7 Behavior at approach to intersections
15-8 Use of deceleration lane

IV OBSERVATION AND UNDERSTANDING OF TRAFFIC

17 Observation

17-1 Observation technique
17-2 Observation of overall picture of traffic, road and surroundings
17-3 Conscious observation of traffic signs
17-4 Use of direction signs

18 Understanding of traffic

18-1 Anticipation
18-2 Making allowance for any traffic situations that may occur
18-3 Reactions to observations made
18-4 Strategy

Proceeding Through Intersection
Speed (S)
Low Traffic Density

The driver will reduce speed before entering a four-way blind uncontrolled intersection.

Correct Response

1. Brakes gently, to 10 to 15 mph, one car length before the corner and continues to cover brake pedal until the traffic checks have been completed.
2. Does not stop or go slowly once into the intersection.
3. Accelerates through the intersection.

Normal Transit Between Intersections
Speed Control (S)
High-medium or Low Traffic Density

The driver will select the appropriate speed for conditions, be[illegible] guided by speed limit signs, laws, and traffic conditions.

Correct Response

1. Does not exceed the legal speed limit at any time between the beginning of the (S) coding and the start of coding the next maneuver.
2. Does not exceed the speed of the traffic flow by more than 4 mph.
3. Does not fall below the speed limit by more than 4 mph unless traffic or potential hazards require it.

Following Distance (F)
High Traffic Density

The driver must maintain at least a 2-second interval from traffic ahead at all times.

Correct Response

Unless there is a significant amount of traffic, there is no opportunity to observe this. If the situation is favorable, there is ample opportunity to observe following distance in normal transit on high density streets. Following distance can also be coded if the driver comes up on slow traffic or traffic stopped at an intersection. Interrupt assessment of following distance to observe mirror check before driver slows down, but then return to following distance as he comes up on traffic. The driver must anticipate slowing of traffic ahead. He must brake gradually enough that he does not throw passengers forward. He must maintain a 2-second distance at all times. Following distance (F) is necessarily indicated on the scoring sheet at specific loca[illegible]ons but refers to the entire segment of the route between two turns. If two F's occur, attempt to code it twice in that segment. Do not code following distances of more than four seconds. If it cannot be coded, underline the F's.

Stop Sign
Limit Line (LL)

Stop sign for the driver's vehicle, but none for cross traffic. The driver must stop behind the limit line (and then continue when traffic permits). If there is no physical limit line, the stop should be made behind a line connecting the two near corners of the street the vehicle is on. The vehicle must not enter the intersecting street.

Correct Response

1. Stops behind limit line.

Mirror Check (M)

The driver will check rear view mirror before any speed reduction or lateral movement and when approaching a traffic light. The coder must attend to the mirror check as soon as the previous coding has been completed, since driver may check early and, if there is no traffic, may not need to repeat.

Gap Acceptance (G)

Gap acceptance is coded on some turns where path and speed on the turn are also called for. The novice should decline the smallest gaps that an experienced driver might accept but should not wait when there is ample time.

Correct Response

1. Accepts a 10-second gap; does not accept a gap smaller than 9 seconds*. The coder should check his judgment by counting seconds (1001, 1002, etc.). If driver accepts too small a gap, code it as X. (Examiner may also code Hazard, X, or Instructor Control, I.)
2. Gap is also wrong if there is no traffic and driver does not move promptly.
3. If there is no traffic and the driver moves promptly, underline G (i.e., a judgment cannot be made).

Pre-operation (Pre-op)

The driver will perform these pre-operation checks before starting the engine:

Correct Response

1. Adjusts seat.
2. Fastens seat belt and shoulder harness.
3. Checks and insures that all passengers are also buckled up.
4. Adjusts both mirrors correctly. If driver must make head adjustments, or adjusts mirrors later, then go back and mark Pre-op wrong.

Shut Down (S.D.)

The driver will perform these shut-down checks:

Correct Response

1. Puts gear selector lever in Park (or gear shift in neutral).
2. Turns ignition off.
3. Sets parking brake.

Y Turnabout
Low Density Traffic (residential)
Location (L)

Driver will chose a safe location for the Y turnabout (three-point turnabout).

Correct Response

1. Chooses a point at least 200 feet from any intersection.
2. Does not start a Y turnabout when pedestrians or vehicles are nearby.
3. If there is no safe place to turn and the driver traverses the whole block without attempting to turn, underline Location (L) and Backing (B). (The instructor will tell the driver how to get back on the route.)

Backing (B)

Driver will look left, right, and back before moving the car in reverse.

Correct Response

1. Looks left and right before backing.
2. Turns head around and looks straight back over right shoulder when moving the car in reverse. Failure to be looking straight back at all times that the car is moving backwards is disqualifying, except for brief checks left, right, and forward.

* Experience drivers may accept smaller gaps, but must not throw passengers off balance nor clear on-coming car by less than 4 seconds.

Right Turn Path (P) Low Density Traffic	The driver must select a path that will allow him to start his turn two to three feet from the curb and finish his turn in the middle of the right half of the street.
Correct Response	1. Begins turning when vehicle is two to three feet from the curb and front wheels are even with the beginning of the bend of the curb. 2. Turns steering wheel smoothly and follows a smooth curve to the center of the right lane on the new street.
Right Turn Speed Control (S) High and Medium Density Traffic	The driver will decelerate smoothly before the turn and accelerate smoothly when clearing the intersection.
Correct Response	1. Decelerates smoothly before the turn to 8-10 mph, or less if traffic warrants. 2. Accelerates smoothly two-thirds of the way through the turn, increasing speed quickly enough so that following traffic in new path would not have to slow down or change lanes for driver's vehicle. (The coder must turn around and observe traffic.) 3. Adjusts speed to flow of traffic. 4. Accelerates promptly; if driver hesitates or starts and stops without cause, speed is coded X.
Right Turn Speed Control (S) Low Density Traffic	Driver must control his speed by braking before the turn and resuming normal speed after completing his turn.
Correct Response	1. Before one car length from the corner, brakes to a speed of 8 to 10 mph. 2. Accelerates smoothly as soon as driver is two-thirds of the way through the turn. 3. Accelerates promptly; if driver hesitates or starts and stops without cause, speed is coded X.
Right Turn Observing (O) High, Medium & Low Density Traffic	Driver will scan the intersection for potential conflicts with vehicles and pedestrians prior to initiating turn.
Correct Response	1. Turns head to the right and looks for pedestrians or vehicles that could block intended path. If a pedestrian is on right near corner, head movement must indicate check of the spot (75° head movement). 2. Turns head to the left and looks for approaching cross traffic. 3. Turns head to the right again and looks at turn path just prior to the execution of the turn. Order of checks is important. (Note: forward scan will usually not be noticeable.) 4. Completes these checks quickly and does not look for more than 2 seconds (count of 1001, 1002) at any spot unless there is traffic and the driver's vehicle is stopped.

Lane Change Path (P) High or Medium Density Traffic Correct Response	The driver must maintain a straight lane position during scanning procedures (mirrors and blind spot). He must signal before he moves and cancel after the move is completed. The driver then steers smoothly with a gradual angular movement into the middle of the new lane without swerving to either side of the lane. 1. Maintains straight path while scanning. 2. Signals before the lane change. 3. Steers smoothly with gradual angular movement. 4. Straightens vehicle in new lane. 5. Cancels a signal.
Lane Change Speed (S) High or Medium Density Traffic Correct Response	Driver will decrease, increase, or maintain speed according to traffic conditions. 1. If flow of traffic of new lane is faster, increases speed when entering new lane. 2. If flow of traffic of new lane is slower, decreases speed when entering new lane. 3. If flow of traffic of new lane is of equal speed, maintains speed when entering new lane.
Lane Change Observing Traffic (O) High or Medium Density Traffic	The driver will scan one or both mirrors, as appropriate, and check blind spot before changing lanes. He will observe traffic ahead in both present and intended lanes for possible slowing. Lane change (right or left)) is necessarily indicated on the scoring sheet at specific locations but refers to the entire segment of the route between two turns. If two lane change arrows occur within a segment (between turns), both of them should be coded whenever they occur. Ignore aborted lane changes. (If they are dangerous, the examiner will code hazard, and mark it wrong.)
Correct Response	1. Checks traffic ahead in present and intended lanes. 2. Checks rear view mirror. 3. Checks outside mirror for left hand change. 4. Checks blind spot by turning the head briefly (appr. 1 second: if the coder counts 1002, it is too long) in the direction of the lane change and then before steering into the new lane, again checks forward traffic. Driver must not look through back window when checking blind spot. If he does, check is wrong (X).
Proceeding Through Intersection Observing Traffic (O) Correct Response	The driver will scan the intersection before entering. 1. The driver will look left and right before entering a four-way controlled intersection. 2. At a four-way uncontrolled blind intersection, the driver will look left and right before entering the intersection. If blind at that point for less than 200 yards, checks left again. 3. At a blind tee intersection, the driver will look briefly in the direction of the adjoining street. 4. For all checks at intersections, the driver will not look in any direction for more than 2 seconds (count of 1001, 1002) at any spot unless there is traffic and the driver's vehicle is stopped.

Maneuvers in Molecular Approach (from Jones, 1978).

Left Turn
Path (P)
High, medium or low traffic density.

The driver will follow a standard path. A standard path runs from the center of the left-most lane of the original street to the center of the left-most lane of the intersecting street*. The turn must commence at a point one-third to one-half of the way into the intersection. The path passes just to the left of the center of the intersection. If the light is red, the driver must stop clearly behind the crosswalk line.

Correct Response

1. Enters intersection in the center of the left-most lane of a 4 (or more) lane street, or center of lane if single lane in each direction, and remains in the center until turning begins.
2. Begins turning when one-third to one-half of the way into the intersection.
3. If the car must stop for oncoming traffic in the intersection, the wheels must remain straight until the turn is started. (After stop, if vision is blocked by a left-turning truck, the driver may move forward into the turn but if he enters the oncoming travel lane and forces vehicles to compensate, examiner will score Hazard or Instructor Control and coder should underline P.)
4. Passes just to left of center of the intersection.
5. Completes turn in center of the left-most lane of intersecting street*. (If that lane is blocked or otherwise inaccessible, for example, a roadwork crew or a disabled vehicle, and the driver selects another lane, the examiner will code as Hazard or Instructor Control (see Examiner's Manual) and coder should underline P.)
6. Stops well behind nearest crosswalk line if light is red.

Left Turn
Speed (S)
High and Medium Density Traffic

The driver will decelerate smoothly before the turn and accelerate smoothly when clearing the intersection. Failure to accelerate promptly is a frequent error of novice drivers.

