Marijuana's effect on actual driving: summary of a 3-year experimental program

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1. Introduction

A program was set up to determine the dose-response relationship between marijuana and objectively and subjectively measured aspects of real-world driving; and, to determine whether it is possible to correlate driving performance impairment with plasma concentrations of the drug or a metabolite. A variety of driving tasks were employed, including: maintenance of a constant speed and lateral position during uninterrupted highway travel, following a leading car with varying speed 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.

The program was sponsored by the U.S. National Highway Traffic Safety Administration, with the exception of the alcohol part of the city driving study which was sponsored by the Dutch Road Safety Directorate of the Dutch Ministry of Road and Public Works. Report writing was still in progress at the time of T92. Therefore, results of the studies could not yet be presented.

2. General Procedures.

All subjects who participated in one of the program's studies were current users of cannabis and in possession of a driver's licence. Furthermore, they had indicated on a questionnaire that they had driven within one hour after smoking cannabis at least once within the preceding year. Subjects were screened in two stages: first from their responses to a combined cannabis use, driving experience and medical history questionnaire; and secondly, on the basis of an interview and physical examination. Furthermore law enforcement authorities were contacted, with the volunteers' consent, to verify that they had no previous arrests or convictions for drug trafficking.

Subjects were instructed to sleep normally on the nights before test days. Alcohol consumption was prohibited for 24 hours before tests, and consumption of beverages containing caffeine, for 2 hours beforehand. Those who smoked tobacco were advised that this would also be prohibited for one hour before testing until its completion. Each subject was required to submit a

urine sample immediately upon arrival at the test site. Samples were later assayed qualitatively for the following common "street drugs" (or metabolites): cannabinoids, benzodiazepines, opiates, cocaine, amphetamines and barbiturates. In addition a breath sample was analyzed on the spot for the presence of alcohol using a Lion-SD3 breath-analyzer.

Blood samples were taken by venepuncture. Two 10 ml aliquots were obtained in every case. These were heparinized and centrifuged within 30 minutes. Plasma was placed in frozen (-20°C) storage prior to analysis. The quantitative chemical analysis of THC and 11-nor-acid in plasma was performed by gas chromatography/ mass spectrometry (GC/MS) using deuterated cannabinoids as internal standards (Möller & Dörr, 1992).

Active and placebo marijuana cigarettes were supplied by the U.S. National Institute on Drug Abuse (NIDA). Cigarettes were smoked through a plastic holder, and in a fashion determined by the subjects.

3. Pilot Study to Select THC Doses

3.1 Introduction

Doses used in all previous studies of inhaled THC have been selected without consulting the subjects beforehand to determine whether these realistically approximated doses they commonly use. To avoid arbitrarily selecting the wrong maximum dose, it seemed necessary to consult the subjects in the context of a "clinical" pilot study. The pilot study's major purpose was therefore to establish the maximum dose for subsequent driving studies. Yet it provided several opportunities for obtaining valuable information about THC pharmacokinetics and its pharmacodynamic effects after marijuana smoking. The secondary purpose became that of specifying relationships between plasma concentrations of THC and its metabolite with changes in the other physiological, performance or subjective variables.

3.2 Methods

Twenty-four healthy volunteers, 12 males and 12 females, volunteered to participate in this study. Subjects' mean (±SD) age was 27.0 (±4.6) and 24.6 (±2.9) for males and females, respectively. Groups of six were treated and tested per night. Sessions were conducted in the evening between 19.00 and 24.00 hours and subjects smoked and were tested at staggered intervals of 10 minutes.

The cigarettes had an average weight of 767 mg and contained 2.57% or about 20 mg THC. The subjects were allowed to smoke part or all of the marijuana content in three cigarettes until achieving the desired psychological

effect. The only requirement was to smoke continuously for a period not exceeding 15 minutes. When subjects voluntarily stopped smoking, cigarettes were carefully extinguished and retained for subsequent gravimetric estimation of THC consumed (difference between amount of THC originally present in the cigarette and the amount of THC remaining in the cigarette butt after smoking). This method of estimating THC amounts consumed is based upon the assumption that THC is equally distributed the cigarette. Perez-Reyes *et al.* (1982) analyzed THC concentrations in the unsmoked portions of marijuana cigarettes of three different potencies and indeed found that they were identical to those in the unlit cigarette.

A test battery which lasted 30 minutes took place before smoking and was repeatedly administered at 30, 90, 150 and 210 minutes after initiation of smoking. The battery consisted of: 1. the critical tracking test (CTT, Jex *et al.*, 1966); 2. a hand steadiness test, in which the number of side contacts were measured that occurred as the subject attempted to hold a 1 mm stylus for 15 seconds within each of five circular holes with successively diminishing diameters; 3. body sway test; 4. heart rate measurement; 5. questionnaires measuring subjects' perceived "high", cognitive and emotional state, and willingness to drive; and, 6. blood sampling.