Correct Response

1. Decelerates smoothly, coming to a stop or near stop if there is traffic. At no time should the tires squeal or the passengers be thrown.
2. Accelerates smoothly, soon after he passes the one-third mark in the turn, steadily increasing to traffic speed.
3. Adjusts speed so that vehicle does not interfere with oncoming traffic.
4. Accelerates promptly; if driver hesitates or starts and stops without cause, speed is coded X.

Left Turn
Speed (S)
Low Density Traffic

The driver will control his speed before the turn by braking to 10-12 mph one car length from the corner. He will accelerate smoothly two-thirds of the way through the turn. (Driver must approach between 20 and 25 mph).

Correct Response

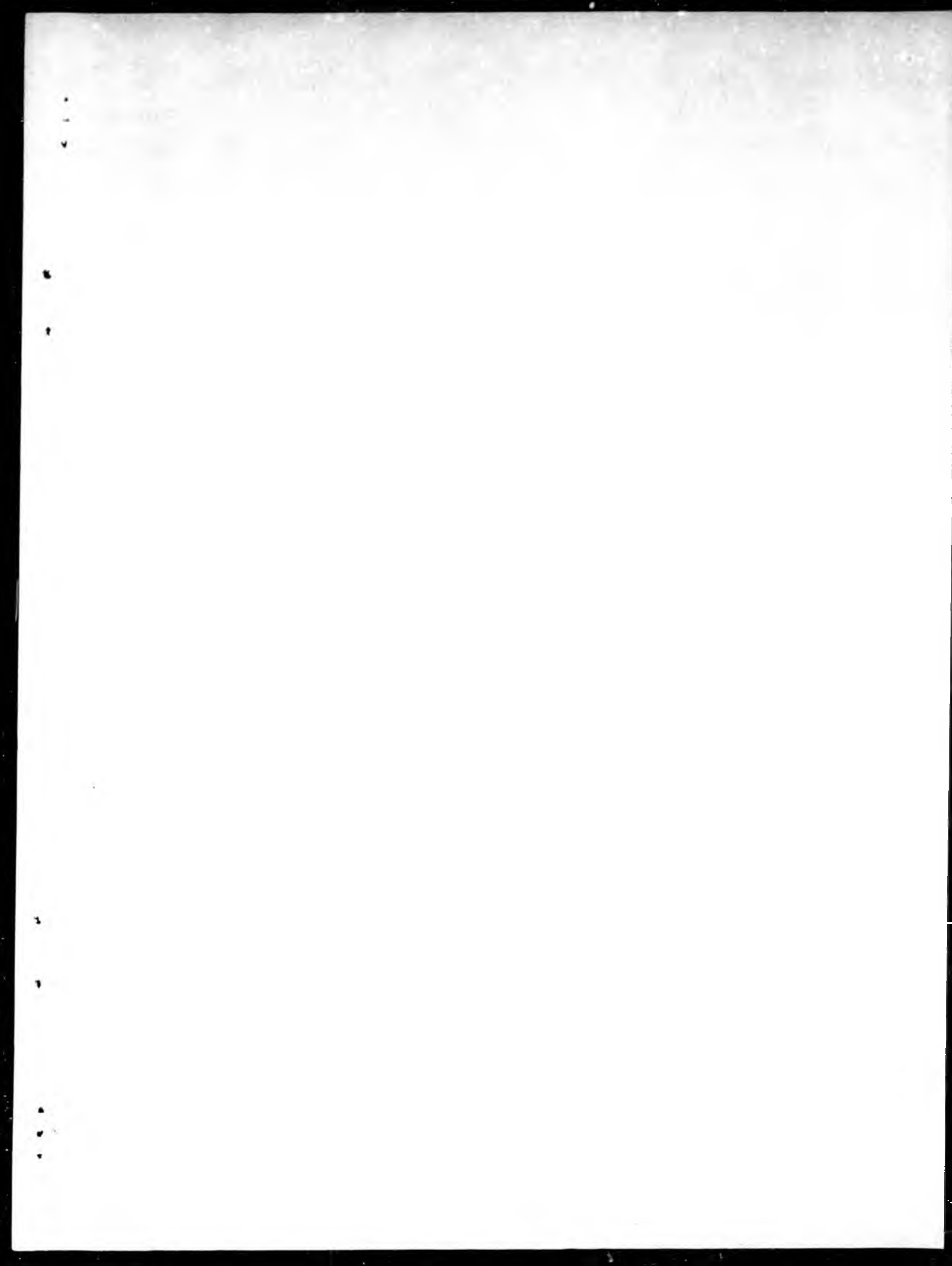
1. Before the turn, brakes to 10-12 mph.
2. Two-thirds of the way through the turn, accelerates smoothly out of the turn.
3. Accelerates promptly; if driver hesitates or starts and stops without cause, speed is coded X.

* For experienced drivers, it is acceptable to end in any open lane if it is safe to do so. This is not acceptable for novice drivers.

V SPECIAL MANEUVERS

27 Turning

27-1 Stopping at the correct place
27-2 Driving slowly, while turning steering wheel rapidly; no use of steering wheel while stopped
27-3 Looking alongside the car when approaching the kerb
27-4 Observing traffic during the entire maneuver



National Library of Medicine MEDLINE Database

TITL: Marijuana use and depression.

AUTH: Green B E; Ritter C

ORGA: Department of Socic ogy, Ohio State University, Columbus 43210, USA. green.446@osu.edu

PUB TYPE: Journal Article.

CITE: *J Health Soc Behav. 2000 Mar; 41 (1): 40-9.*

LANG: ENG; English

ABST: The primary goal of this study is to examine the association between marijuana use and adult depressive symptomatology. The key independent variables examined are age of marijuana initiation, frequency of current marijuana use, the use of other licit and illicit drugs, and whether marijuana was used to cope with problems. The relationships among these variables are assessed using data from the Young Men and Drugs Survey (n = 1,941), a nationally representative sample of men from the 1944-1954 birth cohort. Results show that early marijuana initiation appears to be weakly associated with increased depression in adulthood. This effect, however, is mediated by educational attainment, employment status, marital status, and other drug use, notably alcohol and tobacco use. Adult frequency of marijuana use is not significantly associated with increased depression in adulthood. Finally, marijuana users who use the drug to cope with problems are more depressed than those who do not use to cope with problems.

MJTR: Depression, complications. Marijuana Smoking, adverse effects.

MNTR: Adaptation, Psychological. Adult. Depression, psychology. Humans. Male. Research Support, U.S. Gov't, P.H.S..

GEOT: UNITED STATES

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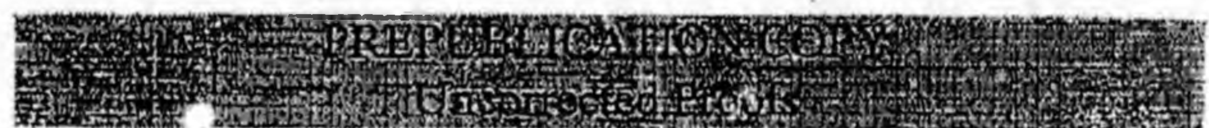

MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE

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Division of Neuroscience and Behavioral Health

INSTITUTE OF MEDICINE

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Preface

Why study the medical value of marijuana now? What circumstances provoked this analysis and report? There have been a variety of influences since the IOM Report of 1982. First, advocates of personal choice with a growing distrust of scientific medicine sought alternatives congruent with their values about health and life. This view was expressed at the ballot box in recent state referenda. Proponents claimed their own "scientific evidence" of marijuana's safety and effectiveness. Others, distressed by the societal ravages of drug abuse, especially among young people, view legalized medical marijuana as a subterfuge enabling liberalization, the potential "gateway" to even more harmful substance abuse. Meanwhile, there have been remarkable and accelerating advances of relevant knowledge in molecular and behavioral neuroscience, in particular newly elaborated systems of transmitters, receptors, and antagonists—all illuminating the physiological effects of cannabinoids, both those found in nature and those normally found in the brain. (Cannabinoids are the group of compounds related to THC, the primary psychoactive ingredient in marijuana.) The new science could inform policies responding to the public divide.

In January 1997, the White House Office of National Drug Control Policy (ONDCP) asked the Institute of Medicine to conduct a review of the scientific evidence to assess the potential health benefits and risks of marijuana and its constituent cannabinoids. That review began in August 1997 and culminates with this report.

Information for this study was gathered through analysis of the relevant scientific literature, scientific workshops, site visits to cannabis buyers' clubs and HIV/AIDS clinics, and extensive consultation with biomedical and social scientists. Three 2-day workshops—in Irvine, California; New Orleans, Louisiana; and Washington, DC—were open to the public and included scientific presentations and also reports, mostly from patients and their families, about their experiences with and perspectives on the medical use of marijuana. Scientific experts in various fields were selected to talk about the latest research on marijuana, cannabinoids, and related topics. In addition, advocates for and against the medical use of marijuana were invited to present scientific evidence in support of their positions. Finally, the Institute of Medicine appointed a panel of nine experts to advise the study team on technical issues.

Public outreach included setting up a Web site that provided information about the study and asked for input from the public. The Web site was open for

comments from November 1997 until November 1998. Some 130 organizations were invited to participate in the public workshops. Many people in the organizations—particularly those opposed to the medical use of marijuana—felt that a public forum was not conducive to expressing their views; they were invited to communicate their opinions (and reasons for holding them) by mail or telephone. As a result, roughly equal numbers of persons and organizations opposed to and in favor of the medical use of marijuana were heard from.

Advances in cannabinoid science of the last 16 years have given rise to a wealth of new opportunities for the development of medically useful cannabinoid-based drugs. The accumulated data suggest a variety of indications, particularly for pain relief, nausea, and appetite stimulation. For patients, such as those with AIDS or undergoing chemotherapy, who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad spectrum relief not found in any other single medication.

Marijuana is not a completely benign substance. It is a powerful drug with a variety of effects. However, the harmful effects to individuals from the perspective of possible medical use of marijuana are not necessarily the same as the harmful physical effects of drug abuse.

Although marijuana smoke delivers THC and other cannabinoids to the body, it also delivers harmful substances, including most of those found in tobacco smoke. In addition, plants contain a variable mixture of biologically-active compounds and cannot be expected to provide a precisely defined drug effect. For those reasons, the report concludes that the future of cannabinoid drugs lies not in smoked marijuana, but in chemically-defined drugs that act on the cannabinoid systems that are a natural component of human physiology. Until such drugs can be developed and made available for medical use, the report recommends interim solutions.

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EXECUTIVE SUMMARY

Public opinion on the medical value of marijuana has been sharply divided. Some dismiss medical marijuana as a hoax that exploits our natural compassion for the sick; others claim it is a uniquely soothing medicine that has been withheld from patients through regulations based on false claims. Proponents of both views cite 'scientific evidence' to support their views and have expressed those views at the ballot box in recent state elections. In January 1997, the White House Office of National Drug Control Policy (ONDCP) asked the Institute of Medicine to conduct a review of the scientific evidence to assess the potential health benefits and risks of marijuana and its constituent cannabinoids (see box: *Statement of Task*). That review began in August 1997 and culminates with this report.

The ONDCP request came in the wake of state "medical marijuana" initiatives. In November 1996, voters in California and Arizona passed referenda designed to permit the use of marijuana as medicine. Although Arizona's referendum was invalidated five months later, the referenda galvanized a national response. In November 1998, voters in six states (Alaska, Arizona, Colorado, Nevada, Oregon, and Washington) passed ballot initiatives in support of medical marijuana. (The Colorado vote will not count, however, because after the vote was taken a court ruling determined there had not been enough valid signatures to place the initiative on the ballot.)

Can marijuana relieve health problems? Is it safe for medical use? Those straightforward questions are embedded in a web of social concerns, most of which lie outside the scope of this report. Controversies concerning the nonmedical use of marijuana spill over onto the medical marijuana debate and obscure the real state of scientific knowledge. In contrast with the many disagreements bearing on social issues, the study team found substantial consensus among experts in the relevant disciplines on the scientific evidence about potential medical uses of marijuana.

This report summarizes and analyzes what is known about the medical use of marijuana; it emphasizes evidence-based medicine (derived from knowledge and experience informed by rigorous scientific analysis), as opposed to belief-based medicine (derived from judgment, intuition, and beliefs untested by rigorous science).

Throughout this report, *marijuana* refers to unpurified plant substances, including leaves or flower tops whether consumed by ingestion or smoking. References to "the effects of marijuana" should be understood to include the composite effects of its various components; that is, the effects of THC, the primary psychoactive ingredient in marijuana, are included among its effects, but not all the effects of marijuana are necessarily due to THC. *Cannabinoids* are the group of compounds related to THC, whether found in the marijuana plant, in animals, or synthesized in chemistry laboratories.

EXECUTIVE SUMMARY

Three focal concerns in evaluating the medical use of marijuan...

- Evaluation of the effects of isolated cannabinoids.
- Evaluation of the health risks associated with the medical use of marijuana.
- Evaluation of the efficacy of marijuana.

EFFECTS OF ISOLATED CANNABINOIDS

Cannabinoid Biology

Much has been learned since a 1982 IOM *Marijuana and Health* report. Although it was clear then that most of the effects of marijuana were due to its actions on the brain, there was little information about how THC acted on brain cells (neurons), which cells were affected by THC, or even what general areas of the brain were most affected by THC. Additionally, too little was known about cannabinoid physiology to offer any scientific insights into the harmful or therapeutic effects of marijuana. That all changed with the identification and characterization of cannabinoid receptors in the 1980s and 1990s. During the last 16 years, science has advanced greatly and can tell us much more about the potential medical benefits of cannabinoids.

CONCLUSION: At this point, our knowledge about the biology of marijuana and cannabinoids allows us to make some general conclusions:

- Cannabinoids likely have a natural role in pain modulation, control of movement, and memory.
- The natural role of cannabinoids in immune systems is likely multifaceted and remains unclear.
- The brain develops tolerance to cannabinoids.
- Animal research demonstrates the potential for dependence, but this potential is observed under a narrower range of conditions than with benzodiazepines, opiates, cocaine, or nicotine.
- Withdrawal symptoms can be observed in animals, but appear to be mild compared to opiates or benzodiazepines, such as diazepam (Valium®).

CONCLUSION: The different cannabinoid receptor types found in the body appear to play different roles in normal human physiology. In addition, some effects of cannabinoids appear to be independent of those receptors. The variety of mechanisms through which cannabinoids can influence human physiology underlies the variety of potential therapeutic uses for drugs that might act selectively on different cannabinoid systems.

RECOMMENDATION 1: Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body. Because different cannabinoids appear to have different effects, cannabinoid research should include, but not be restricted to, effects attributable to THC alone.

Efficacy Of Cannabinoid Drugs

The accumulated data indicate a potential therapeutic value for cannabinoid drugs, particularly for symptoms such as pain relief, control of nausea and vomiting, and appetite stimulation. The therapeutic effects of cannabinoids are best established for THC, which is generally one of the two most abundant of the cannabinoids in marijuana. (Cannabidiol, the precursor of THC, is generally the other most abundant cannabinoid.)

The effects of cannabinoids on the symptoms studied are generally modest, and in most cases, there are more effective medications. However, people vary in their responses to medications and there will likely always be a subpopulation of patients who do not respond well to other medications. The combination of cannabinoid drug effects (anxiety reduction, appetite stimulation, nausea reduction, and pain relief) suggests that cannabinoids would be moderately well suited for certain conditions, such as chemotherapy-induced nausea and vomiting and AIDS wasting.

Defined substances, such as purified cannabinoid compounds, are preferable to plant products which are of variable and uncertain composition. Use of defined cannabinoids permits a more precise evaluation of their effects, whether in combination or alone. Medications that can maximize the desired effects of cannabinoids and minimize the undesired effects can very likely be identified.

Although most scientists who study cannabinoids agree that the pathways to cannabinoid drug development are clearly marked, there is no guarantee that the fruits of scientific research will be made available to the public for medical use. Cannabinoid-based drugs will only become available if public investment in cannabinoid drug research is sustained, and if there is enough incentive for private enterprise to develop and market such drugs.

EXECUTIVE SUMMARY

CONCLUSION: Scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation; smoked marijuana, however, is a crude THC delivery system that also delivers harmful substances.

RECOMMENDATION 2: Clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid-onset, reliable, and safe delivery systems.

Influence Of Psychological Effects On Therapeutic Effects

The psychological effects of THC and similar cannabinoids pose three issues for the therapeutic use of cannabinoid drugs. First, for some patients—particularly older patients with no previous marijuana experience—the psychological effects are disturbing. Those patients report experiencing unpleasant feelings and disorientation after being treated with THC, generally more severe for oral THC than for smoked marijuana. Second, for conditions such as movement disorders or nausea, in which anxiety exacerbates the symptoms, the anti-anxiety effects of cannabinoid drugs can influence symptoms indirectly. This can be beneficial or can create false impressions of the drug effect. Third, in cases where symptoms are multifaceted, the combination of THC effects might provide a form of adjunctive therapy; for example, AIDS wasting patients would likely benefit from a medication that simultaneously reduces anxiety, pain, and nausea while stimulating appetite.

CONCLUSION: The psychological effects of cannabinoids, such as anxiety reduction, sedation, and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations, and beneficial for others. In addition, psychological effects can complicate the interpretation of other aspects of the drug effect.

RECOMMENDATION 3: Psychological effects of cannabinoids such as anxiety reduction and sedation, which can influence medical benefits, should be evaluated in clinical trials.

RISKS ASSOCIATED WITH MEDICAL USE OF MARIJUANA

Physiological Risks

Marijuana is not a completely benign substance. It is a powerful drug with a variety of effects. However, except for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications. The harmful effects to individuals from the perspective of possible medical use of marijuana are not necessarily the same as the harmful physical effects of drug abuse. When interpreting studies purporting to show the harmful effects of marijuana, it is important to keep in mind that the majority of those studies are based on *smoked* marijuana, and cannabinoid effects cannot be separated from the effects of inhaling smoke of burning plant material and contaminants.

For most people, the primary adverse effect of *acute* marijuana use is diminished psychomotor performance. It is, therefore, inadvisable to operate any vehicle or potentially dangerous equipment while under the influence of marijuana, THC, or any cannabinoid drug with comparable effects. In addition, a minority of marijuana users experience dysphoria, or unpleasant feelings. Finally, the short-term immunosuppressive effects are not well established but, if they exist, are not likely great enough to preclude a legitimate medical use.

The *chronic* effects of marijuana are of greater concern for medical use and fall into two categories: the effects of chronic smoking, and the effects of THC. Marijuana smoking is associated with abnormalities of cells lining the human respiratory tract. Marijuana smoke, like tobacco smoke, is associated with increased risk of cancer, lung damage, and poor pregnancy outcomes. Although cellular, genetic, and human studies all suggest that marijuana smoke is an important risk factor for the development of respiratory cancer, proof that habitual marijuana smoking does or does not cause cancer awaits the results of well-designed studies.

CONCLUSION: Numerous studies suggest that marijuana smoke is an important risk factor in the development of respiratory disease.

RECOMMENDATION 4: Studies to define the individual health risks of smoking marijuana should be conducted, particularly among populations in which marijuana use is prevalent.

EXECUTIVE SUMMARY

Marijuana Dependence And Withdrawal

A second concern associated with chronic marijuana use is dependence on the psychoactive effects of THC. Although few marijuana users develop dependence, some do. Risk factors for marijuana dependence are similar to those for other forms of substance abuse. In particular, antisocial personality and conduct disorders are closely associated with substance abuse.

CONCLUSION: A distinctive marijuana withdrawal syndrome has been identified, but it is mild and short-lived. The syndrome includes restlessness, irritability, mild agitation, insomnia, sleep EEG disturbance, nausea, and cramping.

Marijuana As A "Gateway" Drug

Patterns in progression of drug use from adolescence to adulthood are strikingly regular. Because it is the most widely used illicit drug, marijuana is predictably the first illicit drug most people encounter. Not surprisingly, most users of other illicit drugs have used marijuana first. In fact, most drug users begin with alcohol and nicotine before marijuana—usually before they are of legal age.

In the sense that marijuana use typically precedes rather than follows initiation of other illicit drug use, it is indeed a "gateway" drug. But because underage smoking and alcohol use typically precede marijuana use, marijuana is not the most common, and is rarely the first, "gateway" to illicit drug use. There is no conclusive evidence that the drug effects of marijuana are causally linked to the subsequent abuse of other illicit drugs. An important caution is that data on drug use progression cannot be assumed to apply to the use of drugs for medical purposes. It does not follow from those data that if marijuana were available by prescription for medical use, the pattern of drug use would remain the same as seen in illicit use.

Finally, there is a broad social concern that sanctioning the medical use of marijuana might increase its use among the general population. At this point there are no convincing data to support this concern. The existing data are consistent with the idea that this would not be a problem if the medical use of marijuana were as closely regulated as other medications with abuse potential.