3.3 Results

One male's data were dropped from the statistical analyses because no drug was found in any blood sample. The only result that will be reported here regards the THC amount smoked.

Six subjects consumed one cigarette, thirteen smoked two and four smoked three. Total amounts THC consumed are given in Table 1. Statistical analyses failed to reveal a significant difference between the sexes. It should be noted that these amounts of THC represent both the amount inhaled and the portion that was lost through pyrolysis and side-stream smoke during the smoking process. It was decided, on the basis of these results, that the maximum THC dose in subsequent driving studies would be 300 μg/kg.

Table 1. Mean, median and range of amounts THC consumed.

	THC (mg)			THC (μg/kg)		
	mean	median	range	mean	median	range
males	22.3	18.6	14.7-35.2	324	292	203-524
females	19.4	18.9	11.3-28.2	293	292	194-440

4. Marijuana and Driving on a Restricted Highway

4.1 Introduction

The first driving study was executed on a closed section of a public highway. The major objective was to determine the dose-response and dose-response-time relationship between marijuana and lane tracking variability as measured during high-speed highway travel. A secondary objective was to relate objective measures of driving impairment to subjective impressions of driving quality and expressed willingness to drive in the same states of intoxication under normal circumstances.

4.2 Methods

The same subjects who participated in the pilot study served again as the subjects. They were treated on separate occasions with THC doses of 0, 100, 200, 300 μg/kg. Treatments were administered according to a double-blind cross-over design.

Two subjects commenced smoking at a time (t=0). Driving tests were performed twice, beginning at t=40 and 100 minutes and lasting 15-20 minutes. Blood samples were taken before the driving tests at t=30 and 90. The subjects' pulse was taken and their performance measured in two psychomotor tests (CTT and hand steadiness) that began after the driving tests at t=70 and 130. Subjective assessments of perceived "high", cognitive and emotional state, and willingness to drive were made immediately after smoking, and before and after the driving tests. Before the start of the experiment, subjects were individually trained to operate the vehicle under generally the same conditions as the tests later occurred.

The driving test, developed and standardized by O'Hanlon *et al.* (1982, 1986) and applied in more than 40 open- and closed-road studies by three Dutch Institutes during the last decade, measures the ability to control an instrumented vehicle's speed and lateral position. Subjects were instructed to maintain speed at 90 km/h (60 mph), or less if they felt incapable of driving safely at that speed, and a steady lateral position between the delineated boundaries of the traffic lane.

Driving was performed over a 11 km (7 mi) section of a primary highway Two lanes in the same direction were closed to normal traffic between the hours of 19.00 and 24.00 on three consecutive weeknights over four consecutive weeks of testing. Driving began at one end of the section, involved turning at the other and ended with a return to the origin. A licensed driving instructor accompanied each subject. He was charged with responsibility for ensuring safety at all times and was able to intervene, if necessary, using redundant vehicular controls.

Two Volvo station wagons containing essentially the same instrumentation were employed in the study. The first of a pair of subjects who received treatments together departed from the origin driving one vehicle and was followed by the second driving the other after 2½ minutes. The first subject waited for the arrival of the second at the turning point before returning to the origin. The purpose was to avoid having the subjects, travelling in opposite directions, meet enroute.

Speed, steering wheel angle and lateral position were continuously recorded at a 4 Hz sampling rate. The latter was analyzed to yield the primary dependent variable, the standard deviation of lateral position (SDLP), which has been shown to be both highly reliable (typical test-retest correlation of 0.7-0.9) and very sensitive to the influence of sedative drugs and alcohol.

5. Marijuana and Driving on a Normal Highway in Traffic

5.1 Introduction

Upon completion of the first driving study, a second was conducted to come a step closer to driving reality than its predecessor. The methods applied were, with the addition of a car following test, the same as those used in the first driving study. However, driving tests were now conducted on a primary highway in the presence of other traffic.

The major objective of this study was to confirm the relationship between inhaled THC dose and lateral position variability in the context of a standard road-tracking test conducted on a highway in normal traffic. A secondary objective was to measure performance in another actual driving test (i.e. car following) to determine whether degrees of impairment would correlate between the two tests in a manner indicating a general influence of THC on driving behavior. The third objective was to continue efforts to correlate plasma concentrations of THC and 11-nor-acid with driving performance impairment as measured in both tests.

5.2 Methods

Sixteen new subjects, equally comprised of men and women, were selected according to the same inclusion/exclusion criteria as before. Subjects' mean (±SD) age was 28.3 (±7.4) and 25.0 (±4.6) for males and females, respectively.