CONCLUSION: Present data on drug use progression neither support nor refute the suggestion that medical availability would increase drug abuse. However, this question is beyond the issues normally considered for medical uses of drugs, and should not be a factor in evaluating the therapeutic potential of marijuana or cannabinoids.

USE OF SMOKED MARIJUANA

Because of the health risks associated with smoking, smoked marijuana should generally not be recommended for long-term medical use. Nonetheless, for certain patients, such as the terminally ill or those with debilitating symptoms, the long-term risks are not of great concern. Further, despite the legal, social, and health problems associated with smoking marijuana, it is widely used by certain patient groups.

RECOMMENDATION 5: Clinical trials of marijuana use for medical purposes should be conducted under the following limited circumstances: trials should involve only short-term marijuana use (less than six months); be conducted in patients with conditions for which there is reasonable expectation of efficacy; be approved by institutional review boards; and collect data about efficacy.

The goal of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but rather as a first step towards the possible development of nonsmoked, rapid-onset cannabinoid delivery systems. However, it will likely be many years before a safe and effective cannabinoid delivery system, such as an inhaler, will be available for patients. In the meantime, there are patients with debilitating symptoms for whom smoked marijuana might provide relief. The use of smoked marijuana for those patients should weigh both the expected efficacy of marijuana and ethical issues in patient care, including providing information about the known and suspected risks of smoked marijuana use.

Statement of Task

The study will assess what is currently known, and not known about the medical use of marijuana. It will include a review of the science base regarding the mechanism of action of marijuana, an examination of the peer-reviewed scientific literature on the efficacy of therapeutic uses of marijuana, and the costs of using various forms of marijuana versus approved drugs for specific medical conditions (e.g., glaucoma, multiple sclerosis, wasting diseases, nausea, and pain).

The study will also include an evaluation of the acute and chronic effects of marijuana on health and behavior; a consideration of the adverse effects of marijuana use compared with approved drugs; an evaluation of the efficacy of different delivery systems for marijuana (e.g., inhalation vs. oral); and an analysis of the data concerning marijuana as a gateway drug; and an examination of the possible differences in the effects of marijuana due to age and type of medical condition.

Specific Issues

Specific issues to be addressed fall under three broad categories: the science base, therapeutic use, and economics.

Science Base

- Review of neuroscience related to marijuana, particularly relevance of new studies on addiction and craving
- Review of behavioral and social science base of marijuana use, particularly assessment of the relative risk of progression to other drugs following marijuana use
- Review of the literature determining which chemical components of crude marijuana are responsible of possible therapeutic effects and for side effects

Therapeutic Use

- Evaluation of any conclusions on the medical use of marijuana drawn by other groups
- Efficacy and side-effects of various delivery systems for marijuana compared to existing medications for glaucoma, wasting syndrome, pain, nausea, or other symptoms
- Differential effects of various forms of marijuana that relate to age or type of disease.

Economics

- Costs of various forms of marijuana compared with costs of existing medications for glaucoma, wasting syndrome, pain, nausea, or other symptoms
- Assessment of differences between marijuana and existing medications in terms of access and availability

These specific areas, along with the assessments described above will be integrated into a broad description and assessment of the available literature relevant to the medical use of marijuana.

Recommendations

RECOMMENDATION 1: Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural functions of cannabinoids found in the body. Because different cannabinoids appear to have different effects, cannabinoid research should include, but not be restricted to, effects attributable to THC alone.

Scientific data indicate the potential therapeutic value of cannabinoid drugs for pain relief, control of nausea and vomiting, and appetite stimulation. This value would be enhanced by a rapid onset of drug effect.

RECOMMENDATION 2: Clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid-onset, reliable, and safe delivery systems.

The psychological effects of cannabinoids are probably important determinants of their potential therapeutic value. They can influence symptoms indirectly which could create false impressions of the drug effect or be beneficial as a form of adjunctive therapy.

RECOMMENDATION 3: Psychological effects of cannabinoids such as anxiety reduction and sedation, which can influence perceived medical benefits, should be evaluated in clinical trials.

Numerous studies suggest that marijuana smoke is an important risk factor in the development of respiratory diseases, but the data that could conclusively establish or refute this suspected link have not been collected.

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Recommendations, *continued*

RECOMMENDATION 4: Studies to define the individual health risks of smoking marijuana should be conducted, particularly among populations in which marijuana use is prevalent.

Because marijuana is a crude THC delivery system that also delivers harmful substances, smoked marijuana should generally not be recommended for medical use. Nonetheless, marijuana is widely used by certain patient groups, which raises both safety and efficacy issues.

RECOMMENDATION 5: Clinical trials of marijuana use for medical purposes should be conducted under the following limited circumstances: trials should involve only short-term marijuana use (less than six months); be conducted in patients with conditions for which there is reasonable expectation of efficacy; be approved by institutional review boards; and collect data about efficacy.

If there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their synthetic derivatives. Isolated cannabinoids will provide more reliable effects than crude plant mixtures. Therefore, the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but such trials could be a first step towards the development of rapid-onset, nonsmoked cannabinoid delivery systems.

RECOMMENDATION 6: Short-term use of smoked marijuana (less than six months) for patients with debilitating symptoms (such as intractable pain or vomiting) must meet the following conditions:

- **failure of all approved medications to provide relief has been documented,**
- **the symptoms can reasonably be expected to be relieved by rapid-onset cannabinoid drugs,**
- **such treatment is administered under medical supervision in a manner that allows for assessment of treatment effectiveness,**
- **and involves an oversight strategy comparable to an institutional review board process that could provide guidance within 24 hours of a submission by a physician to provide marijuana to a patient for a specified use.**

RECOMMENDATION 6: Short-term use of smoked marijuana (less than six months) for patients with debilitating symptoms (such as intractable pain or vomiting) must meet the following conditions:

- **failure of all approved medications to provide relief has been documented;**
- **the symptoms can reasonably be expected to be relieved by rapid-onset cannabinoid drugs;**
- **such treatment is administered under medical supervision in a manner that allows for assessment of treatment effectiveness;**
- **and involves an oversight strategy comparable to an institutional review board process that could provide guidance within 24 hours of a submission by a physician to provide marijuana to a patient for a specified use.**

Until a non-smoked, rapid-onset cannabinoid drug delivery system becomes available, we acknowledge that there is no clear alternative for people suffering from *chronic* conditions that might be relieved by smoking marijuana, such as pain or AIDS wasting. One possible approach is to treat patients as n-of-1 clinical trials, in which patients are fully informed of their status as experimental subjects using a harmful drug delivery system, and in which their condition is closely monitored and documented under medical supervision, thereby increasing the knowledge base of the risks and benefits of marijuana use under such conditions.

The Drug Policy Letter

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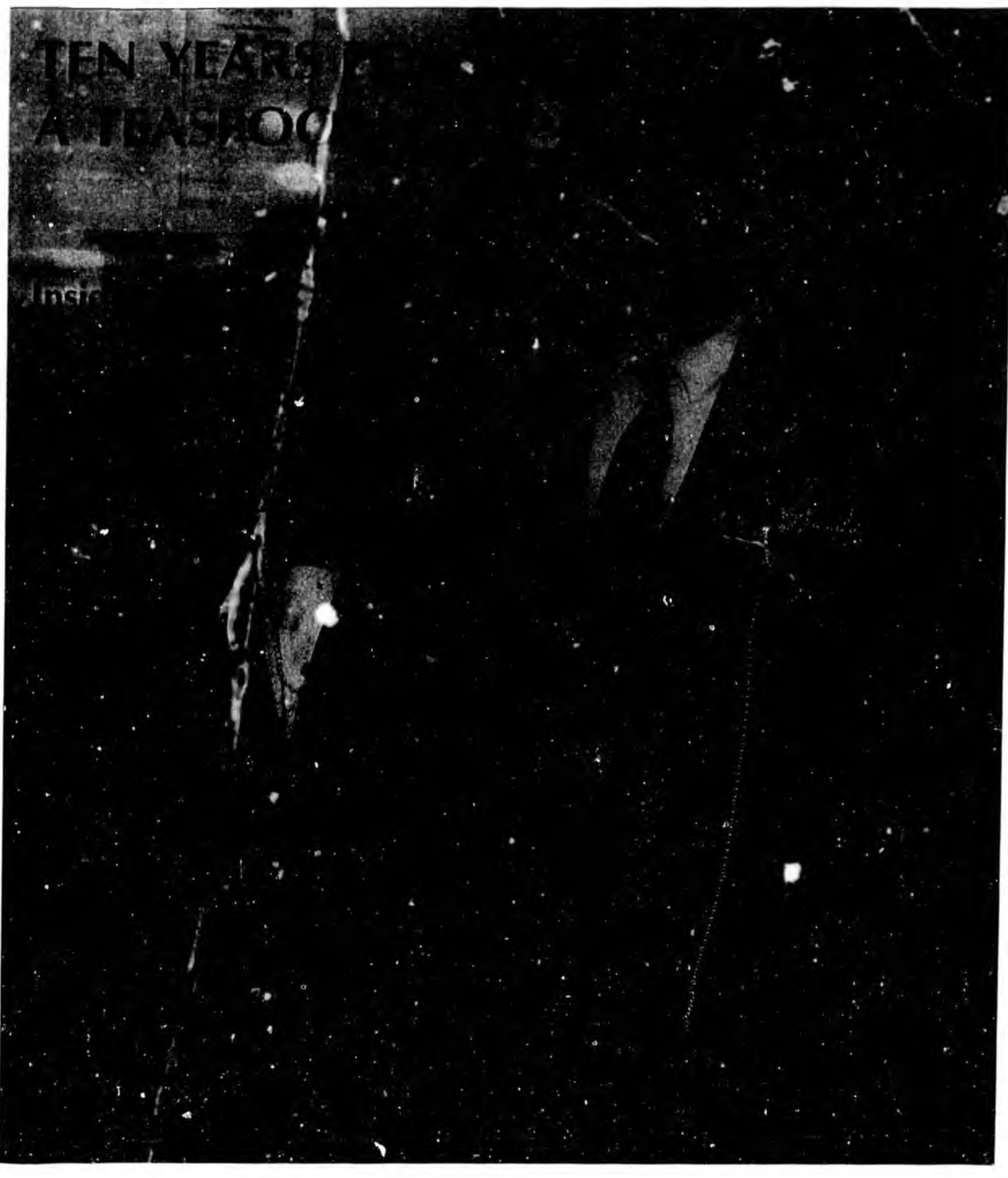

MARIJUANA HAS 'MODERATE' EFFECT ON DRIVING, ALCOHOL BIGGEST DANGER ON THE ROAD

The National Highway Traffic Safety Administration (NHTSA) released two studies this year on drug use and driving.

"The Incidence and Role of Drugs in Fatally Injured Drivers" is dated October 1992, but was released February 1994. The study found that, out of a sample of 1,882 drivers killed in car, truck and motorcycle accidents from 1990 to 1991, alcohol was found in just over half the cases. By comparison, only 17.8 percent of the fatally injured drivers showed traces of other drugs, the majority of whom also had intoxicating levels of alcohol in their system. (A person with a blood/alcohol content (BAC) greater than 0.1 percent is considered intoxicated in most states.) Of the drugs that showed up in the fatally injured drivers, the most frequent was cannabis, in 6.7 percent of the drivers. Other drugs that showed some prevalence were cocaine (5.3 percent), benzodiazepines (2.9 percent), amphetamines (1.9 percent) and barbiturates (1.5 percent).

In addition to measuring for drug presence, the study also attempted to measure causal contributions to the accidents by the various drugs. This was accomplished by conducting a "responsibility analysis" of each accident, and comparing the responsibility rates of those with a drug or drugs in their system with the "drug-free" control group. The responsibility rates were as follows:

- alcohol with a BAC greater than 0.1 percent, 93.9 percent;
- alcohol with a BAC under 0.1 percent, 75.8 percent;
- amphetamines, 83.3 percent;
- drug-free, 67.7 percent;
- benzodiazepines, 66.7 percent;
- THC, the active ingredient in marijuana, 57.9 percent; and
- cocaine, 57.1 percent.

Even though the responsibility rates in the THC and cocaine-only groups were lower than the drug-free group, the differences were rated as statistically insignificant because of the low number of persons in these categories.

The report concluded: "Although drugs other than alcohol were the basic focus of this study, the dominance of alcohol in fatal crashes was inescapable.... No single drug, nor all the drugs combined, approached the prevalence of alcohol."

The second report, "Marijuana and Actual Driving Performance," reached similar conclusions. Just as the previous

[*continued on page 35*]

TWO STUDIES RATE DRUG TREATMENT A BARGAIN OVER LAW ENFORCEMENT

What's the best way to fight drug abuse? There is plenty of room for debate, but two recent reports concluded that drug treatment provides more bang for the buck.

The nonprofit RAND Corporation released a report on how to control cocaine markets and treat the drug's users. They concluded that too much money was spent on "attack" type supply-reduction strategies and far too little was available for treatment programs. The study established that one dollar spent on a drug treatment program would save seven dollars' worth of supply reduction efforts.

The report, "Controlling Cocaine: Supply versus Demand Programs," weighed the positive and negative aspects of supply control techniques. Authors C. Peter Rydell and Susan S. Everingham from RAND's Drug Policy Research Center demonstrated that treatment pays for itself by reducing the costs of crime and lost productivity, whereas supply-side techniques end up costing the taxpayer more money. As Rydell and Everingham discovered: Source eradication operations save only about $.15 per dollar, interdiction is worth $.32 per dollar and domestic

[*continued on page 35*]

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SOURCES FOR "WAS KEVIN ELDERS SET UP? YOU BE THE JUDGE" (p. 8)

1, 3, 5: Prosecution. **2, 4:** Defense. **6:** Walraven testimony; sources to *The Drug Policy Letter*. **7:** Walraven testimony. **8:** Friend of Walraven to *DPL*. **9:** Sources to *Arkansas Democrat-Gazette*. **10:** Friends of Walraven to *DPL*. **11:** Prosecution to *DPL*. **12:** Police and friends of Walraven to *DPL*. **13:** Walraven police statement. **14:** Walraven testimony. **15:** Police to *DPL*. **16:** Walraven testimony. **17:** Prosecution to *DPL*. **18:** Dr. Elders' letter to Judge Plegge. **19:** Prosecution to *DPL*. **20:** Kevin Elders testimony.

SOURCES FOR THE DRUG INDEX (p. 16)

1, 2: Department of Justice. **3-5:** Office of National Drug Control Policy. **6-8:** DOJ. **9:** Peter D. Hart Research Associates poll. **10:** *CBS News/America Tonight* poll. **11:** Louis Harris & Associates poll. **12:** *CBS News/America Tonight* poll. **13:** DOJ. **14, 15:** *Congressional Quarterly Researcher*. **16, 17:** DOJ.

PHOTO CREDITS

p. 5: Stanton Breidenthall, *Arkansas Democrat-Gazette*. **pp. 6, 7, 9:** Cynthia Cotts. **p. 12:** James Kelly. **p. 14:** Scripps Howard News Service. **p. 15:** Robert Chapman, Office of Baltimore Mayor Kurt Schmoke. **p. 17:** Washington Convention and Visitors Association. **p. 24:** Dupont Photographers. **p. 33:** MTV Networks.

LETTERS TO THE EDITOR

[*continued from page 3*]

jurisdiction in an Article III Court is supposedly provided in § 801 of Title 21. The Congress molded the language of the preamble to the U.S. Constitution, using "We the People of the United States, in Order to ... promote the general Welfare..." to mean, "we the government." The Constitution was written to protect "we the people" against overbroad government. The language of the preamble has been subverted to justify the prosecution of state citizens in federal courts.

In summary, § 801 argues that the Congress cannot tell the difference between drugs which have traveled in interstate commerce and those which have not. Therefore, because Congress *wanted* to create a federal prohibition, it *needed* jurisdiction over all drugs, in the interest of promoting the public welfare. I am unable to find any authority in the Constitution which allows Congress to pass a law because it wants to.

Perry McCullough
Phoenix, AZ

MARIJUANA HAS 'MODERATE' EFFECT ON DRIVING

[*continued from page 29*]

study found that there was no indication that marijuana by itself was a cause of fatal accidents," this study found that "THC's adverse effects on driving performance appear relatively small."

The study, conducted in the Netherlands and sponsored by NHTSA, measured the effects of marijuana on drivers on a closed road, but with traffic, and compared the effects of a modest dose of THC to alcohol (BAC of 0.04 percent). The report concluded that:

1) "Marijuana, when taken alone, produces a moderate degree of driving impairment, ... manifesting itself mainly in the ability to maintain a steady lateral position on the road,"

2) "The magnitude of impairment is not exceptional in comparison with changes produced by many medicinal drugs and alcohol,"

3) "It is not possible to conclude anything about a driver's impairment on the basis of his/her plasma concentrations of THC," and

4) When comparing the effects of alcohol with marijuana, marijuana's effects on driving, even at the highest dosage tested (300 micrograms/kg), never exceeded alcohol's effects at BACs of 0.08 percent. The marijuana users also tended to overestimate the adverse effects of the drug on their driving quality and compensated for this by increasing effort and/or slowing down. Alcohol had the opposite effect: Drivers under its effect tended to underestimate the adverse effects of the drug and did not "invest compensatory effort."

As the researchers stated: "THC's effects differ qualitatively from many other drugs, especially alcohol. For example, subjects drive faster after drinking alcohol and slower after smoking marijuana.... This evidence strongly suggests that alcohol encourages risky driving whereas THC encourages greater caution, at least in experiments. Another way THC seems to differ qualitatively from many other drugs is that the former's users seem better able to compensate for its adverse effects while driving under the influence."

It would be a mistake to infer from either report that it is safe to drive under the influence of any drug.

— SE

TREATMENT STUDIES

[*continued from page 29*]

enforcement equals $.52 per dollar. By contrast, drug treatment programs reduced crime and productivity to save $7.46.

The authors recommend developing more demand reduction programs in the United States. They point out that even if the treatment does not completely alter drug use rates, 80 percent of the people enrolled in treatment do not use drugs during that time.

To reach their conclusions, the RAND researchers created a mathematical model of cocaine users and how much cocaine they consume. They used the mathematical models to project several likely directions in which the phenomenon of cocaine use could move.

Meanwhile, an August study commissioned by the state of California found, as did RAND, that treatment was more cost-effective than law enforcement.

The report, "Evaluating Recovery Services: The California Drug and Alcohol Treatment Assessment (CALDATA)," interpolated population data and concluded, in part, that:

- each day of treatment pays for itself by the end of the day because of the cost of crime avoided during that time.
- The benefits from different treatment programs outweigh the costs, depending upon the type of program, at ratios ranging from 4:1 to 12:1.
- A two-thirds reduction in the amount of crime within the population sample selected occurred during the time from before to after treatment.

This report, which was commissioned in 1992, found that treatment yielded a $7 return on every dollar spent. Further, by treating 150,000 people at a cost of $2 million, the taxpayers saved about $1.5 billion, mostly from the reductions in crime.

To acquire a copy of the RAND report, write RAND Distribution Services, 1700 Main St., P.O. Box 2138, Santa Monica, CA 90407-2138, call (310) 451-7002, fax (310) 451-6915, or e-mail via the Internet: order@rand.org.

To acquire a copy of the report, "Evaluating Recovery Services: The California Drug and Alcohol Treatment Assessment (CALDATA)," write the California Department of Alcohol and Drug Programs Resource Center, 1700 K Street, Sacramento, CA 95814, or call (800) 879-2772 or (916) 327-3728.