The study was conducted according to an ascending dose series design where both active drug and placebo conditions were administered, double-blind, at each of three THC dose levels. THC doses were the same as those used in the previous study, namely 100, 200 and 300 μg/kg. Cigarettes appeared identical at each level of treatment conditions and were smoked within a time

limit of 10 minutes.

Two subjects at a time commenced smoking at t=0. Thirty minutes after onset of smoking (t=30 min) the subjects performed a battery of laboratory tests (tracking, hand steadiness and body sway) and yielded a blood sample at t=40 min. They were then transported to a primary highway (A76, different than in the previous study) between the Dutch cities of Maastricht and Heerlen were the driving tests were performed. Two instrumented vehicles, the same as those in the previous study, were employed in this study. At t=55 min, one subject started the car following test (below) in the eastward direction whilst the other subject was sitting in the passenger's seat of the preceding car involved in the same test. The test was conducted on a 16 km (10 mi) circuit of the highway and lasted about twelve minutes. At the end of the circuit the car turned at a signalized intersection and parked at a service station, whereupon the subjects reversed roles to repeat the test running in the opposite direction. The new driver reentered the highway and began his/her car following test at t=70 min. After conclusion of the car following test, the subject left the highway at an exit ramp and reentered in the opposite direction on the associated entrance ramp. Thereupon both vehicles parked on the paved shoulder.

Both subjects then commenced the standard driving test (below) in separate instrumented vehicles at t=85 and 88, respectively. The test circuit was the same as for the car following test. Subjects drove twice around the circuit without stopping in about 50 minutes. At the conclusion of this test, both subjects participated again in the car following test in the same order as before at t=140 and 155 min, respectively. Subjects were then transported back to the laboratory where they yielded a blood sample (t=190) and repeated the test battery (t=195).

The standard test was the same as described in the previous study except for its duration and the presence of other traffic. Subjects were instructed to maintain a constant speed of 95 km/h (59 mph) and a steady lateral position between lane boundaries in the right traffic lane. They were allowed to deviate from this only if it would become necessary to pass a slower vehicle in the same lane. Standard deviation of lateral position (SDLP) was the primary dependent variable.

The car following test measures drivers' ability to perceive changes in a preceding vehicle's speed and to react in a manner maintaining a constant headway. It began as the preceding and the following vehicle, respectively driven by one of the driving instructors and the subject, operated in tandem on the slower traffic lane while travelling at a speed of 100 km/h (62 mph). The subject was instructed to maintain a 50 m (164 ft) headway however the preceding vehicle's speed might vary. After driving in this manner for about one minute, the operator of the preceding vehicle released the accelerator pedal allowing its speed to fall to 80 km/h (50 mph). Immediately thereafter, the operator of the preceding vehicle accelerated to 100 km/h (62 mph). The duration of one deceleration and acceleration maneuver was approximately 50

seconds and six to eight, depending upon traffic density, were executed during one test. The dependent variables were mean headway, coefficient of variation of headway, and mean reaction time to perceived speed changes of the preceding car.

6. Marijuana, Alcohol and City Driving

6.1 Introduction

The program then proceeded into the third driving study which involved tests conducted in high-density urban traffic. A marijuana dose of 100 µg/kg and placebo were given to subjects who would now operate in an urban driving test. A second group also participated in this study and undertook the same driving test, but then after drinking alcohol (reaching an average BAC of 0.04 g%), and a placebo. This was done for two reasons; first, the alcohol condition served as a control whether the employed tools to assess driving performance were sensitive; and, secondly, it made a comparison possible between low doses of alcohol and THC.

6.2 Methods

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. Subjects' mean (±SD) age was 23.7 (±2.7) and 22.4 (±3.5) for those in the alcohol and marijuana group, respectively.

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). 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. The subjects in the marijuana group were treated on separate occasions with THC doses of 0 and 100 µg/kg. Cigarettes were smoked within a time limit of 5 minutes, and driving tests commenced 30 minutes after initiation of smoking. Active drug and placebo conditions were administered double-blind and in a counter-balanced order in each group.

Immediately prior to and following the driving tests subjects performed the hand steadiness and time perception task, yielded a blood sample, and were administered the same subjective questionnaires used in the previous

studies.

Driving tests were conducted on central city and residential streets and on urban highway during daylight hours, and lasted about 45 minutes. Two persons accompanied the subject while driving: a licensed driving instructor sitting in the passenger's seat and an trained observer sitting in the center rear seat. The former had access to redundant controls and his primary responsibilities were controlling safety and giving the route instructions.

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 evaluating driving proficiency. Her method was also applied in the present study. It involves the employment of a 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 11-nor-acid measured at about the same time.

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