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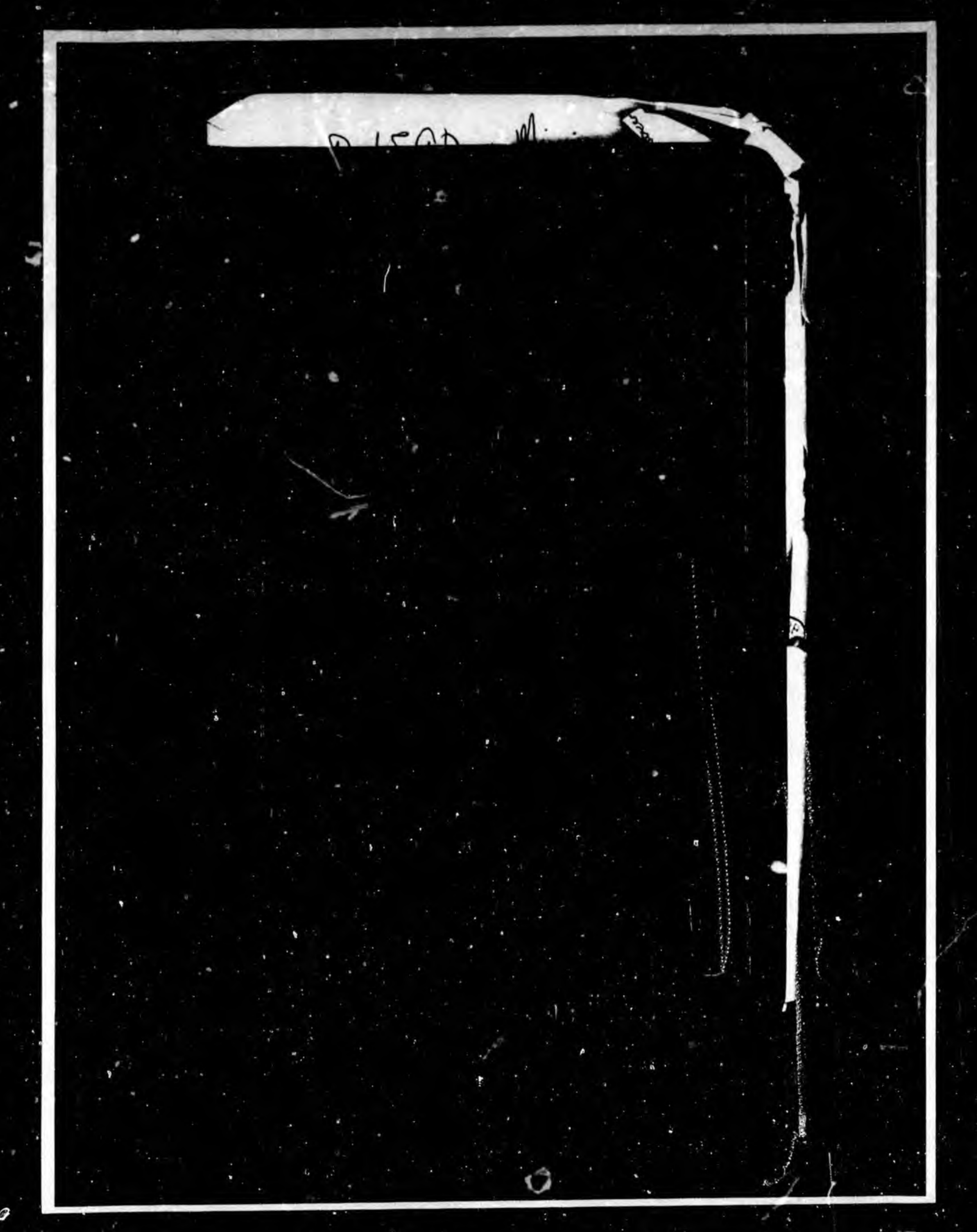

as phenothiazines and butyrophenones. It usually occurs early in treatment and rarely during maintenance treatment. It develops in up to 3% of patients started on antipsychotics. Risk is increased in agitated male patients who have received large and rapidly increased doses. No genetic component is apparent. Its pathophysiologic basis is believed to be blockade of central dopamine receptors. Characteristic signs are muscle rigidity, hyperpyrexia, tachycardia, hypertension, tachypnea, change in mental status, and autonomic dysfunction. Laboratory abnormalities include respiratory and metabolic acidosis, myoglobinuria, elevated CK, and leukocytosis. Mortality approaches 30%.

Treatment includes cessation of antipsychotic drugs, supportive care, and aggressive treatment of myoglobinuria, fever, and acidosis. The dopamine agonist bromocriptine 2.5 to 20 mg tid or dantrolene up to 10 mg/kg IV q 4 h may be used as a muscle relaxant. Treatment is usually in an ICU. After recovery, reintroduction of the antipsychotic drug retriggers the syndrome in up to 1/3 of patients.

Malignant hyperthermia, induced by inhalation of potent anesthetics or succinylcholine, is clinically similar to neuroleptic malignant syndrome; however, the pathophysiology and susceptibility appear to be different in most cases (see under PHARMACODYNAMIC VARIATION in Ch. 301). When patients with neuroleptic malignant syndrome require anesthesia, trigger agents for malignant hyperthermia should be avoided, although malignant hyperthermia has not been reported in these patients or their family members.

Legal Considerations

In most states, when a patient expresses the intention to harm a particular person, the evaluating clinician is required to warn the intended victim and notify a specified law enforcement agency. Specific requirements vary by state. Typically, state regulations also require reporting suspected abuse of children, the elderly, and spouses.

Criteria and procedures for involuntary hospitalization vary by jurisdiction. Usually a physician or psychologist and one additional clinician must certify that the patient has a psychiatric disorder, is a danger to himself or others, and refuses treatment.

195 / DRUG USE AND DEPENDENCE

(Substance Use Disorders; Drug Addiction; Drug Abuse; Drug Habituation)

A single definition for drug dependence is neither desirable nor possible. Some illicit drug use, although considered abuse because it is illegal, does not involve dependence of any kind. Drug dependence of a specific type (eg, cocaine dependence) emphasizes that different drugs have different effects, including type and risk of dependence.

Two concepts contribute to the definition of drug dependence: **tolerance,** which describes the need to progressively increase the dose to produce the effect originally achieved with smaller doses, and **physical dependence,** a state of physiologic adaptation to a drug, manifested by a withdrawal (abstinence) syndrome. In a withdrawal syndrome, untoward physiologic changes occur when the drug is discontinued or when its effect is counteracted by a specific antagonist that displaces the agonist from its binding site on cell receptors. Physical dependence does not accompany all forms of drug dependence.

Psychologic dependence is accompanied by feelings of satisfaction and a desire to repeat the drug experience or to avoid the discontent of not having it. This anticipation of effect is a powerful factor in the chronic use of psychoactive drugs and, with some drugs, may be the only obvious factor associated with intense craving and apparent

compulsive use. Drugs that cause chiefly psychologic dependence include cocaine, marijuana, amphetamine, and hallucinogens, such as lysergic acid diethylamide (LSD), 3,4-methylenedioxymethamphetamine (MDMA), and peyote.

Drugs that produce strong physical dependence (eg, heroin, alcohol) are prone to abuse, and dependence is difficult to treat. If a drug does not cause physical dependence, discontinuing the drug does not cause a major stereotypical withdrawal syndrome. However, most psychoactive drugs cause tolerance, and in some cases, reactions after discontinuation resemble a withdrawal syndrome (eg, depression and lethargy after withdrawal of cocaine or amphetamine; characteristic changes in the EEG after withdrawal of amphetamine). Commonly used psychoactive drugs vary in their potential for different types of dependence (see TABLE 195-1).

Drugs that produce dependence act on the CNS and have one or more of the following effects: reduced anxiety and tension; elation, euphoria, or other mood changes pleasurable to the user; feelings of increased mental and physical ability; altered sensory perception; and changes in behavior.

Addiction, a concept without a consistent, universally accepted definition, is used here to refer to a lifestyle characterized by compulsive use and overwhelming involvement with a drug; it may occur without physical dependence. Addiction implies the risk of harm and the need to stop drug use, whether the addict understands and agrees or not.

Drug abuse is definable only in terms of societal disapproval. It may involve experimental and recreational use of drugs, which is usually illegal with risk of arrest; unsanctioned use of psychoactive drugs to relieve problems or symptoms; or use of drugs first for the previous two reasons but later because of dependence and the need to continue at least partially to prevent the discomfort of withdrawal. Abuse of prescription and illegal drugs occurs in all socioeconomic groups, including among persons with advanced education and professional status. However, the most devastating use of psy-

TABLE 195-1. POTENTIAL FOR DEPENDENCE WITH COMMONLY USED DRUGS

Drug	Physical Dependence	Psychologic Dependence	Tolerance
CNS depressants			
Alcohol	+ + +	+ + +	+ +
Barbiturates	+ + +	+ + +	+ +
Ethchlorvynol	+ + +	+ + +	+ +
Glutethimide	+ + +	+ + +	+ +
Methaqualone	+ + +	+ + +	+ +
Methyprylon	+ + +	+ + +	+ +
Opioids	+ + + +	+ + + +	+ + + +
Synthetic opioids	+ + + +	+ + + +	+ + + +
Anxiolytics			
Alprazolam, oxazepam, temazepam (short-acting)	+ +	+ + +	+
Chlordiazepoxide, diazepam (long-acting)	+	+ + +	+
Stimulants			
Amphetamine	?	+ + +	+ + + +
Cocaine	0	+ + +	+ +
Methamphetamine	?	+ + +	+ + + +
Hallucinogens			
LSD	0	+ +	+ +
Marijuana			
(low-dose Δ-9-THC)	0	+ +	0
(high-dose Δ-9-THC)	0	+ +	+
Mescaline, peyote	0	+ +	+

LSD = lysergic acid diethylamide; THC = tetrahydrocannabinol; 0 = no effect; + = slight effect to + + + + marked effect.

TABLE 195–2. PHYSICAL DEPENDENCE WITH SOME COMMON SEDATIVES AND ANXIOLYTICS

Drug	Doses Producing Dependence (mg/day)	Time Necessary to Produce Dependence (days)	Dose Equivalent to Phenobarbital 30 mg (mg/day)*
Amobarbital ("blues")	500–600	30	100
Amobarbital-secobarbital combination ("rainbows")	500–600	30	100
Chloral hydrate	2000–2500	30	500
Chlordiazepoxide	200–300	60	25
Diazepam	60–100	40	10
Ethchlorvynol	1500–2000	60	500
Glutethimide	1250–1500	60	500
Meprobamate	2000–2400	60	400
Methaqualone	1800–2400	30	300
Methyprylon	1200–1500	60	300
Pentobarbital ("yellow jackets")	500–600	30	100
Secobarbital ("reds")	500–600	30	100

*Drugs on which a patient is dependent can be replaced by a dose of phenobarbital equivalent to 1/3 the average dose of that drug.

ance level can be determined by repeating the test q 3 to 4 h with a larger dose. Severe anxiety or agitation may increase the patient's tolerance. Once the 24-h dose still tempered by tolerance is determined, that dose is usually given qid for 2 or 3 days to stabilize the patient and is then decreased by 10% a day.

Alternatively, phenobarbital can be used. It does not produce the "high" of more rapidly acting drugs, and it is the anticonvulsant of choice. Rapid-onset barbiturates, other sedative-hypnotics, or minor anxiolytics can be replaced by a dose of phenobarbital equivalent to 1/3 the average daily dose of the drug on which the patient is dependent (see TABLE 195–2); eg, for secobarbital 1000 mg/day, the stabilizing dose of phenobarbital is 300 mg/day or 75 mg q 6 h. Phenobarbital is given orally qid, and the initial phenobarbital dose is reduced by 30 mg/day until the patient is drug-free. Because the initial daily dose must be estimated from the patient's history, a potential for error exists, and the patient must be observed closely for the first 72 h. If he remains agitated or anxious, the dose should be increased; if he is drowsy or dysarthric or has nystagmus, the dose should be decreased. While patients are being detoxified, other sedatives and psychoactive drugs should be avoided. However, if the patient is also taking antidepressants, especially tricyclics, the antidepressant should not be abruptly discontinued; the dose should be reduced over 3 to 4 days.

CANNABIS (MARIJUANA) DEPENDENCE

Chronic or periodic use of cannabis producing some psychologic dependence but no physical dependence.

Any drug that causes euphoria and diminishes anxiety can cause dependence, and cannabis is no exception. However, heavy use and complaints of inability to stop are unusual. Cannabis can be used episodically without evidence of social or psychologic dysfunction. The term dependence probably is misapplied to many users. No withdrawal syndrome occurs when the drug is discontinued, but some heavy users report disrupted sleep and nervousness when they stop.

Use of cannabis is widespread. Surveys that showed diminishing prevalence of use from 1979 to 1991 show an increase in use by persons 12 to 17 yr old until 1995. Prevalence may have leveled recently. Of the 65 to 70 million Americans who have tried cannabis, about 2 to 3% are daily or near-daily users. Not all daily users are addicts. Use of cannabis is a drug problem (as indicated by the increase in prevalence and in the number of persons seeking help to control its use), although its toxicologic importance is unclear. The number of users who have sought treatment or counseling to help them stop may be exaggerated because persons who test positive in the workplace are often ordered to seek treatment, then followed with compulsory testing.

In the USA, cannabis is commonly smoked in cigarettes made from the flowering tops and leaves of the dried plant or as hashish, the pressed resin of the plant. Dronabinol, a synthetic form of Δ-9-tetrahydrocannabinol (the principal active constituent of marijuana), is used to treat nausea and vomiting associated with cancer chemotherapy and to enhance appetite in AIDS patients. This form does not appear on the street.

Symptoms and Signs

Smoked cannabis produces a dreamy state of consciousness in which ideas seem disconnected, unanticipated, and free-flowing. Time, color, and spatial perceptions may be altered. In general, a feeling of well-being and relaxation (a "high") results. These effects last 2 to 3 h after inhalation. There is no persuasive evidence of a prolonged or hangover effect. Tachycardia, conjunctival injection, and dry mouth occur regularly. Many of the psychologic effects seem to be related to the setting in which the drug is taken. Panic reactions have occurred, particularly in naive users, but have become unusual as the culture has become more familiar with the drug. Communicative and motor abilities are decreased, depth perception and tracking are impaired, and the sense of timing is altered—all hazardous in certain situations (eg, driving, operating heavy equipment). Schizophrenic symptoms may be exacerbated by marijuana, even in patients being treated with antipsychotic drugs (eg, chlorpromazine). Appetite often increases.

Critics of marijuana cite much scientific data regarding adverse effects, but most of the claims regarding severe biologic impact are unsubstantiated, even among relatively heavy users and in areas intensively investigated, such as immunologic and reproductive function. However, high-dose smokers of marijuana develop pulmonary symptoms (episodes of acute bronchitis, wheezing, coughing, and increased phlegm), and pulmonary function may be altered. This is manifested by large airway changes of unknown significance. Even daily smokers do not develop obstructive airway disease. Pulmonary carcinoma has not been reported in persons who smoke only marijuana, possibly because less smoke is inhaled than during cigarette smoking. However, biopsies of bronchial tissue sometimes show precancerous changes, so carcinoma may occur. In a few case-control studies, some tests detected diminished cognitive function in small samples of long-term high-dose users; this finding awaits confirmation. Studies in newborns have not found evidence of fetal harm due to maternal use of cannabis. Decreased fetal weight has been reported, but when all factors (eg, maternal alcohol and tobacco use) are accounted for, the effect on fetal weight disappears. Δ-9-Tetrahydrocannabinol is secreted in breast milk. Although no harm to breastfed babies has been shown, breastfeeding mothers, like pregnant women, are advised to avoid using cannabis.

Because cannabinoid metabolites persist, urine tests after one-time use remain positive for days or weeks after discontinuation in regular users. Tests that identify an inactive metabolite identify use only, not dysfunction; the smoker may be free of drug effect by the time his urine is tested. The test can detect extremely small amounts and so is of little value in identifying the pattern of use.

COCAINE DEPENDENCE

Psychologic dependence, sometimes leading to profound psychologic addiction, produced by high doses of cocaine, which can cause euphoric excitement.

Tolerance occurs, but physical dependence has not been confirmed; no stereotypical withdrawal syndrome occurs when the drug is discontinued. However, the tendency to continue taking the drug is strong.

Most users are episodic recreational users who voluntarily curtail their use. However, cocaine use and the development of addictive behavior in some users has increased in North America, although recent declines are recorded.

Although most cocaine in the USA is snorted intranasally, smoking crack cocaine has become widely publicized. The imported hydrochloride salt is converted to a more

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Psychoactive substance use and the risk of motor vehicle accidents

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Abstract

The driving performance is easily impaired as a consequence of the use of alcohol and/or licit and illicit drugs. However, the role of drugs other than alcohol in motor vehicle accidents has not been well established. The objective of this study was to estimate the association between psychoactive drug use and motor vehicle accidents requiring hospitalisation.

A prospective observational case-control study was conducted in the Tilburg region of The Netherlands from May 2000 to August 2001. Cases were car or van drivers involved in road crashes needing hospitalisation. Demographic and trauma related data was collected from hospital and ambulance records. Urine and/or blood samples were collected on admission.

Controls were drivers recruited at random while driving on public roads. Sampling was conducted by researchers, in close collaboration with the Tilburg police, covering different days of the week and times of the day. Respondents were interviewed and asked for a urine sample. If no urine sample could be collected, a blood sample was requested.

All blood and urine samples were tested for alcohol and a number of licit and illicit drugs. The main outcome measures were odds ratios (OR) for injury crash associated with single or multiple use of several drugs by drivers.

The risk for road trauma was increased for single use of benzodiazepines (adjusted OR 5.1 (95% CI: 1.8–14.0)) and alcohol (blood alcohol concentrations of 0.50–0.79 g/l, adjusted OR 5.5 (95% CI: 1.3–23.2) and $\geq$0.8 g/l, adjusted OR 15.5 (95% CI: 7.1–33.9)). High relative risks were estimated for drivers using combinations of drugs (adjusted OR 6.1 (95% CI: 2.6–14.1)) and those using a combination of drugs and alcohol (OR 112.2 (95% CI: 14.1–892)). Increased risks, although not statistically significantly, were assessed for drivers using amphetamines, cocaine, or opiates. No increased risk for road trauma was found for drivers exposed to cannabis.

The study concludes that drug use, especially alcohol, benzodiazepines and multiple drug use and drug–alcohol combinations, among vehicle drivers increases the risk for a road trauma accident requiring hospitalisation.
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Keywords: Traffic accidents; Injured drivers; Alcohol; Drugs; Medicines; Case-control study

1. Introduction

The Grand Rapids Study convincingly showed that driving under influence of alcohol is an important risk factor for traffic accidents (Borkenstein et al., 1974). The role of drugs other than alcohol in motor vehicle accidents, however, has not been well established. Many medicines (prescription or over-the-counter) and illicit drugs affect the nervous system (Ramaekers, 1998). Driving under the influence of drugs other than alcohol is considered to be an increasing cause of traffic accidents worldwide (Morland, 2000).

Several classes of drugs, including amphetamines, antihistamines, cannabis, hypnotics, tranquillizers and tricyclic antidepressants, have been shown to impair driving skills in laboratory tests and driver-simulation studies (O'Hanlon and Volkerts, 1986; Smiley, 1987; Robbe, 1998). These studies are restricted in various ways, e.g. with regard to subject selection and divergent behaviour or sample size. Their generalization to a 'real' traffic situation is debated. Many observational studies have shown that drug use as determined by biological sampling among drivers is prevalent and increasing (Gjerde et al., 1993; Soderstrom et al., 1997; Morland, 2000). Several studies tried to provide

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accident risk estimates related to drug use by linking drug prescription records to hospital admission records involving motor vehicle accidents, police reports, or health insurance records (Skegg et al., 1979; Ray et al., 1992; Leveille et al., 1994; Neutel, 1995; Hemmelgarn et al., 1997; Barbone et al., 1998; McGwin et al., 2000). In addition, a few studies have been conducted in which non-trauma patients were included as controls (Honkanen et al., 1980; Marquet et al., 1998). These studies provided risk estimates, but a limitation is that the control groups were not taken from moving traffic.

The objective of our study was to estimate the association between the use of various psychoactive substances and serious traffic injuries needing hospitalisation by comparing exposure frequencies (prevalences) of these substances in injured and non-accident involved drivers.

2. Methods

2.1. Setting

The study was conducted in co-operation with a large general teaching hospital (St. Elisabeth Hospital) and the police department located in the Dutch city of Tilburg, covering a population of approximately 350,000 persons. The hospital has all the facilities comparable with a highly equipped trauma centre. The source populations of our study were injured and non-accident involved drivers throughout the period from May 2000 until August 2001. The hospital's Medical Ethics Committee approved the study protocol and informed consent was obtained for the use of medical records from patients or their relatives.

2.2. Study design

A prospective case-control study was conducted to assess the relationship between drug use and trauma injuries requiring hospitalisation caused by motor vehicle accidents. Only injured car or van drivers were included in the study.

2.3. Selection of cases

All injured car or van drivers who were admitted to the emergency room of the hospital were prospectively identified. Demographic, accident and injury characteristics were obtained from medical and ambulance records, and the emergency's department electronic medical data system (Vles et al., 2000). The physicians at the emergency department were trained to fill in a detailed questionnaire about the crash circumstances. The severity of injuries was graded according to the Injury Severity Scale (ISS) (Baker et al., 1974). Urine and/or blood samples were taken directly in the emergency room.

2.4. Selection of controls

Control patients were randomly selected from moving traffic during 20 roadside survey sessions. In order to be able to construct a representative control sample, the week was systematically divided into 6 h periods. Each survey session covered a 6 h period because of work-time reasons. The survey was conducted among a representative sample of locations along main roads in the Tilburg police district, which covers the area of the St. Elisabeth Hospital. Frequent change of location was intended to minimize the predictability of the surveys with respect to time and place.

The police stopped cars and the drivers were asked to co-operate on a voluntary basis. The survey sessions were combined with normal police enforcement activities regarding drink-driving. Respondents were interviewed on their drug and medicine use and subsequently requested to produce a urine specimen. If they were not able or willing to urinate they were requested to deliver a blood specimen. A trained research nurse performed the vena-puncture. Subjects who delivered a urine or blood specimen were compensated by a small amount of 10 Dutch guilders (approximately € 5). The interview and specimen sampling took place in a specially equipped mobile research unit with a private toilet. After the interview and specimen sampling, all subjects were breath tested for alcohol by a police officer, using a Dräger Alcotest 7410 Plus screening device. The breath test was compulsory for all drivers who were stopped. Data collection also comprised date and time of selection, gender and age of the driver, and signs of intoxication.

2.5. Drug exposure assessment

Both cases and controls were tested for the presence of alcohol, amphetamines, barbiturates, benzodiazepines, cannabis, methadone, opiates, and tricyclic antidepressants.

Urine samples were screened at the Dutch Laboratory for Drugs Doping, Tilburg, The Netherlands. Screening was performed by enzyme multiplied immunoassay technique (EMIT® II Plus). For benzodiazepines, a special high sensitivity protocol was used with on-line deglucuronidation. The risk for false-positive results was avoided by confirmation analysis of the positive urine samples (amphetamines and opiates) with appropriate gas chromatography mass spectrometry (GC–MS) techniques.

Drug screening in serum was performed by The Netherlands Forensic Institute (NFI), Rijswijk, The Netherlands. Opiates and cannabis screening was performed by Cozart® enzyme immunoassay (EIA). Confirmation was performed using GC–MS. For the other drugs and pharmaceuticals, a high-performance liquid chromatography (HPLC) method was used, which was developed by NFI.

Concerning the cases medical and ambulance records were examined to control for drugs administered during transport and at the emergency department. When urine or blood specimens were positive for drugs given during

transport, or in the emergency room before sampling, the specimens were considered to be negative.

2.6. *Potential confounders*

The following covariates were studied as possible confounding factors: age, gender, blood alcohol concentration, concomitant drug exposure, season, and time of day. Time of day was categorised as day (10 a.m.–10 p.m.) or night (10 p.m.–10 a.m.).

2.7. *Statistical analysis*

For both cases and controls, the baseline characteristics were determined. An ANOVA/Student's *t*-test was performed to assess the significance of differences in the mean of continuous variables between cases and controls. Differences in proportions of categorical variables were tested for significance by a chi-square (χ^2) test. To estimate the association between drug use, and any other potential risk factor and road trauma requiring hospitalisation adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were calculated using multivariate unconditional logistic regression (Hosmer and Lemeshow, 1989). All potential confounding factors were entered in the logistic model. In this model the odds ratio can be interpreted as a relative risk. Unadjusted ORs are not presented because this study was not designed to determine a causal relationship for each single drug separately. Data were analysed using SPSS 10.0 statistical software.

3. Results

We were able to identify and include 110 injured motorists. The relatives of two deceased patients refused consent and their data were excluded from analysis. The mean ISS for the case patients was 14 (range 1–75); of the 1029 controls, 816 (79.3%) drivers complied to participate. In the case group 39% of the specimens consisted out of urine compared to 85% in the controls, respectively. Overall, 74% of the study subjects were men. The mean age was 38.6 years. Control subjects were older than case patients (39.1 versus 34.6, $P = 0.002$).

Table 1 shows the distribution of demographic variables and of the frequencies of drugs and alcohol use. Male patients were more frequently exposed to cannabis and cocaine. Drugs and/or alcohol were more frequently detected in injured drivers than in non-accident involved drivers.

Forty percent of all case patients were positive for one or more drugs and/or alcohol in comparison with 14% of the controls (Fig. 1). Eight percent of all case patients were both exposed to (multiple) drugs and alcohol. Only one control subject had used a drug–alcohol combination.

The use of benzodiazepines (adjusted OR 5.1 (95% CI: 1.8–14.0)) and alcohol was significantly associated with road accidents (Table 2). Drivers with a blood alcohol concentration (BAC) ≥0.8 g/l were at the highest risk (adjusted OR 15.5 (95% CI: 7.1–33.9)). Users of amphetamines, cocaine, and opiates had a twofold increased risk, however, not statistically significant. No association was found for cannabis and tricyclic antidepressants, and no estimates could be calculated with regard to methadone and barbiturates.

A sixfold increased risk (adjusted OR 6.1 (95% CI: 2.60–14.10)) was found for the concurrent use of two, or more drugs compared with no drug use. This effect was even more pronounced in patients concomitantly exposed to alcohol and one or more drugs, which showed the highest risk for road accidents (adjusted OR 112.2 (95% CI: 14.1–892.9)).

Table 1
Characteristics of cases and controls

Characteristics	Cases, $N = 110$ (%)	Controls, $N = 816$ (%)
Gender		
Male	81 (74)	602 (74)
Female	29 (26)	214 (26)
Age group (year)		
18–25	31 (28)	144 (18)
25–34	35 (32)	228 (28)
35–49	28 (26)	237 (29)
≥50	16 (14)	207 (25)
Season		
January–March	25 (23)	269 (33)
April–June	21 (19)	172 (21)
July–September	37 (34)	147 (18)
October–December	27 (25)	228 (28)
Time of day		
10 a.m.–10 p.m.	54 (49)	496 (61)
10 p.m.–10 a.m.	56 (51)	320 (39)
Drugs and alcohol		
Amphetamines	7 (6)	13 (2)
Barbiturates	2 (2)	0 (0)
Benzodiazepines	11 (10)	12 (1.5)
Blood alcohol concentration (g/l)		
<0.5	84 (76)	796 (97)
0.5–0.79	3 (3)	7 (1)
≥0.8	23 (21)	13 (2)
Cannabis	13 (12)	49 (6)
Cocaine	10 (9)	16 (2)
Methadone	1 (1)	0 (0)
Opiates	8 (7)	20 (3)
Tricyclic antidepressants	1 (1)	4 (0.5)

4. Discussion

This study indicates that use of alcohol, amphetamines, benzodiazepines, cocaine, and opiates places drivers at increased risk for motor vehicle accidents requiring hospitalisation. Users of drug–drug combinations were at a sixfold increased risk. Vehicle drivers who were exposed

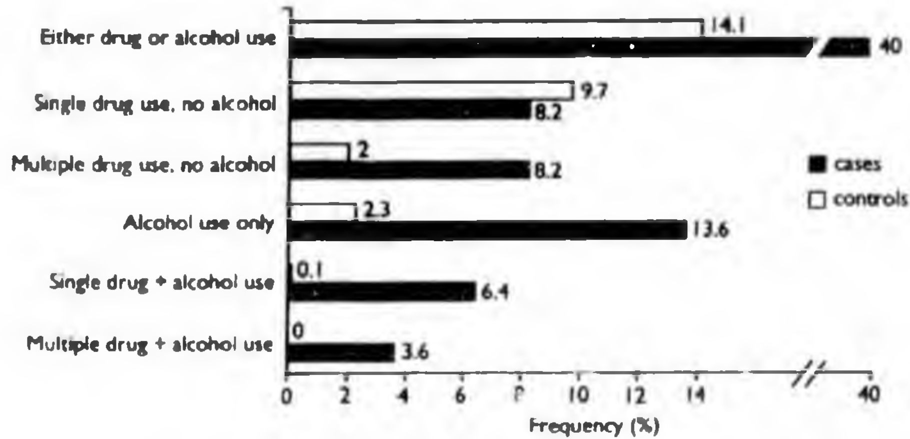

Fig. 1. Use of drugs and or alcohol (>0.5 g/l) for cases and controls.

to drug–alcohol combinations were at the highest risk of experiencing injurious road accidents.

The prevalence for drug and alcohol found in this study is consistent with literature on impaired drivers, or drivers injured or killed in road accidents. However, prevalence figures are hard to compare because of time trends and local differences in drug use habits, patterns, and legislation (Morland, 2000). Our study confirms the well-known association between alcohol and traffic accidents (Borkenstein et al., 1974).

For drivers using benzodiazepines, a fivefold increased injury risk (95% CI: 1.8–14.0) was found, which is in concordance with other studies. In the late 70s, Skegg and co-workers linked drug prescription records with hospital admission and showed that people who used minor tranquillizers had a fivefold higher risk of a serious road accident (Skegg et al., 1979). A similar result was concluded in a related study, which found a four times increased risk for persons taking benzodiazepines within 4 weeks of receiving the prescription (Neutel, 1995). Also more recent data showed that users of benzodiazepines were at increased risk of experiencing road accidents (Barbone et al., 1998). In contrast, other studies using a comparable methodology showed no increase of accident risk with the use of benzodiazepines and sedatives (Jick et al., 1981; Leveille et al., 1994). However, Honkanen and others found a twofold increased accident risk among car drivers using benzodiazepines compared to controls. They selected controls randomly from car drivers at petrol stations, which comes closest to the methodology used in our study (Honkanen et al., 1980). Further research is necessary to establish whether within the group of benzodiazepines specific substances or doses bear a higher or lower risk than others due to differences in pharmacokinetic and pharmacodynamic properties.

The most common therapeutically used opioids studied in relation to traffic accidents are morphine and codeine. In our study, a twofold increased risk was found, which is in concordance with the literature (Ray et al., 1992; Leveille et al., 1994). We found a relatively high prevalence of opiates in injured drivers. After analytical confirmation 6-monoacetylmorphine (6-MAM) the first heroin metabolite was found in the urine of only one case, and two control patients. This figure may underestimate the real number of heroin users because 6-MAM is very rapidly metabolised into morphine and can therefore not always be detected.

The use of amphetamines (including ecstasy) and cocaine has been related with driving impairment (Dussault et al., 2001; Logan and Couper, 2001). In our study, we found that use of amphetamines or cocaine, and opiates places drivers at a twofold increased risk for motor vehicle accidents, however, not statistically significantly. The differences in the prevalence's of these drugs among drivers involved in an accident and non-accident drivers possibly indicates that these drugs are important risk factor for traffic accidents.

In our study, no association was found between exposure to cannabis and road accidents. Experimental and epidemiological studies have provided conflicting data about the

Table 2
Risk for personal injury in road accidents associated with current use of psychoactive substances in real moving traffic

Substance	OR[a]	95% CI
Amphetamines	2.10	0.66–6.73
Benzodiazepines	5.05	1.82–14.04
Cannabis	1.22	0.55–2.73
Cocaine	2.04	0.69–6.09
Opiates	2.35	0.87–6.32
Blood alcohol concentration (g/l)		
<0.5	1.00[b]	
0.5–0.79	5.46	1.28–23.22
≥0.8	15.5	7.09–33.90
Multiple drugs vs. no drug	6.05	2.60–14.10
Drug–alcohol combination vs. no drug	112.22	14.10–893

Adjusted in the multivariate logistic model for age, gender, alcohol, amphetamines, benzodiazepines, cannabis, cocaine, opiates, season, and time of day.

[a] OR: odds ratio.

[b] Reference category.